

- 7:30–8:00 Coffee and Pastries
- 7:30–7:45 Case of the Day
Austin Wand, MD
- 7:45–8:00 Case of the Day
Eric A. Jensen, MD

The Chest Radiograph

Moderator: John C. Wandtke, MD

- 8:00–8:20 Value in Thoracic Radiology
E. James Potchen, MD, JD
- 8:20–8:40 Analysis of Mediastinal Contours
James C. Reed, MD
- 8:40–9:00 Things That Are Not What You Thought They Were on the Chest Radiograph:
Confusing Findings Resolved by CT
J. David Godwin II, MD
- 9:00–9:20 Chest Radiographic Interpretation of Interstitial Lung Disease:
Review of a Dying Art
Wallace T. Miller, Jr, MD
- 9:20–9:40 Misconceptions in Chest Radiology
Murray G. Baron, MD
- 9:40–10:00 Evaluating Competence in the Interpretation of Chest Radiographs
Phillip N. Cascade, MD
- 10:00–10:10 Questions
- 10:10–10:25 Break

AIDS

Moderator: Georgeann A. McGuinness, MD

- 10:25–10:45 Lung Disease in HIV-Positive Individuals without AIDS
Mark A. King, MD
- 10:45–11:05 Airway Disease in the AIDS Patient
Georgeann A. McGuinness, MD
- 11:05–11:25 The Changing Face of PCP in AIDS Patients
Phillip M. Boiselle, MD
- 11:25–11:45 Pulmonary Neoplasms in AIDS
Keith J. Edinburgh, MD, MEd
- 11:45–12:05 Emerging Infections in AIDS
Linda B. Haramati, MD, Elizabeth R. Jenny-Avital, MD

Monday



Value in Thoracic Radiology

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In understanding transactions in the marketplace the value of a product can be viewed as what someone will pay for and how much they are willing to pay. What is it worth? Why should someone want it? Some form of compensation for an activity is necessary if that activity is to be continued.

The concept of adding value is a basic principle in the analysis of any human enterprise. Value is defined as the relationship between someone and something they desire. Value is not intrinsic within an object; it depends on the relation of that object to something else. The value of chest imaging cannot be determined without knowing its purpose.

Why do people get chest x-rays? The value of anything can only be assessed in the context of its intended use. The value of a chest radiograph in a patient with pneumonia differs from the value of a study when used to screen for lung cancer. The value of any diagnostic test is limited to its ability to diminish uncertainty. That, in part, is determined by how much a priori uncertainty exists. For the most part a radiologist will add more value when reading a bone film for a primary care physician than for an orthopedic surgeon. Similarly, radiologists have the prospect of contributing more value when reading chest x-rays for primary care physicians than for pulmonologists. In general more information will be provided to a primary care physician by a radiologist, than to a specialist. The specialist may know more about the interpretation of the radiograph and its implications to the patient.

In this context, when advocating a screening test the physician has a responsibility which differs from that when performing a diagnostic exam on a patient with symptoms. Diagnostic radiology is the business of uncertainty reduction. Screening tests have a unique relation to uncertainty reduction. The patient begins with the presumption of being healthy. Anything that changes that presumption may increase uncertainty. In this situation false positive exams increase uncertainty while false negative exams do not. The uncertainty equilibrium is shifted by a false positive exam. The value of a diagnostic procedure is heavily determined by the a priori presumption of probable illness.

The prospect of using low dose spiral CT to screen for lung cancer is one of the most exciting recent events in thoracic radiology. The proposed ACRIN project promises to reveal the merit of advocating this screening test. With the relative frequency of benign pulmonary nodules exceeding that of malignant nodules, the prospects for inappropriate false positive examinations may become a barrier to widespread use of what could eventually become a very valuable approach to reduce death from lung cancer. In my view the biggest barrier to a successful outcome of this project is the number of false positives due to benign pulmonary nodules. We therefore should do whatever we can to diminish this prospect.

Observer performance studies have revealed remarkable variation in the performance of radiologists and other physicians when reading plain chest films. It is likely that this variation will increase as we are faced with the massive volume of images encountered when interpreting screening CT examinations. In screening mammography computer assisted detection (CAD) can reduce variation in observer performance. Computer assisted detection has the prospect of adding more value to screening CT studies than it has to routine chest radiology.

CAD can help resolve the probable difficulties in establishing the value of advocating screening CT exams to detect early lung cancer in asymptomatic patients at high risk for this disease. We can approach nodule distinction by applying at least four distinguishing features to automated computer assessment of pulmonary nodules detected by spiral CT. The computer can be used to estimate the probable malignancy of any nodule detected. Three-dimensional data provides considerable greater opportunity for CAD to add to what the human eye can readily detect in evaluating these CT studies. The higher the resolution in three dimensions the greater the contribution from computer assistance up to a limit of perfectibility. That limit remains to be found.

Four measurements may be useful adjuncts to this study. We do not know which of these are necessary to reach a threshold of certainty sufficient to add value to screening pulmonary CT. Optimal



metrics can be determined once the value of each measurement has been investigated independently. Some combination may be sufficient to effectively exclude the probability that a nodule reaches a threshold for malignancy that would warrant a further more invasive diagnostic procedure.

I would propose beginning with the following four measurements:

1. Diameter variation – The standard deviation of the average diameter determined in multiple three-dimensional projections will provide an assessment of the sphericallity of the nodule. The wider the variation in diameter the more likely the prospect of malignancy.
2. Density Variation – The standard variation in voxal density within the boundaries of the nodule can be used to assess the degree of calcification. The more the variation the less likely the lesion is malignant.
3. Surface area – Can be used to apply fractal analysis to a nodule. The more spiculated the nodule, the larger the surface area per average diameter. Surface area to diameter ratio can be used as a predictor of probable malignancy.
4. Airway connectivity – Bronchogenic carcinoma is found in proximity to an airway. Zerhouni, et. al. have developed methods for automatic bronchial airway tracing. This can be used to define the relative proximity of the lesion to an airway. The greater the airway connectivity, the more likely the lesion is malignant.

These measurements independently or in some combination may be considered with other indicia of malignancy in establishing a CAD system defining the threshold required for advocating further (more invasive) diagnostic procedures in response to an apparent abnormality detected on a screening pulmonary CT.

The prospective value of CAD as an adjunct to screening pulmonary CT will have to be studied using some form of observer performance study. These studies allow one to measure the value of a diagnostic procedure in terms of its capacity to reduce uncertainty. The methods used to evaluate the performance of radiologists when reading standard chest x-rays will be useful as a basis for designing the means to maximize the prospects for success when evaluating the merits of new technology as exemplified by screening CT for lung cancer detection.

The assessment of value in chest imaging may properly depend upon whether the quality was impacted throughout the entire process. Opportunities to augment quality throughout the entire system and

continuous quality improvement will increase the value of whatever is done. Initially, quality assurance in radiology was directed to image quality. How much image improvement is enough? What is an optimal image? Can digitized images work as well as films? How much spatial and contrast resolution do we really need to have the maximum impact. Now with screening CT, CAD may add more value than was possible in plain film radiography. CAD may be useful to enhance detection and even more importantly reduce the false positives. Indeed without such adjuncts we may not discover the true value of advocating screening CT to detect lung cancer in asymptomatic high-risk patients.

The value of any diagnostic test depends upon relating quality to cost. Excessive false positives will markedly diminish the prospective value of any test used for screening asymptomatic patients. As with any diagnostic procedure, the purpose of chest imaging is to decrease uncertainty. Value is added in diagnostic imaging through reducing uncertainty by optimizing the performance of the entire system of chest imaging.

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Analysis of Mediastinal Contours

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Objectives:

1. Review normal variations of mediastinal anatomy.
2. Correlate plain film, CT and MR analysis of mediastinal contours.
3. Improve perception of mediastinal abnormalities.

Perception of mediastinal abnormalities requires a thorough knowledge of normal mediastinal contours. There are numerous mediastinal abnormalities which may be readily detected and diagnosed by plain film analysis; however, others frequently require multi-planar imaging with CT, MR, or image-guided biopsy. This presentation will review normal mediastinal anatomy and a wide variety of mediastinal abnormalities.

Mediastinal contours are visualized as a result of the interface of the mediastinal pleura with the lung. Abnormalities are perceived when there are alterations in the normal mediastinal structures. Additional structures such as masses, cysts, or aneurysm displace the pleura while other invasive processes such as invasive cancers, lymphoma and some infections may cross the mediastinal pleura eradicating the normal lung-pleural interface.

Analysis of mediastinal contours may be facilitated by dividing the mediastinum into four quadrants and reviewing anatomy with plain film, CT and MR. The right superior mediastinal contours are determined by the following: brachiocephalic veins, superior vena cava, azygous vein, paratracheal line, and the right main bronchus. The left superior mediastinal contours include the bronchocephalic vein, subclavian vein and artery, aortic arch, aorticopulmonary window, main pulmonary artery and left pulmonary artery. The heart is the largest contour in the inferior mediastinum, but the inferior vena cava and vertebrae are identifiable on the right and the descending aorta and paraspinal stripe should be visualized on the left.

Sagittal MR, the lateral plain film and axial images permit examination with emphasis on anterior to posterior anatomy. Anteriorly, we may identify abnormalities of the thymus, lymph nodes, fat, and right heart. The middle structures include the trachea, esophagus, azygous, superior vena cava, aorta, great vessels, and lymph nodes. Posteriorly we observe the descending aorta, azygous vein, spine and paraspinal lines.

Pulmonary consolidations should be distinguishable from mediastinal abnormalities by the presence of ill-defined or irregular borders and the presence of

air-bronchograms or even lucent spaces. Lung masses are often irregular and sometimes heterogeneous, but may be smooth and when closely applied to the mediastinal pleura could be difficult to distinguish from a mediastinal mass. Lung masses which are firm and round may form a characteristic sulcus with the mediastinal pleural. This appearance is often distinctive from the expected tapered interface that is seen when a mediastinal mass displaces the pleura into the lung. Primary lung cancers may be even more difficult to evaluate because they are locally invasive and may extend directly into the mediastinum or they may metastasize to the mediastinal nodes. In contrast with invasive primary lung tumors, mediastinal lymphomas arise in the mediastinal nodes or thymus and may also be locally invasive and spread into the lung. Serial films may document the progression of the tumor and provide reliable signs for distinguishing lung tumors from lymphoma, but this often requires biopsy when patients present with advanced disease. Infrequently, other mediastinal tumors in particular malignant thymoma may be locally invasive and mimic the appearance of lymphoma or extensive metastatic disease.

Chest wall abnormalities that arise anteriorly from the sternum or from posterior ribs may suggest a mediastinal abnormality on the plain film, but they can be accurately identified by the presence of destruction of bone or by multiplanar images that show extension of the abnormality into the chest wall. Pleural abnormalities that arise from the medial pleura may be more difficult to correctly localize and are often indistinguishable from primary mediastinal abnormalities.

Since a number of mediastinal contours are the result of the interface of vascular structures with the lung, there are important differences in mediastinal contours based on the patient's age. This is especially true of the contours of the heart and great vessels, especially the aorta and superior vena cava. Enlarged vessels and vascular abnormalities must always be distinguished from mediastinal masses especially before consideration of biopsy.

Masses are challenging to evaluate, but processes that spread diffusely through the mediastinum produce an even less distinctive radiographic appearance of diffuse mediastinal widening. Mediastinal widening may result from hematoma, vascular abnormali-





ties, invasive masses, infection, fibrosis, accumulations of fat and abnormalities of the esophagus.

Mediastinal lipomatosis is a common variant of normal in obese patients. It is also seen in patients with endocrine disturbances such as Cushing's or those on high dose steroid therapy. The opacity of fat is between that of the mediastinal soft tissues and the aerated lung. This is sometimes recognized on plain film, but usually requires CT for confirmation. Lipomatosis is a benign normal variant that must be distinguished from more serious causes of mediastinal widening such as lymphoma.

While the expected appearance of adenopathy may be that of circumscribed masses, very extensive adenopathy from both infectious and neoplastic causes may diffusely widen the mediastinum. Clinical correlation is essential, for example, patients with AIDS who develop mediastinal adenopathy often have very extensive adenopathy involving multiple node groups. This requires consideration of infections by mycobacteria, or fungi, and may also result from Kaposi's sarcoma or lymphoma. While reactive lymph node hyperplasia may cause progressive generalized adenopathy this is not a frequent cause of nodes that are detectable by plain film and rarely causes adenopathy with nodes greater than 1cm on CT.

Mediastinitis is caused by both acute bacterial and granulomatous infections. In addition, spondylitis may spread into the mediastinum with paraspinous abscess or mediastinitis. Staphylococcus and tuberculosis are the two most common causes of spondylitis with paraspinal abscess.

Mediastinal hematoma should be suspected in patients following major trauma who develop mediastinal widening. However, mediastinal hematomas may also occur with fractures of the sternum and vertebrae. Additionally, there are non-traumatic vascular abnormalities which widen the mediastinum including atherosclerotic dilatation of vessels, aortic dissection, and occasionally aneurysm. Even congenital

abnormalities such as left-sided superior vena cava and coarctation of the aorta may alter the mediastinal contours and widen the mediastinum.

Summary:

Careful analysis of mediastinal contours is required to distinguish primary mediastinal from pleural, pulmonary and chest wall abnormalities. Most mediastinal abnormalities are detected with plain films, and in some cases the correct diagnosis may be suspected, but most require CT, MR or biopsy. Basic clinical correlation is essential. The appearance of a widened mediastinum must be evaluated in context of the patient's clinical presentation in order to determine the appropriate choice of imaging procedures.

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Things That Are Not What You Thought They Were on the Chest Radiograph: Confusing Findings Resolved by CT

J. David Godwin II, MD

CT has improved our understanding of normal and pathologic anatomy as portrayed on plain radiographs of the chest. The goal of this presentation is to present some points in this new understanding and to clarify the potentially confusing manifestations of:

Thoracic veins

- normal structures and variants causing pseudotumors, including the retroaortic anastomoses of the azygos system, the left superior intercostal vein (forming an “aortic nipple”), or a dilated azygos vein

Thoracic arteries

- tortuous, dilated brachiocephalic artery causing mediastinal pseudotumor
- the apical opacity of Proto

Extrapleural fat

- fat “in the fissures” [*not really in the fissures*]; fissural fat causing pseudopneumonia
- chest wall fat resembling pleural plaque
- mediastinal lipomatosis; pseudotumors caused by displaced mediastinal fat
- paraspinal fat resembling posterior lymphadenopathy

The apical cap

The pulmonary ligament [*sense and nonsense*]

The juxtaphrenic peak in upper lobe volume loss [*caused not by the pulmonary ligament, but by the inferior accessory fissure*]

The phrenic nerve and the sublobar septum [*frequently misinterpreted as the pulmonary ligament*]

The retrosternal stripe caused by mediastinal rotation [*not caused by excess “areolar” tissue or by accessory hemidiaphragm*]

“Herniation of the lung” across the midline [*not real herniation, but another manifestation of mediastinal rotation*]

Osseous pseudotumors caused by the vertebral lamina, osteophytes, vertebral transverse processes, costal cartilages, healed rib fractures, the scapulae and arms

Pseudopneumothorax caused by pneumomediastinum

Misleading Findings Caused by Veins

The **left superior intercostal vein** (LSIV) collects the 2nd, 3rd, and 4th intercostal veins into a common trunk that passes alongside the aortic arch to terminate in the left brachiocephalic vein. It may be visible as a small bump (the “**aortic nipple**”) along the aortic arch or just above or below it, where it can be mistaken for lymphadenopathy in the aortopulmonary window. Although an “aortic nipple” can be a normal variant, dilation of the LSIV can reflect elevated systemic venous pressure or excess flow in the azygos-hemiazygos system. Excess flow could reflect a congenital venous anomaly or obstruction of a major vein, such as the SVC, IVC or a brachiocephalic vein. The same conditions can dilate the **azygos vein**.

There are several normal connections between the azygos vein and the hemiazygos or accessory hemiazygos vein, known as the **retroaortic anastomoses**. On CT scans these connections may be visible as oval masses anterior or anterolateral to the spine. If these veins are not clearly enhanced by contrast, they may be mistaken for enlarged lymph nodes.

Arterial Pseudotumors

In an elderly patient with a dilated, elongated, and tortuous aorta, the **right brachiocephalic artery** is often similarly dilated and tortuous. It bulges to the right and creates superior mediastinal pseudotumor. The tortuosity of the brachiocephalic artery results not only from its own elongation, but also from elongation of the aorta, which elevates the arch and forces the brachiocephalic artery above it to buckle. On CT scans, the normal brachiocephalic artery is circular, whereas a tortuous artery is cylindrical or ovoid. Its dense contrast enhancement helps to distinguish the tortuous brachiocephalic artery from tumor or lymphadenopathy.

Proto demonstrated that the right or left subclavian artery can indent the lung apex within the arc of the first rib and create a vague round opacity suggest-



ing tumor. Rarely, the connection of this opacity to the vertical segment of the subclavian artery is recognizable, helping to establish the vascular cause of the round opacity. CT is definitive in excluding a real lung lesion as the cause of this **apical opacity of Proto** and in demonstrating its vascular cause.

Confusing Manifestations of Extrapleural Fat

Extrapleural fat in the chest wall is mobile and plastic because it is embedded in loose connective tissue. Fat rearranges in response to inward traction on the parietal pleura. Thus, where lung scarring tethers the visceral pleura, the traction is transmitted to the parietal pleura, pulling it inward and stretching and thickening the overlying extrapleural fat in the chest wall.

The parietal pleura can be drawn into a lung fissure by the normal (negative) pleural pressure, and subjacent extrapleural fat is pulled along, resulting in a wedge-shaped fat deposit on lateral view. This fat appears to be “in the fissure,” but is actually covered by parietal pleura and is thus extrapleural—it is not in the pleural space. If extrapleural fat is drawn into a major fissure that intersects the apex of the hemidiaphragm, the fat may “silhouette out” the diaphragm on the frontal view, falsely suggesting pneumonia (“**pseudopneumonia**”).

Mediastinal fat, also extrapleural, is as mobile and plastic as chest wall fat. Thus, lung scarring (e.g., from IPF or from radiation fibrosis) or volume loss (e.g., from lobectomy) can draw mediastinal fat into strange configurations that resemble mediastinal masses. The usual clinical setting is irradiated Hodgkin’s disease. Mediastinal lymphadenopathy initially shrinks after radiation, but as radiation fibrosis develops in the lung, the mediastinum again widens, suggesting tumor recurrence. CT may show that the widening is really from rearranged mediastinal fat caused by lateral retraction of mediastinal pleura by adjacent lung fibrosis.

Mediastinal lipomatosis, sometimes idiopathic, is more often caused by administration of corticosteroids. The widening usually involves the superior portion of the mediastinum, and the borders are usually straight rather than convex. Convex borders raise the possibility of tumor. Of course, noncontrast CT readily distinguishes fat from tumor.

Paraspinal fat deposits can be prominent, particularly in middle-aged or older men. The deposits create paraspinal stripes that are convex or straight and usually bilateral, resembling lymphadenopathy. The differential diagnosis is particularly troublesome in a patient who has lymphoma or a retroperitoneal tumor (such as renal or testicular cancer). Once

again, CT readily distinguishes fat from lymphadenopathy.

The Cause of the Apical Cap

A smooth stripe between the lung apices and the undersurface of the first rib is a normal finding. It should not be taken as an indication of tuberculosis. Although an apical cap has been called “apical pleural thickening,” the pleura itself is usually normal. If there is any scarring contributing to the cap, it is usually subpleural *lung* scarring, which has been attributed to the relative ischemia of tissue at the extreme apex of the lung.

The most common cause of an apical cap is normal intercostal muscle or extrapleural fat. If there is not a pronounced convexity of the stripe toward the lung and there are no symptoms to suggest apical lung cancer, some asymmetry of the apical caps on the two sides is acceptable. Even a gentle convexity of the cap laterally between the first and second ribs is normal.

The Inferior Pulmonary Ligament, Sublobar Septum, Inferior Accessory Fissure, and Phrenic Nerve

At the hilum, the visceral pleura of the lung is continuous with the parietal pleura of the mediastinum. Instead of forming a simple tube that surrounds the bronchi and pulmonary vessels as they exit the mediastinum and enter the lung, the pleural reflection between the mediastinum and lung is prolonged downward below the hilum, binding the lower lobe to the mediastinum alongside the esophagus. This downward prolongation, which consists of two fused pleural layers, is the **pulmonary ligament**.

The pulmonary ligament is invisible on normal chest radiographs. However, its effects in tethering the lower lobe to the mediastinum are apparent in the presence of pleural effusion. As pleural effusion gets large enough to elevate the lung base, the pulmonary ligament keeps the medial portion of the lower lobe fixed along the lower mediastinum. Thus, only the lateral part of the lower lobe can rise.

On CT scans the pulmonary ligament is sometimes visible as a small laterally-directed beak of mediastinal pleura near the esophagus. The effect of the pulmonary ligament is dramatic in the presence of pleural effusion. The lateral aspect of the lower lobe floats anteriorly, rotating around the pulmonary ligament, which acts as a hinge attaching the lobe to the mediastinum.

CT scans often show the **sublobar septum**, a linear structure extending from the medial pleura of the lower lobe (near the pulmonary ligament) posterolaterally into the lung toward a basal pulmonary vein.



This structure has been mistaken for the pulmonary ligament. Similarly, about 40% of persons have at least a shallow **inferior accessory fissure** (which delimits the medial basal segment from the other basal segments of the lower lobe). This structure may be visible as a curved line that extends laterally from near the pulmonary ligament and then arcs anteriorly to join the major fissure. *The sublobar septum is probably the incomplete portion of the inferior accessory fissure.* A third linear structure that extends laterally from the mediastinum is the **phrenic nerve**, which has also been mistaken for the pulmonary ligament. However, it is too far anterior to be the ligament, which is always near the esophagus: on the right, the phrenic nerve extends laterally from the IVC, and on the left it extends laterally from the heart.

Mediastinal Rotation and “Lung Herniation”

The position of the mediastinum in the chest is determined by the balance of the (negative) pleural pressure between the two hemithoraces. Volume loss on one side (e.g., from lung hypoplasia, lung resection, atelectasis or scarring) will draw the mediastinum ipsilaterally; the mediastinum rotates as if the descending aorta were the hinge. As the mediastinum rotates, its leading edge is dragged laterally along the anterior chest wall in front of the lung. On the lateral view, this interposed tissue forms a **retrosternal stripe** that separates the lung from the anterior chest wall. Although this stripe has been attributed to an excess of areolar tissue or to the presence of accessory hemidiaphragm (a rare congenital anomaly), CT has shown that it is caused solely by mediastinal rotation.

As the mediastinum rotates, the anterior junction line between the two lungs also rotates. The resultant anterior extension of one lung across the midline has been termed, “**herniation of the lung,**” but this terminology is incorrect and misleading. A real hernia requires a hole in a barrier. However, in mediastinal rotation, there is no hole in the barrier (the anterior junction line); the barrier has just rotated.

Pseudopneumothorax Caused by Pneumomediastinum

Since the mediastinum is extrapleural, gas causing **pneumomediastinum** can extend along extrapleural tissue planes out from the mediastinum and over the apices of the lungs or behind the sternum. In either case, the parietal pleura is displaced from the chest

wall, creating a visible pleural line that suggests pneumothorax (“**pseudopneumothorax**”). However, signs of pneumothorax in other locations are usually absent. Furthermore, connective tissue strands may be visible within the pseudopneumothorax. Finally, on decubitus views, the gas collection does not shift its location, as true pneumothorax almost always does.

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Chest Radiographic Interpretation of Interstitial Lung Disease: Review of a Dying Art

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Educational Objectives

1. To recognize four basic chest radiographic patterns of interstitial lung diseases and to understand what characteristic differentiate one pattern from another.
2. To learn what are the most common entities to cause each pattern of interstitial lung disease.

Introduction

The plain film interpretation of diffuse interstitial lung disease is one topic which often seems difficult, if not impossible, to many radiologists. However, when armed with a systemic approach to analyze the radiograph, in many instances a short differential diagnosis may be easily generated; and if sufficient clinical history is available, a specific diagnosis may be made.

The vast majority of interstitial diseases may be classified as “reticulonodular”. Any pattern of criss-crossing lines, will create small polygonal networks a reticular group, and focal interstitial thickening or the junctions of the crossing lines and lines, seen end on, will appears nodular opacities. One of the first hurdles to overcome in separating the various interstitial diseases is to recognize the more specific underlying pattern. These underlying patterns may be classified as: linear, peripheral reticular, cystic (central reticular), and nodular patterns. Distribution of opacities, lower lung zone predominant, mid lung zone predominant, upper lung zone predominant, or diffuse distribution may play an important adjunctive role in distinguishing interstitial diseases as well as the recognition of other bony or soft tissue abnormalities which may relate to the primary disorder.

Linear Pattern

The linear pattern appears as long white lines, radiating from the hilum and also line running perpendicular to the chest wall. These are Kerley A and B lines. Most radiologists readily recognize Kerley B lines, an important clue to this pattern. As you may have guessed, the most common cause of this pattern is hydrostatic interstitial pulmonary edema. The

other causes of the linear pattern include lymphangitic carcinomatosis and pneumocystis pneumonia (PCP), and rarely interstitial pneumonias, such as cytomegalovirus (CMV), respiratory syncytia virus (RSV), as well as mycoplasma, and congenital chlamydia infections. These appear more or less as CHF, and so a radiograph which reminds you of interstitial pulmonary edema, should make you think of the differential for the linear pattern.

Differentiation of the causes of the linear pattern is largely based on clinical history. Usually it is advisable to “rule out” CHF with a combination of a therapeutic trial of diuretics and a follow-up chest radiograph. If the interstitial pattern disappears, then the cause was CHF. If it does not improve then lymphangitic carcinomatosis, PCP or interstitial pneumonias should be considered. Lymphangitic carcinomatosis, PCP and interstitial pneumonias are more likely to be asymmetrically distributed.

Most patients with lymphangitic carcinomatosis will have a clinical history of a malignancy known to cause this pattern of metastasis, such as breast, lung, stomach or pancreatic carcinoma. However, occasionally this is the first manifestation of disease. Asymmetry of the linear interstitial pattern is an important clue to this diagnosis.

With the occurrence of the AIDS epidemic, PCP has become a common infection in inter-city hospitals. Patients with AIDS and other causes of immunosuppression, such as organ transplant recipients and patients with lymphoproliferative disorders are predisposed to this opportunistic infection and, therefore, the presence of a linear interstitial pattern in these patients should alert you to the possibility of PCP.

Interstitial pneumonias in adults are rare. They are usually symmetric and diffuse, but occasionally may be asymmetric or focal in distribution. Clinical symptoms suggestive of pneumonia, such as cough, fever, and dyspnea, are usually present and are the major clue to the diagnosis. Patients may also be in a risk group prone to a particular interstitial pneumo-



Patterns of Diffuse Interstitial Lung Disease

Radiographic Pattern

Radiographic clues

Linear Pattern

1. interstitial pulmonary edema
2. lymphangitic malignancies
 - carcinoma, lymphoma, leukemia
3. interstitial pneumonias
 - mycoplasma, viruses

changes rapidly
may be asymmetric

may be asymmetric

Peripheral Reticular Pattern

1. idiopathic pulmonary fibrosis
2. collagen vascular disorders
 - RA, scleroderma, MCTD,
 - dermatomyositis, SLE
 - Sjogren's syndrome
3. asbestosis
4. bronchiolitis obliterans
organizing pneumonia
5. sarcoidosis

clavicle erosions, dilated esophagus
skin calcifications

pleural plaques

mid/upper lung predominance, adenopathy

Cystic (Central Reticular) Pattern

1. honeycomb lung (end stage fibrosis)
2. diffuse bronchiectasis
3. eosinophilic granuloma
4. lymphangioleiomyomatosis (LAM)
5. tuberous sclerosis
6. emphysema

course, well defined walls
well defined ring shadows
nodules, hyperinflation, upper lobe predominance
hyperinflation
hyperinflation
hyperinflation

Nodular Pattern

1. metastasis
2. granulomatous diseases
 - a. sarcoidosis
 - b. miliary infections
 - TB
 - fungi (histo, cocci, crypto, blasto)
 - c. hypersensitivity pneumonitis
 - d. eosinophilic granuloma
3. pneumoconiosis
 1. silicosis
 2. coal workers pneumoconiosis
 3. berylliosis
 4. talcosis

Hx of cancer, especially thyroid, breast

mid/upper lung predominance, adenopathy
may be very tiny nodules

indistinct nodules
cysts, hyperinflation, upper lung predominance

upper lung predominance, adenopathy
progressive massive fibrosis
upper lung predominance, adenopathy
progressive massive fibrosis

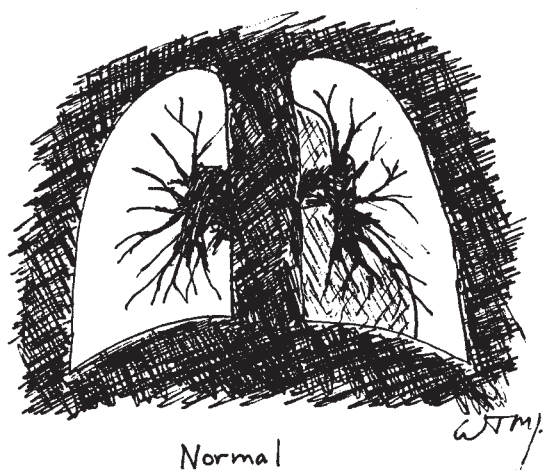
nia, such as the association of CMV infection with organ transplant recipients.

Peripheral Reticular Pattern

As the name implies, the dominant feature of this group of diseases is the appearance of a fine network of lines producing a series of tiny polygonal spaces, usually less than 5 mm. in diameter, as if it were a honeycomb made by ant-sized bees. Characteristi-

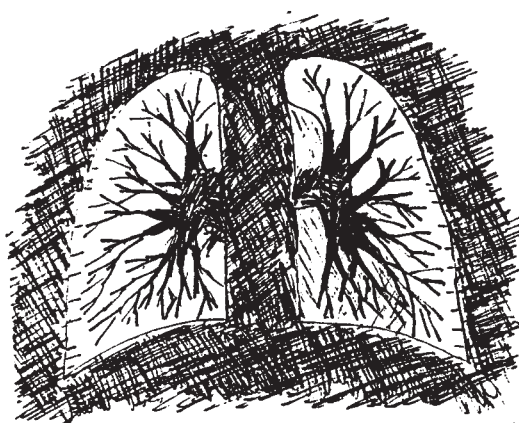
cally this network is very delicate and often likened to lace. These are Kerley C lines. This pattern is always predominant in the periphery of the lung and is usually seen best in the costophrenic angles. While occasionally diffuse, these lines usually have a basilar predominance. The three common causes of this pattern are idiopathic pulmonary fibrosis, asbestosis, and collagen vascular diseases, particularly scleroderma and rheumatoid arthritis. Rarely this may be





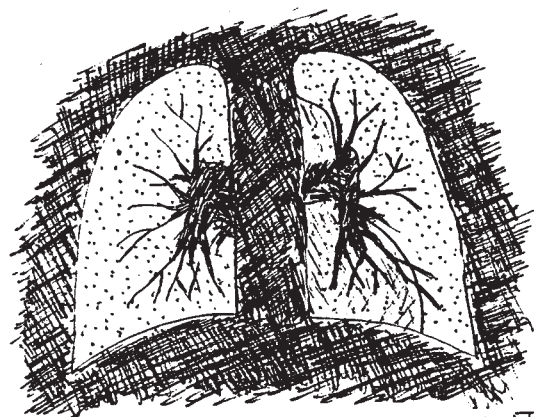
Normal

WTM



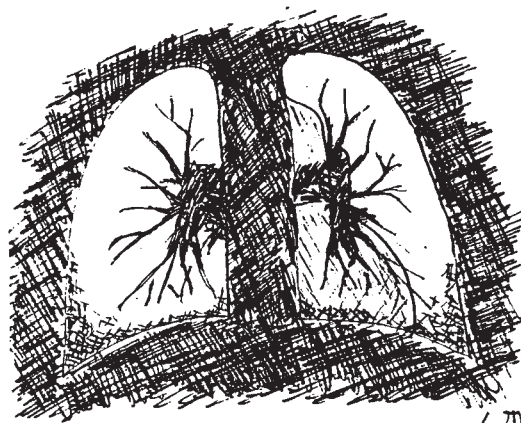
Linear Pattern

WTM



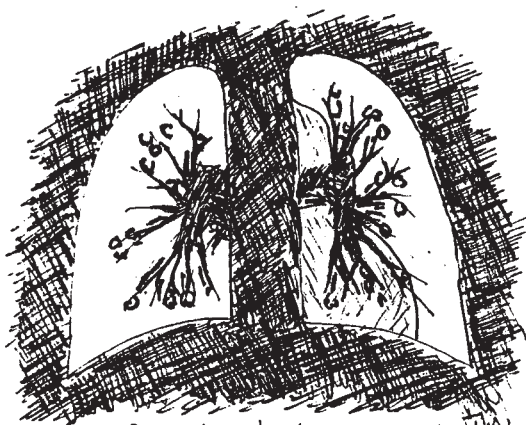
Nodular Pattern

WTM



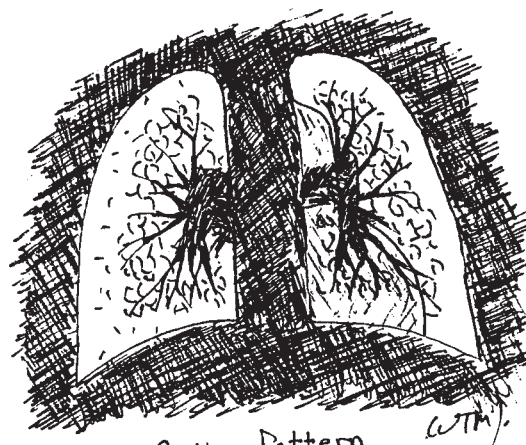
Reticular Pattern

WTM



Bronchiectasis

WTM



Cystic Pattern

WTM

seen with bleomycin or Carmustine (BCNU) toxicity, bronchiolitis obliterans organizing pneumonia (BOOP) and sarcoidosis.

Differentiation of the causes of this pattern is dependent on clinical history. Patients with asbestosis will have a large exposure to asbestos dust which will be readily discovered with a good occupational history. It is typically seen in miners, shipyard workers, insulation workers, boilermakers, construction work-

ers and roofers as well as in other occupations. Casual exposure to asbestos as in most non-occupational exposures is usually not sufficient to produce radiographically detectable asbestosis. Pleural plaques may be a radiographic clue to the diagnosis.

The majority of individuals with reticular interstitial disease due to collagen vascular disorders (CVD) will have a known history of such, prior to the development of interstitial lung disease. The most common





causes are rheumatoid arthritis (RA) and progressive systemic sclerosis (scleroderma), but the pattern may also be seen with other disorders such as polymyositis/dermatomyositis, mixed connective tissue disorder (MCTD), systemic lupus erythematosus (SLE) and Sjogren's syndrome. The presence of clavicle erosions in RA or a dilated esophagus in scleroderma may be radiographic clues to the diagnosis.

BCNU and Bleomycin use may be obvious to the clinician caring for the patient, but such history may not be typically sought by the radiologist! Interstitial lung disease is very rare because the toxicity is dose dependent and oncologists usually maintain doses below the toxic threshold.

Idiopathic pulmonary fibrosis is a diagnosis of exclusion. However, this is the most common cause of this pattern. Characteristically, it is seen in elderly patients and will occasionally have a more rapid radiographic progression than the other causes of the reticular pattern.

Cystic Pattern (Central Reticular Pattern)

In this pattern the network of lines tends to take a rounded contour, producing moderate sized (5-15 mm.) spaces which are seen in the more central portions of the lung. This is in contrast to the peripheral reticular pattern which has smaller spaces (usually less than 5 mm.) and is seen in the peripheral regions of the lung. In some instances, the cystic pattern is seen as prominent ring shadows. In others, the overall appearance is of an indistinct reticular network made of a large series of circular lines. The causes of this pattern are diffuse bronchiectasis, lymphangiomyomatosis (LAM), tuberous sclerosis (TS), eosinophilic granuloma of the lung (EG), and end stage fibrosis or honeycomb lung.

Diffuse bronchiectasis will usually show coarse ring shadows which are well defined and may be localized to one lobe or asymmetrically and haphazardly distributed. Often, this is a straight-forward diagnosis. When diffuse, bronchiectasis usually implies a systemic disease. Most commonly this is cystic fibrosis (CF); however, other causes include allergic bronchopulmonary aspergillosis (ABPA), immotile cilia syndrome (Kartaganer's syndrome), and a variety of immunodeficiency states such as common variable hypogammaglobulinemia, and hyper-IgE syndrome.

Lymphangiomyomatosis and the lung disease of tuberous sclerosis are pathologically identical diseases in which proliferation of interstitial smooth muscle results in air trapping and the production of small uniform cystic spaces. These are readily seen on high resolution CT of the lung but, if carefully sought out, can also be seen on chest radiographs. At

best, these rings are quite apparent. At worst, the interstitial lines are very faint and the radiograph resembles emphysema. The presence of air trapping is an important clue to the diagnosis of lymphangiomyomatosis and tuberous sclerosis. They are among the few causes of interstitial disease and hyperinflation on the chest radiograph; the other major cause is eosinophilic granuloma of the lung or Histiocytosis X.

Eosinophilic granuloma of the lung is another cause of the cystic pattern of interstitial disease. Besides the presence of fine cysts, other clues to the diagnosis of EG include hyperinflation, the presence of fine interstitial nodules, and an upper lobe predominance to the disease. The nodular appearance of EG tends to be a manifestation of early disease and the cystic appearance is often a latter finding. EG is also associated with smoking and therefore in the late stages of disease there may be concomitant emphysema present.

Nodular Pattern

The nodular pattern, as the name implies, appears as numerous tiny nodular densities. Unfortunately, this interstitial pattern has one of the longer differentials. Causes include pneumoconiosis (silicosis, coal workers pneumoconiosis and berylliosis), tiny metastasis (thyroid carcinoma and breast carcinoma), and granulomatous diseases such as sarcoidosis, chronic hypersensitivity pneumonitis, eosinophilic granuloma of the lung (Histiocytosis X), and miliary infections (tuberculosis, cryptococcosis, coccidioidomycosis, histoplasmosis, etc.). Silicosis, coal workers pneumoconiosis, sarcoidosis, and histiocytosis, usually have a mid and upper lung zone predominance, a finding which may help narrow the differential. Sarcoidosis and silicosis may have associated hilar and mediastinal adenopathy, and frequently have a mid and upper lung zone distribution of opacities. Progressive massive fibrosis, a mass-like region of fibrosis in the upper lobes with cicatricial emphysema peripheral to the mass, may be found in silicosis and coal workers pneumoconiosis and may be a diagnostic clue.

Once again in most cases, clinical history is essential to arrive at a specific diagnosis. Patients with miliary infection will usually have fever and they may have other clinical clues associated with them. For example, a history of immunosuppression suggests miliary TB or diffuse fungus such as cryptococcosis. Travel to the southwest U.S. is a clue to coccidioidomycosis. Patients with nodular pneumoconiosis will have a history of occupational exposure to the appropriate dust. Those patients with small nodular metastatic tumor will usually have a



known malignancy. Hypersensitivity pneumonitis is a rare and difficult diagnosis. Often the appropriate clinical inquiry occurs only after the radiograph raises a suspicion of the disease. The nodules of hypersensitivity pneumonitis are usually somewhat indistinct, a feature which is also seen in sarcoidosis but is less common in other causes of the nodular pattern. Sarcoidosis and histiocytosis are often seen in younger patients without significant medical history. Sarcoidosis in its latter stages will often have a characteristic symmetric mid and upper lung zone scarring. This appears as coarse linear bands which extend horizontally from the hilum and produce upward retraction of the hilum. When seen, this is sufficiently characteristic to

be diagnostic of sarcoidosis. Pulmonary alveolar microlithiasis is an exceedingly rare cause of the nodular pattern which is characterized by sharply defined, calcified, small, "sandlike" opacities. The density of the nodules is so characteristic that it is usually diagnostic of this idiopathic disorder.

Conclusion

The plain film evaluation of diffuse interstitial lung disease is often a daunting task. However, armed with a systematic approach to evaluate the radiograph, a pertinent differential diagnosis may be generated, and with appropriate clinical history, a specific diagnoses may often be made.



Misconceptions in Chest Radiology

Murray G. Baron, MD

Objectives:

To understand the underlying processes resulting in the roentgen images of “discoid atelectasis”, “diaphragmatic tenting”, free pleural effusion and the post-pneumonectomy thorax.

Advances in diagnostic radiology result from the gathering of data by observation and/or experimentation and the interpretation of this data. If one or more of the processes is incorrect, the results will be incorrect. Even though the error of the result may not be recognized immediately, it rapidly becomes evident when it fails in practice. Rarely, the reverse can happen: although the preliminary work is faulted, the results come out correctly – the right hypophysis is accepted for the wrong reasons. Then, because of the association between the process and the conclusion, the preliminary steps are assumed to be correct and take on a life of their own, creating unanswerable questions and interfering with the understanding and application of the conclusions.

Discoid Atelectasis

Atelectasis of a pulmonary sub-segment, from obstruction of its bronchus, results in linear shadows in the lungs. This was first described by Dr. Felix Fleischner in 1936, in relation to pulmonary embolization and infarction. He felt that because the bronchi are stiffer than the lungs, and because they are oriented along the long axis of the sub-segment, the lung cannot collapse in all directions around the occluded bronchus. Instead, the sub-segment would fold into a flat pancake, hence the term “discoid” or “plate-like” atelectasis.

Problems:

1. The original pleural surface of the sub-segment is contracted from its original area to a line, representing the edge of the atelectatic plate. Why is there no wrinkling of the pleural surface?
2. In the presence of a pneumothorax, the entire lung usually collapses into a ball at the pulmonary hilum. Evidently, even the major bronchi can fold.
3. Frequently, the line formed by the atelectatic plate is too fine to represent collapsed portion of the lung.

Normally, when a sub-segmental bronchus is occluded, the lung does not collapse, as there is air drift

from the adjacent sub-segments through the pores of Cohn. However if there is congestion or infiltration in these adjacent segments, there is no collateral air drift and the sub-segment collapses. It is more likely that the segment collapses in all directions around the obstructed bronchus and pulls in a double layer of visceral pleura. When the expanded lung is viewed, a puckering of the pleural surface can be seen over this point. The linear shadow on the chest film is due to the double layer of pleura, any fluid within it and the infiltration of the adjacent sub-segments, when viewed on end.

Frequently, the bronchial obstruction is caused by a mucous plug. When this is coughed up, air re-enters the sub-segment, it expands to its original volume and the linear atelectatic streak disappears. However, if, while the sub-segment is collapsed, the two layers of pleura become adherent, the sub-segment is prevented from ever re-expanding, the adjacent infiltration clears and a fine linear shadow remains a pulmonary scar.

Diaphragmatic Tent

The usual explanation for the upward tenting of a portion of the diaphragm is that it is caused by retraction of a pulmonary scar attached to the diaphragm.

Problems:

1. The tent can form in a very short period of time.
2. The tent can clear completely.
3. When a pneumothorax is induced, the tent disappears.

A diaphragmatic tent results from discoid atelectasis in the lung, facing on the diaphragm. As the sub-segment collapses, it draws the visceral pleura and associated extra pleural tissues inward, producing the appearance of a tent. In the presence of a pneumothorax, the air separates the lung from the diaphragm showing that there is no adhesion. The air fills the atelectatic cleft in the lung and the diaphragm assumes its normal curve. When the air in the pleura is absorbed, the tent reforms.

The Pleural Fluid Meniscus

A meniscus is the curved air-fluid interface seen in small bore tubes or pipettes, caused by surface attraction. In the erect chest film, a free pleural fluid collection usually has a curved upper border that resembles



a meniscus. Over the years, the use of this term has changed form resembling a meniscus to being a meniscus. A large proportion of radiologists-in-training, when asked to indicate the upper level of the pleural effusion will carefully trace the slanted curve of this “meniscus”.

Problems:

1. No meniscus is seen with a hydropneumothorax.
2. Fluid does not flow uphill.

The medial base of the lung is usually tethered by the inferior pulmonary ligament so that the lung cannot float on the pleural fluid with the patient erect as it does when the patient is supine. The free pleural fluid encircles the lung except on its medial aspect. Because of gravity, the fluid layer around the lung is very thin near the top of the effusion and gets progressively thicker lower down, towards the diaphragm. On an erect frontal chest film, the fluid layer is usually too thin to cast a significant shadow when it is viewed *en face*. What is seen is the shadow of the fluid laterally, where it displaces the lung inward from the chest wall. Essentially the fluid is visualized in a mid-coronal section and its free margin resembles a meniscus. The true fluid level is easily demonstrated if radio-opaque oil is injected into the effusion. The oil floats on the fluid and a nice horizontal line of oil droplets outlines the upper extent of the fluid – exactly as it is outlined by air when there is a hydropneumothorax.

The Post Pneumonectomy Space Becomes Filled with Fluid

Following removal of a lung, the hemithorax decreases in size: the heart and mediastinum shift to the involved side, the ribs become shingled and the diaphragm is elevated. The remaining space is then

filled with fluid, which, over the years, becomes organized into fibrous tissue.

The fact that the hemithorax fills with fluid is absolutely correct. But the concept that the outpouring of fluid is the primary mechanism is misleading.

Problems:

1. Why does the fluid form? It does not in a pneumothorax.
2. Why does the fluid production stop when the hemithorax is filled – or can it go on too long?

What does happen is that the air in the thorax is absorbed exactly in the same way as when there is a pneumothorax. In the latter case the lung expands to occupy the space relinquished by the disappearing air. Since there cannot be a vacuum, when there is no lung, fluid is drawn into the chest to replace the air and when all the air is absorbed no more fluid is formed. We follow the patient post operatively to make sure that the air space in the thorax gradually diminishes and is replaced with fluid. Any increase in the air space is indicative of a bronchopleural fistula. After the hemithorax is completely opacified, shift of the heart and mediastinum indicates excessive fluid production, almost always due to bleeding in the chest. Rarely this can be caused by a virulent infection.

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Evaluating Competence in the Interpretation of Chest Radiographs

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Preface

The primary objective of this presentation is to describe a method for assessing competency of chest radiologists. A second objective will be to delineate weaknesses in the method, and to make recommendations for future improvements.

Introduction

Political and regulatory pressures in this era of managed care are compelling health care delivery systems to put in place mechanisms for ensuring the competence of physicians. The quality of care delivered by radiologists can be monitored effectively in some aspects such as interventional radiology where complication and technical success rates are easily quantified (1). However, assessing competence in diagnostic radiology is a more complex and difficult task (2). A competent radiologist must master the ability to visualize and recognize visual patterns. In addition, radiologists must combine the visual findings with a vast knowledge base in order to make clinical decisions and derive diagnoses. Radiologists must also continually update their base of knowledge, especially in light of rapidly changing technology. Given this complexity of practice, what is the best way to evaluate competence of diagnostic radiologists?

Published methods of evaluating performance are limited to question and answer tests of knowledge, tests of observation ability, or reviews of a restricted batch of cases from clinical practice (3-7). There are questions about the validity of these methods. Does the ability of a radiologist to interpret images or answer questions in a test situation such as written and oral American Board of Radiology examinations reflect competency in clinical practice (8)? Does a review of a limited batch of cases accurately reflect the overall performance of a diagnostic radiologist, and is the process cost-effective?

This presentation describes the continuous five-year experience of evaluating faculty members in an academic radiology department, measuring their relative capability to interpret chest radiographs in practice by detecting missed diagnoses and determining individual error rates. The effort to detect missed diagnoses represents randomized sampling, not an ex-

act representation of the actual total number of errors made. The results of our experience are presented along with potential bias errors.

Methods

In April of 1991, members of the faculty in the chest section of a large academic center began to collect cases where there was a disagreement in the interpretation of a bedside or standard chest radiographic examination. Disagreements were usually discovered when new examinations were compared to prior studies and reports. A few cases were referred from the institutional risk-management department, and others were communicated to chest faculty members by referring physicians. Faculty members were encouraged to communicate these disagreements to the author who maintained a database. The database was protected for security reasons with a secret code identifier for each radiologist and patient. The database included the coded identity of the source of the disagreement in diagnosis to evaluate for potential case selection bias.

Cases of disagreement were reviewed every three months by the chest faculty. Raw data containing names and record numbers of patients were discarded after peer review. Each case was reviewed to evaluate whether a missed diagnosis had been made, either false positive or negative. All cases were reviewed in a blinded fashion as only the presenter had knowledge of the radiologists involved in the disagreement. In addition, a severity score was assigned by group consensus when it was determined that an error had been made. The scoring system classifies missed diagnoses on a scale from class I-IV, from least to most obvious (9). Class I is a diagnosis that would not be expected to be made, even in retrospect. One example from our experience was a case of a posteroanterior view of the chest that showed a calcification over the right lung base that was called a granuloma. A subsequent examination including a lateral view showed that the calcification was in the breast. The diagnosis was not made initially because of the limitations inherent in the study, not because of individual error. A class II miss is one where the diagnosis was difficult, not ordinarily expected to be made. Class III cases are those where





the diagnosis should usually be identified and class IV when the diagnosis should have been made consistently. Only classes III and IV were considered significant misdiagnoses and the clinical outcomes were not considered for this study. When consensus could not be reached and there was irreconcilable split in voting between two scores, the lower score was assigned. On occasion, cases were excluded when the group determined that a case was not a “miss” despite the disagreement in interpretation.

Data for six chest faculty members were recorded. Four were “majors” in chest radiology, spending approximately 80% or more of their clinical time in chest, and two were “minors” with regular but less frequent assignments. Other faculty members interpreting chest radiographs as part of a night or weekend assignment, but without regular chest assignments, were grouped together as “other” in the database. Fellows in chest radiology were considered in the “other” category. When the same misdiagnosis was made on the same patient by two different radiologists on different examinations, each was graded separately. When more than two faculty members made the same error on a patient, the cases were excluded from this study as the database defined this category as “multiple” and no record was kept for individuals.

Billing data were used to determine the total number of chest examinations read by each radiologist, and for the sum of cases read by the non-chest faculty designated as “other”. Although case reviews were begun in 1991, this report only covers the period from January 1, 1994 to December 31, 1998. Cases before 1994 were not considered, as there was no mechanism to determine the total number of cases reported by each radiologist before that time.

Results

There was no statistical difference in the rate of misdiagnosis for faculty members with a major or regular minor assignment in the Division of Chest Radiology. However, there was a statistically significant higher rate of class III and class IV misses for faculty without usual assignments in chest radiology. No significant bias in reporting of disagreements was found. Following are the types of false positive and negative diagnoses in order of prevalence: pulmonary nodules, hilar and mediastinal masses, musculoskeletal abnormalities, pneumothorax, cardiovascular abnormalities and miscellaneous other findings.

Discussion

Because our system consists of a sampling of the total number of errors made, cases of misdiagnosis must be discovered and reported at random if the re-

sults are to accurately represent relative individual error rates. The group consensus process of grading must be consistent and reproducible. Many potential biases exist that could distort the findings.

Bias

Disease Prevalence and Patient Demographics

If the case-mix differs with variations in disease prevalence for each radiologist, then the number of missed diagnoses could be skewed. For example, if one radiologist reads a larger proportion of outpatient chest radiographs from a walk-in clinic with a low incidence of disease, the number of false positives might be expected to be lower when compared to another radiologist who reads a larger proportion of patients with cancer. Other related covariates include the age and sex distribution of the patient population interpreted by individual radiologists. An additional factor relates to the relative availability of accurate histories, although there is some argument about the influence of histories on accuracy of interpretation.

Data Collection/Case Selection

It is important that cases be noted at random in order to have findings most representative of clinical practice. In our series, more cases of disagreement were discovered and noted by faculty with appointments in chest radiology compared to other sources. The number of cases noted also differed between chest faculty members. The uneven distribution of case identification raises the possibility of selection bias.

Influence of Clinical Factors

When reaching consensus on scoring, the group should know the history available to the reader at the time of interpretation and whether comparisons were available. For example, the relative scoring of a missed pneumothorax could be influenced if a history of attempted line placement was, or was not, provided on the requisition.

Inter-observer Variation

There may be inherent differences in the relative scoring of missed diagnoses between individuals at the peer-review sessions. All faculty members were likely influenced to some degree when realizing that they might or might not be the radiologist involved in the case. There also appeared to be an inherent difference in overall scoring with some participants being “easy” and others “tough” when assigning the class of misdiagnosis. This difference in approach may relate to differences in the point of the ROC curve that each radiologist operates.

Truth in Diagnosis

The truth as to whether a case is truly a “miss” or not is best determined by subsequent objective measures. Our study dealt exclusively with chest radiography. Most cases were substantiated by subsequent



secondary imaging tests such as CT, or surgery. However, some cases were scored on the basis of group consensus alone such as small pneumothoraces that resolved spontaneously.

Attempts were made to minimize bias in our methodology. The case-mix among faculty members with regular assignments in chest radiology was similar as individuals rotated through the same reading assignments over a period of five years. We monitored case identification and found no evidence of bias between faculty members. The method of reaching consensus on classifying errors at the peer-review sessions was consistent. However, there was no way to ensure that the discovery of "missed diagnoses" was truly randomized and that the results reflected reliable relative rates of misses.

Some Conclusions

There is no method of assessing competence of radiologists in the interpretation of chest radiographs that is not subject to some form of bias. Our method attempts to minimize bias and has benefits when compared to other methodologies. Our process is continuous, involves many cases covering a broad range of abnormalities, and has an educational and quality improvement benefit. The process does not disrupt our daily practice, is not time consuming, and is cost-effective. We believe that the finding that non-chest radiologists have a significant increased rate of class III and IV missed diagnoses compared to chest radiologists is probably true. We also believe that there is no significant difference in diagnostic capability between radiologists that read large numbers of studies on similar groups of patients. However, the potential for bias in our method makes our findings questionable.

What would have happened had we discovered a significant difference in the rate of missed diagnoses for a chest radiologist? Our intent at the beginning of this project was to have a process in place to assess competence. Our Division of Chest Radiology policy stipulates that the results of our method would only act as a "flag" that there could be a problem. If

such a "flag" were to be raised, further evaluation would be undertaken including further retrospective review, direct observation and proctoring.

Given the weaknesses and potential for bias in existing methods of assessing competence, we should strive to improve on the process. Efforts are underway that will lead to the development of a standardized, computer generated reporting system for chest radiography. This would be analogous to the BiRads™ method for mammography (10). With a computer reporting tool we can develop databases that will automatically determine subsequent outcomes of patients by tracking the results of subsequent diagnostic tests and surgical results. Thus we may be able to determine our individual receiver operating curves and work to improve our diagnostic capabilities.

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Lung Disease in HIV-Positive Individuals without AIDS

Mark A. King, MD

Objectives

1. To provide the attendee with an understanding of the effects of HIV on the lung early in the course of infection;
2. To demonstrate morphological changes in the lung of HIV-infected patients prior to the onset of advanced immunosuppression;
3. To describe alterations in the inflammatory environment of the lung that may be relevant to the morphological changes seen on CT

Introduction

In 1989, Kuhlman et al [1] reported an apparent increased incidence of emphysema on CT scans of patients with AIDS. These investigators theorized that HIV may play a role in the development of this “premature bullous damage”. Later, Diaz et al [2] published a cohort of four HIV-positive individuals without AIDS in whom changes of pulmonary emphysema visible on CT scans were thought to be significantly greater than what would be expected given the patients’ trivial smoking histories. The authors of this study theorized that HIV itself may promote the development of emphysema in infected individuals.

Along these lines, several investigators studying pulmonary function in HIV-positive individuals have noted abnormalities, especially a decline in the diffusing capacity for carbon monoxide even before these patients develop AIDS [3-5]. Recently, HIV-positive individuals without AIDS-related pulmonary complications have been shown to have an increased incidence of emphysema, bronchial dilatation, and focal air trapping on CT scans. These findings suggest that HIV may cause pulmonary damage early in the course of the disease. Damage to the lung matrix may compromise the ability of the lung to respond to infection later in the disease, making the infectious pulmonary complications of AIDS more difficult to treat.

Why is the lung a target of HIV infection?

- A. Infection by HIV-1 → local exaggeration of immunosuppression; therefore, more complications of AIDS occur in the lungs than in other organs
- HIV infects pulmonary cells at the early stages of disease
 - Alveolar macrophages are unusually susceptible to infection with HIV [6, 7]

- B. HIV-1 infection induces “upregulation” of various cytokines, including tumor necrosis factor (TNF)- α , granulocyte macrophage-colony stimulating factor (GM-CSF), and matrix metalloproteinases (MMP)
- TNF- α : proinflammatory cytokine, → increased HIV replication
 - GM-CSF: stimulates influx of neutrophils and macrophages
 - MMP: role in development of emphysema
- C. Stimulation of cytotoxic lymphocytes [8]
- D. Macrophage alveolitis [9]

Morphologic Observations and Possible Mechanisms

Emphysema

Emphysema is more prevalent and more severe in HIV-positive individuals than it is in HIV-negative individuals [10]. In a recent CT study, emphysema CT scores were significantly greater in HIV-positive individuals than they were in smoking history-matched HIV-negative individuals. Cigarette smoking is an important cofactor for development of emphysema in these individuals [11], and the severity of emphysema is greater in patients with HIV infection than it is in HIV-negative individuals with similar smoking histories.

The cellular mechanisms that predispose HIV-positive individuals to develop accelerated changes of emphysema are unclear, but there are a few aspects of an HIV-related phenomenon that may be relevant to our understanding of the pathogenesis of emphysema. Recent work suggests a possible relationship between the proportion of cytotoxic lymphocytes in HIV-infected patients and emphysema [10]. There is experimental evidence that suggests that virally-induced activation of cytotoxic lymphocytes may have damaging effects on the lung parenchyma [12]. Alterations in lung lymphocyte populations may be important in the pathogenesis of smoking-related lung injury in the general population [13, 14]. A morphometric analysis of lung biopsy specimens from HIV-negative smokers demonstrated a high correlation between lymphocyte numbers and the presence of emphysema [13]. Furthermore, increased CD8 lymphocytes and decreased CD4 lymphocytes have been found in the bronchial subepithelium of smokers with clinical evidence of



COPD compared to asymptomatic smokers [14]. An increased ratio of cytotoxic lymphocytes to CD4 lymphocytes observed in HIV-positive subjects with emphysema [10] does not prove cause and effect, but it is interesting in the context of data derived from recent work on the pathophysiology of emphysema.

In conventional models of COPD pathogenesis, the neutrophil is most often implicated as the inflammatory cell responsible for the destructive changes associated with emphysema, theoretically by causing elevated local concentrations of free elastase. In patients infected with HIV, alveolar macrophages produce increased quantities of granulocyte-macrophage colony stimulating factor (GM-CSF), a strong chemoattractant for neutrophils [15]. An increase in numbers of neutrophils may increase the free elastase burden in the lung, thereby promoting elastolytic activity that may result in potentiation of the development of emphysema.

An increased production of matrix metalloproteinases in HIV-positive individuals may help to potentiate the development of emphysema. Recently, several investigators have examined the role of matrix metalloproteinases in the development of emphysema [16], ARDS [17], and bronchiectasis [18]. Production of these enzymes by monocytes is enhanced by HIV infection. In fact, Dhawan, et al [19] showed that HIV-infection stimulates monocytes to invade basement membrane matrix and secrete increased quantities of metalloproteinase-9.

Bronchial Dilatation and Focal Air Trapping

McGuinness et al [20] reported an increased incidence of bronchial dilatation in patients with AIDS. Although most of the patients in that study had a history of pyogenic pulmonary infection, the authors thought the bronchiectasis was more severe than would be expected in healthy hosts. They theorized that HIV may potentiate the development of bronchiectasis in these individuals.

Interestingly, abnormal airway function has been reported in HIV-positive individuals without AIDS [3, 21, 22]. Similarly, Wallace et al [23] found that HIV-positive individuals without AIDS had a significantly higher incidence of acute bronchitis than did HIV-negative control subjects. Bronchial dilatation [24] and focal air trapping [25] have been found on CT scans of patients with HIV infection and no history of pulmonary complications of AIDS. HIV-positive individuals with bronchial dilatation on CT have, in general, significantly longer duration of HIV infection, lower DLCO, and greater percentages of neutrophils in BAL fluid than do HIV-positive patients with normal bronchi on CT [24]. These results suggest that airway abnormalities begin early in HIV infection, before the onset of opportunistic infection.

There are several possible mechanisms for development of bronchial dilatation in HIV-positive individuals. Pyogenic infection has been described as a possible cause of bronchiectasis in AIDS patients) [20], but none of the HIV-positive subjects with bronchial dilatation in a recent CT study had any evidence of infection at BAL [24]. Bronchial dilatation has been described in patients with AIDS and lymphocytic interstitial pneumonia [20, 26], presumably secondary to peribronchial infiltration of lymphocytes with resultant obstruction and atelectasis [26]. Whether this mechanism could be largely responsible for bronchial dilatation in patients with HIV infection is not known. A direct effect of increased numbers of neutrophils in the airways is another potential mechanism for developing bronchial dilatation in these individuals. As was mentioned earlier, there is a biological basis for recruitment of neutrophils to the lungs of HIV-positive individuals through increased production of GM-CSF by alveolar macrophages. Increased numbers of neutrophils would theoretically increase the local free elastase burden, and it is possible that resultant proteolytic activity may damage the elastic layer of the airway walls, resulting in bronchial dilatation. This mechanism is supported by the elevated levels of neutrophils found in the BAL fluid of HIV-positive patients with bronchial dilatation. Lastly, bronchial dilatation may be occurring in these individuals as a result of loss of lung elastic recoil. Diffuse parenchymal damage, such as may occur in the setting of diffuse, low grade emphysema, may be below the limit of resolution of thin-section CT. The fact that the presence of bronchial dilatation correlated with decreased DLCO supports the possibility that bronchial dilatation may accompany a diffuse loss of diffusing surface in the lung. We are currently studying the possible relationship between lung elastic recoil and morphologic changes in the airways.

An increased incidence of focal air trapping on expiratory CT has been observed in HIV-positive individuals, supporting the findings of physiologic studies that have reported abnormal airway function during the course of HIV infection. HIV-positive patients with focal air trapping on CT have significantly lower FEV1, FEF25-75, and DLCO than do individuals without CT evidence of air trapping [25]. The severity of focal air trapping on CT in these patients is related to duration of HIV infection, and inversely related to CD4 count, suggesting that airway damage is progressive in these individuals.

Summary

A number of reports have suggested that HIV-positive individuals may develop an accelerated form of lung injury prior to the development of AIDS-related



pulmonary complications, evidenced by reports of morphologic abnormalities (AIDS-associated emphysema and bronchiectasis), functional abnormalities (e.g. decreasing DLCO and abnormal airway function) and symptoms of pulmonary disease (dyspnea and bronchitis). The possibility that HIV-positive individuals have a heightened susceptibility to develop accelerated parenchymal changes may have important implications for the study of the pathogenesis of emphysema. Since HIV infection is associated with changes in the immune and inflammatory environment of the lung, it is possible that these changes may be relevant to the pathogenesis of infections and neoplasms as immunosuppression becomes more advanced.

Lung abnormalities (morphologic and functional) clearly occur in the early stages of HIV infection, prior to the onset of pulmonary complications of AIDS. Emphysema, bronchiectasis and focal air trapping are evidence of abnormal lung structure and function. These frequently pre-existing abnormalities may predispose HIV-positive individuals to more severe pulmonary manifestations of AIDS after the onset of advanced immunosuppression.

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Airway Disease in the AIDS Patient

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Course Objectives

1. Recognize the range of diseases in the AIDS patient, both infectious and noninfectious, which affect the airways.
2. Demonstrate the radiographic and CT findings in each entity.
3. Integrate clinical features, which allow refinements of differential possibilities.
4. Determine the role of CT in guiding biopsy techniques.

AIDS related neoplasms and infections commonly affect the lung parenchyma. Specific involvement of the airways within this spectrum of diseases is less well recognized, and imaging findings therefore are less familiar. The manifestations of airway disease in AIDS, correlated with imaging findings when possible, will be reviewed.

Central Airway Disease (Vocal Cords through Lobar Bronchi)

Infection

Tracheobronchitis can be due to bacterial, viral, or fungal infections. Bacterial infections are most commonly due to *H. influenzae* or *S. pneumoniae*.

Pyogenic infections in the large airways is primarily mucosal, and will not be appreciated at CT. Bronchoscopy will reveal inflamed, friable mucosa, with variable purulence. Diagnosis is through sputum smear and culture.

Bacillary angiomatosis is an unusual vascular proliferative disorder which produces mass lesions in the skin, lymph nodes, bones and viscera of AIDS patients. It is caused by infection by a rickettsial bacillus, *Rochalimaea henselae*. Polyploid, exophytic endotracheal and endobronchial lesions have been reported. The gross appearance of the mucocutaneous lesions is very similar to KS, which is primary differential consideration. At bronchoscopy the lesions may also appear as pale, white, and friable. Good therapeutic response is achieved with antibiotics. Diffuse interstitial lung disease has been described. Endoluminal filling defects may be seen at CT.

Viral infection of the upper airways may be due to herpes or cytomegalovirus (CMV). Herpes tracheobronchitis produces discrete, shallow, punctate ulcerations similar in appearance to herpes ulcerations of the mucosa of the GI tract. These shallow ulcerations are not usually visible at CT. Necrotizing tracheitis

due to CMV is typically a diffuse inflammatory process, with thickening of central airway walls noted at CT. A rare case of tracheal obstruction secondary to an exophytic inflammatory ulcerated mass due to CMV has been reported.

Fungal infections may be due to *Candida* or *Aspergillus* infection. Tracheobronchial Candidiasis is characterized by inflammation of the mucosa of the airways with exudative inflammatory accumulations noted at bronchoscopy. It is reasonable to speculate that irregularity of the mucosa may be seen a CT, although CT findings in this entity have not been described.

Invasive aspergillus is a late manifestation of AIDS, and often occurs in the presence of other risk factors, including corticosteroid therapy, granulocytopenia, or intravenous drug abuse. Classically, tissue invasion by aspergillus usually targets the blood vessels, but may also invade the trachea and bronchi. Unusual forms of aspergillosis in AIDS involve the large airways, including obstructing bronchial aspergillosis, and pseudomembranous necrotizing bronchial aspergillosis. Obstructing bronchial aspergillosis usually presents radiographically as bilateral, diffuse, lower lobe infiltrates, presumably due to post-obstructive local atelectasis, at chest radiography. CT appearances have not been described. Patients generally have progressive cough, and fungal casts of the airways may be expectorated. In contrast with allergic bronchopulmonary aspergillosis, no inflammation of the bronchi is seen pathologically. Pseudomembranous bronchial aspergillosis is characterized by exudative membranes covering the bronchial mucosa. Local invasion of the peribronchial tissue may be seen without invasion of the pulmonary parenchyma.

Neoplasm

Both Kaposi's sarcoma (KS) and AIDS Related Lymphoma (ARL) can involve the upper airways, although it is common in KS, and uncommon in ARL.

Pulmonary involvement with KS occurs in approximately 20% of patients with epidemic KS, preceded by documented cutaneous or visceral involvement in almost all cases. KS may involve the vocal cords, in which case hoarseness is often the presenting symptom. Bulky tumors from KS in the upper airways may result in stridor, or if in smaller lobar or segmental bronchi may result in airway



obstruction causing atelectasis. Such masses are visible as soft tissue filling defects impinging into the lumen of the airways at CT. Radiographic findings in patients with pulmonary parenchymal KS have been well described, and in such a setting even subtle irregularities of the airway walls should be viewed as suspicious for endoluminal involvement. It must be emphasized, however, that CT is not sensitive in the detection of endobronchial or endotracheal KS. At bronchoscopy the characteristic raised erythematous plaques, and appearance that should be considered pathognomonic of KS, will be noted in many areas prospectively interpreted as normal CT.

Thoracic involvement in ARL is usually extranodal. Involvement of the thorax is less common than CNS, abdominal, and osseous involvement. A typical presentation is that of single or multiple pulmonary masses. These are characteristically discrete, well defined, and without associated adenopathy. Endoluminal airway disease is rare.

FOB Correlation

Despite non-invasive means of establishing some diagnoses, such as PCP, most AIDS patients suspected of having pulmonary disease should be evaluated bronchoscopically. CT is of value prior to FOB, not only to identify optimal sites of parenchymal disease for transbronchial biopsy or lavage, but also to evaluate the airways and map the extent and precise location of intrathoracic lymph nodes. Transbronchial needle aspiration (TBNA) has proved an effective means of establishing many diagnoses in AIDS patients, in particular mycobacterial infection. In an ongoing series of TBNA in AIDS patients with adenopathy in our institution the diagnostic yield is 53%. Twenty-one of the 23 cases of mycobacterial infection were diagnosed by TBNA, in 57% of these cases it was the only diagnostic specimen obtained.

Fiberoptic bronchoscopy is important in the evaluation of the patient with KS because it allows direct visualization of the characteristic violaceous airway lesion. Despite early reports of severe hemorrhage at biopsy of this vascular lesion, the diagnosis can be made safely with endobronchial biopsy. Most bronchoscopists, however, consider recognition of the characteristic lesion sufficient for diagnosis. An overlap in appearance with the much more unusual lesion of BA has recently been noted.

FOB and bronchoalveolar lavage is sensitive in the detection of *Aspergillus*, but biopsy is needed to prove tissue invasion. A wide range of diagnostic yield at transbronchial biopsy is reported in proven invasive aspergillosis, although all series are very small.

Small Airway Disease

Bronchiolitis

Most inflammation of the small airways in AIDS is probably due to pyogenic infections. AIDS patients are predisposed to bacterial infections and this vulnerability also likely increases the probability of bacterial bronchitis and bronchiolitis. The CT findings in bronchiolitis have recently been well described. Small (approximately 3 mm) centrilobular somewhat ill defined densities, which may have a Y or V configuration represent bronchioles impacted with inflammatory material at HRCT. There may be peribronchiolar inflammation. These findings may be seen in association with dilatation of the small airways.

Bronchiolitis may also be due to viral infections. Necrotizing cytomegalovirus bronchiolitis in the absence of airspace disease has been described. Airway changes are common in the setting of CMV pneumonitis. CMV bronchiolitis may be seen in conjunction with bronchiectasis.

Bronchial and peribronchial inflammatory changes due to mycobacterial infection was initially described as the HRCT appearance of a "tree in bud" in reference to tuberculous bronchiolitis in non-AIDS patients. Endobronchial or endobronchiolar mycobacterial infection in AIDS, either due to *M. tuberculosis* (MTB) or *M. avium* complex (MAC) may have an identical appearance. Bronchiectasis is often present.

Pneumocystis carinii pneumonia (PCP) is the most common pulmonary infection in AIDS. Airway disease associated with PCP is rarely reported. HRCT evaluation of 11 patients with PCP revealed bronchial wall thickening in nine cases, and bronchial dilatation developing in three cases during the healing phase.

An unusual variant of invasive aspergillosis involving small airways has been described. Chronic cavitary parenchymal disease is associated with aspergillosis of small bronchi and bronchioles. Necrotic debris and aspergillus organisms fill respiratory bronchioles and extend into alveolar airspaces. Chronicity of this process is indicated by the presence of dystrophic calcifications.

AIDS Bronchiectasis

Two recent studies report an accelerated, aggressive form of bronchiectasis in AIDS. In most cases this occurs in patients who have had lung infections, either pyogenic or opportunistic. Both series report patients with bronchiectasis and no history of pneumonia, however. It is speculated that vulnerability of the lungs to infection may reflect direct effects of HIV infection on the pulmonary immune system. T-cell dysfunction, impaired humeral immunity, and impaired function of pulmonary monocytes and macrophages from HIV infection may all predispose

to an accelerated form of bronchiectasis. High resolution CT confirms bronchiectasis in the absence of airspace consolidation.

Both MTB and MAC in AIDS may be associated with bronchiectasis.

Bronchiolitis Obliterans and Bronchiolitis Obliterans Organizing Pneumonia

Histopathologic evidence of bronchiolitis obliterans has been described in up to 36% of patients with biopsy proven PCP.

Histopathologically classic bronchiolitis obliterans organizing pneumonia in the absence of infection is a rare cause of respiratory failure in AIDS patients. It is an important diagnosis to establish, however, because as in non-AIDS patients it is responsive to steroid therapy. CT findings are identical to those in non-AIDS patients.

Respiratory Physiology

We have noted a mosaic pattern of perfusion in the parenchyma of some AIDS patients at HRCT without definite evidence, clinically or radiographically, of active parenchymal infection. Focal areas of relative hyperlucency can be demonstrated with inspiratory and expiratory scans as due to geographic zones of air-trapping and resultant focal vasoconstriction. This may indicate small airway disease such as bronchiolitis obliterans or inflammatory bronchitis. This proved true at histopathologic examination in one case. Most of these cases, however, lack pathologic proof. This observation will require further prospective evaluation.

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The Changing Face of PCP in AIDS Patients

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Learning Objectives:

1. To review the classic radiographic and CT findings of PCP in AIDS patients.
2. To describe the changing trends in the typical imaging features of this infection.
3. To familiarize the attendee with the various atypical imaging manifestations of PCP.

Introduction

Despite a declining incidence secondary to improved prophylaxis, *Pneumocystis carinii* pneumonia (PCP) remains the most common cause of life-threatening pulmonary infection in HIV-positive patients. Although the classic radiographic presentation of PCP is well-recognized, the more unusual manifestations of this infection are less familiar. Because advances in the treatment and prevention of PCP have been associated with an increased frequency of unusual manifestations, it has become increasingly important for radiologists to be aware of the entire spectrum of radiologic manifestations of this infection. The purpose of this lecture is to illustrate and review the varied radiologic presentations of PCP and to provide an updated classification of the typical and atypical imaging features associated with this infection.

Pneumocystis carinii

Pneumocystis carinii is a unicellular organism with a controversial taxonomy. Although it exhibits protozoan-like behavior, the *Pneumocystis* organism is classified as a fungus. *Pneumocystis carinii* consist of small cysts, each of which produce up to eight, intracystic sporozoites. Upon maturity, the cysts rupture and release the sporozoites. The sporozoites differentiate into trophozoites, which subsequently develop into cysts and repeat the cycle.

Because *P. carinii* cannot be grown in culture, a diagnosis of PCP requires morphologic identification of the organism. The cyst capsule of *P. carinii* is the easiest structure to identify, and its visualization is enhanced by special stains, including methenamine silver and toluidine blue. The standard method of diagnosis is the cytologic analysis of specimens obtained from induced sputum or bronchoalveolar lavage. In a minority of cases, however, transbronchial biopsy or open lung biopsy may be necessary for diagnosis.

In recent years, an alternative, cost-effective approach has been gaining increased acceptance. This approach calls for empiric therapy of patients who present with typical clinical and radiographic features of PCP. Using this approach, costly diagnostic procedures are reserved for patients with atypical presentations and for those who fail to respond to empiric therapy.

Typical Features

Classic Radiographic Features

The classic chest radiographic presentation of PCP is a bilateral perihilar or diffuse symmetric interstitial pattern, which may be finely granular, reticular, or ground-glass in appearance. If left untreated, the parenchymal opacities may progress to airspace consolidation.

Importantly, the chest radiograph may be normal at the time of presentation in as many as 39 % of cases. Moreover, the widespread use of PCP prophylaxis has been associated with a trend toward more subtle radiographic presentations. CT, particularly high-resolution CT, is more sensitive than chest radiographs for detecting PCP, and thus may be helpful in evaluating symptomatic patients with normal or equivocal radiographic findings.

Classic CT Features

The classic high-resolution CT finding in PCP is extensive ground-glass attenuation, which corresponds to the presence of intra-alveolar exudate, consisting of fluid, organisms and debris. It is often distributed in a patchy or geographic fashion, with a predilection for the central, perihilar regions of the lungs. Ground-glass attenuation is occasionally accompanied by thickened septal lines, and foci of consolidation may also be evident in severe cases.

New Trends in Typical Features

The face of PCP is changing. The classic radiographic pattern is being encountered less frequently, and several features of PCP that were once considered unusual should now be considered as typical manifestations of this infection. These features include cystic lung disease, spontaneous pneumothorax, and an upper lobe distribution of parenchymal opacities. In the past, these findings were described predominately in patients



receiving aerosolized pentamidine prophylaxis. In recent years, however, these manifestations have been increasingly recognized outside of this setting, as aerosolized pentamidine has been largely replaced by more effective prophylactic agents, including trimethoprim-sulfamethoxazole and dapsone.

Cystic Lung Disease

The most prevalent trend has been an increased frequency of cystic lung disease, which is now recognized as a relatively common manifestation of this infection. On chest radiographs and CT scans of patients with PCP, the prevalence of cysts ranges from approximately 10% to 34%.

Cysts may vary in appearance, with differing shapes and sizes, and varying degrees of wall thickness. Cysts are usually multiple and bilateral, and they may be found in either a subpleural or an intraparenchymal location. Although an upper lobe predominance has been reported, cysts may involve any portion of the lungs. The identification of cystic lesions in an HIV-positive patient is highly suggestive of PCP, particularly when such cysts are accompanied by the presence of adjacent ground glass attenuation.

Spontaneous Pneumothorax

Cystic PCP is associated with an increased incidence of spontaneous pneumothorax, which is thought to occur secondary to rupture of subpleural cysts. In a series of 100 patients with PCP, Chow et al. reported that 35% of patients with cystic PCP developed a pneumothorax versus 7% of patients with noncystic PCP, a statistically significant difference.

The identification of a spontaneous pneumothorax in an HIV-positive patient is virtually diagnostic of PCP. Conversely, the presence of subpleural cysts in a patient with PCP should alert one to the possible development of a pneumothorax.

Upper Lobe Distribution

Although an upper lobe distribution of parenchymal opacities has been a well-recognized manifestation of PCP in patients receiving aerosolized pentamidine prophylaxis, it is now increasingly recognized in patients who have not used this prophylactic agent. In a recent study by Gruden et al., which assessed the role of high-resolution CT in patients with suspected PCP who had normal, equivocal or nonspecific radiographic findings, all patients with proven PCP demonstrated an upper lobe predominance of parenchymal opacities on high-resolution CT scans.

In a recent study that assessed the various etiologies of localized consolidation on chest radiographs of HIV-positive patients, Amin et al. reported that PCP accounted for nearly half the cases of upper lobe consolidation in their series. Interestingly, only a minority of these patients (30%) had received inhaled pentamidine prophylaxis. The results of these studies

emphasize the importance of considering PCP in the differential diagnosis of upper lobe parenchymal opacities, regardless of whether or not the patient has been receiving pentamidine prophylaxis.

Atypical Features

In recent years, the spectrum of radiographic findings associated with PCP has broadened, and it now includes abnormalities involving the lung parenchyma, airways, lymph nodes, and pleura. Because the radiologist is often the first to suggest the diagnosis of PCP, an awareness by radiologists of the entire spectrum of imaging findings associated with this infection is important.

Atypical manifestations include: parenchymal abnormalities, including lung nodules and masses, lobar consolidation, and interstitial fibrosis; airway abnormalities, including bronchiectasis, bronchiolitis, bronchiolitis obliterans, and, rarely, an endobronchial lesion; mediastinal and hilar lymphadenopathy; and pleural effusions.

Parenchymal Abnormalities

Lung Nodules and Masses

There are a variety of nodular patterns that may be associated with PCP. Nodules may vary in size from 2-3 mm diameter "miliary" nodules to larger nodules measuring greater than 1 cm in diameter. Although multiple nodules are usually present, PCP can rarely present as a solitary pulmonary nodule or as a focal mass.

Histologically, nodules and masses have been shown to represent granulomas. Granulomatous inflammation is now a well-recognized manifestation of PCP, occurring in approximately 5% of cases. Nodules and masses are usually encountered relatively early in HIV-infection, when patients are still capable of mounting a granulomatous response.

In an HIV-positive patient, lung nodules are much more commonly associated with other infectious entities, especially mycobacterial and fungal infections, as well as neoplastic conditions, including Kaposi's sarcoma and lymphoma. With regard to parenchymal masses, bronchogenic carcinoma and lymphoma are the most common etiologies in the HIV-positive patient. Thus, a diagnosis of PCP in a patient with a nodular pattern or a focal mass is usually made by biopsy.

Lobar Consolidation

Although lobar consolidation is most commonly associated with bacterial pneumonias, it is important to be aware that PCP may also present with this radiographic pattern. In a study that assessed the radiographic findings in PCP and bacterial pneumonia in HIV-positive patients, Boiselle et al. reported the presence of focal consolidation in 11% of cases of



PCP versus 61% of cases of bacterial pneumonia. When PCP presents as lobar or segmental consolidation, it frequently has an upper lobe distribution.

Interstitial Fibrosis

Interestingly, a subset of patients with atypical imaging features will also present with an atypical clinical presentation. Unlike the typical clinical presentation of PCP, in which symptoms develop over a period of weeks, these patients have a prolonged clinical course, with relatively stable symptoms and radiographic findings over a period of months to years. This subset has been referred to as chronic PCP. Affected patients demonstrate a chronic fibrosing response to the organism that is characterized pathologically by the presence of extensive interstitial fibrosis, which may be associated with both giant cell and granulomatous reactions.

The primary radiologic features of chronic PCP are thickened septal lines, reticular opacities, traction bronchiectasis and honeycombing. These findings may be accompanied by cystic lesions. Although interstitial fibrosis is the primary feature of chronic PCP, residual fibrotic changes and cystic lesions can also be seen following treatment of an acute PCP episode.

Airway Abnormalities

Bronchiolitis

An infectious bronchiolitis is an unusual manifestation of PCP. In HIV-positive patients, bronchiolitis is much more commonly associated with bacterial and mycobacterial infections than PCP. CT findings of bronchiolitis include small, poorly defined centrilobular opacities, which often have a branching, Y- or V-shaped configuration. These opacities represent bronchioles that are impacted with inflammatory material.

Bronchiolitis Obliterans

Interestingly, bronchiolitis obliterans has been reported in 36% of lung biopsy specimens of patients with AIDS and PCP. However, it is infrequently reported on imaging studies. The reason for this discrepancy is uncertain, but it is likely related to the fact that chest radiographs are often normal in patients with bronchiolitis obliterans. The CT findings of bronchiolitis obliterans include a mosaic pattern of lung attenuation, which is accentuated on expiratory images, and bronchiectasis. The mosaic pattern of lung attenuation related to air-trapping may go unrecognized unless expiratory images are performed.

Endobronchial Lesion

There has been one case report of PCP presenting as an obstructing endobronchial lesion. Thus, this should be considered as a truly rare manifestation of *Pneumocystis* infection.

Mediastinal and Hilar Lymph Node Enlargement

CT scans reveal enlarged lymph nodes in approxi-

mately 18% of cases of PCP. Involved lymph nodes are usually only mildly enlarged. Thus, chest radiographs infrequently demonstrate lymph node enlargement in patients with PCP. Pathologic studies of involved lymph nodes reveal nodal necrosis, calcification, loss of normal nodal architecture and replacement by *Pneumocystis* organisms.

Both calcified and noncalcified lymph node enlargement has been described in association with PCP. The presence of punctate calcifications within enlarged mediastinal lymph nodes is characteristic of disseminated *Pneumocystis* infection. Additional findings may include calcified abdominal lymph nodes, and focal calcifications within the liver, spleen, and kidneys. A disseminated mycobacterial infection may have a similar imaging appearance.

Pleural Effusions

Although spontaneous pneumothorax is a well-recognized complication of PCP, involvement of the pleural space is a relatively uncommon complication of this infection. Pleural effusions associated with PCP may represent a sequelae of persistent subpleural pulmonary infection that has been complicated by invasion and subsequent extension into the pleural space.

In HIV-positive patients, pleural effusions are more commonly associated with other infectious processes, especially mycobacterial and bacterial infections, and neoplastic entities, including lymphoma and Kaposi's sarcoma. Because pleural effusions are infrequently associated with PCP, diagnostic thoracentesis is generally recommended in order to exclude a secondary process.

A characteristic imaging appearance has been described with pleural involvement from disseminated PCP. In this setting, a pleural effusion may be accompanied by punctate calcifications along the pleural surface.

Summary

The classic presentation of PCP is a bilateral interstitial pattern, which may be characterized as finely granular, reticular, or ground-glass opacities. When chest radiographic findings are normal or equivocal, high-resolution CT may be helpful, because it is more sensitive than chest radiographs for detecting PCP. The typical CT finding is extensive ground-glass attenuation.

The face of PCP is changing. The classic radiographic presentation is being encountered less frequently. Increasingly recognized characteristic patterns of PCP include cystic lung disease, spontaneous pneumothorax, and an upper lobe distribution of parenchymal opacities. The spectrum of abnormalities associated with PCP is broadening, and now includes abnormalities of the lung parenchyma, airways, lymph nodes, and pleura. An awareness of



the varied presentations of PCP is important, as the radiologist is often the first to suggest the diagnosis of PCP.

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Pulmonary Neoplasms in AIDS

Keith J. Edinburgh, MD, MSED

I. OVERVIEW

A. Major Thoracic Complications of AIDS

1. Infections
 - a. Pneumocystis Carinii Pneumonia (PCP)
 - b. bacterial infections
 - c. Tuberculosis (TB)
 - d. fungal infections
2. Neoplasms
 - a. Kaposi sarcoma (KS)
 - b. Lymphoma

B. Pulmonary Neoplasms in AIDS

1. Kaposi sarcoma
2. Lymphoma
3. Lung Cancer

II. KAPOSI SARCOMA

A. Clinical features

1. most common AIDS-related malignancy
2. accounts for appx 85% of AIDS-related pulmonary neoplasms
3. incidence proportional to risk factors
 - a. increased incidence in homosexuals
 - b. decreased incidence in IVDU
4. CD4 count typically < 100
5. pulmonary involvement in 20-50% of patients with cutaneous KS
6. pulmonary involvement without cutaneous involvement in 15%
7. 65% of patients with pulmonary KS have a second pulmonary diagnosis

B. Imaging features

1. distribution of pulmonary KS
 - a. central predominance: 90%
 - b. mid/lower zone predominance: 95%
 - c. upper zone sparing: 90%
2. CXR findings
 - a. Kerley B-lines: 60%
 - b. peribronchovascular thickening: 55%
 - c. perihilar coalescence: 50%
 - d. pleural effusions: 45%
 - e. nodules: 35%
 - f. lymphadenopathy: 30%
3. CT/HRCT findings
 - a. thickening of the central peribronchovascular interstitium
 - b. nodules
 1. ill-defined
 2. > 1 cm in diameter
 3. peribronchovascular distribution
 - c. interlobular septal thickening
 - d. pleural effusions
 - e. lymphadenopathy

III. LYMPHOMA

A. Clinical features

1. second most common AIDS-related malignancy
2. accounts for appx 15% of AIDS-related pulmonary neoplasms
3. high grade/stage at presentation (80% stage IV)
4. CD4 count typically < 50
5. pulmonary involvement variably reported (5-65%)
6. extranodal involvement in 85%
7. 60% of patients with pulmonary involvement have a second pulmonary diagnosis

B. Imaging features

1. nodules (60%)
 - a. well-defined
 - b. > 1 cm in diameter
 - c. non-specific distribution
2. pleural effusions: 55%
3. consolidation: 35%
4. lymphadenopathy: 30%

IV. LUNG CANCER

A. Two Key Questions

1. Are HIV-infected individuals at increased risk for the development of lung cancer compared to non-HIV-infected individuals?
2. Does the natural history of lung cancer in HIV-infected individuals differ from that in non-HIV-infected individuals?

B. Risk

1. Data
 - a. 5 large cohort studies
 - b. Johnson et al Am J Epidem 1997 n=1073
Gabutti et al Eur J Epidem 1995 n=317
Parker et al Chest 1998 n=26181
Significantly increased risk of lung cancer in HIV patients
 - c. Rabkin et al J Nat Cancer Inst 1994
Slightly increased risk of lung cancer in HIV patients
 - d. Reynolds et al Am J Epidem 1993
n=1756
No increased risk of lung cancer in HIV patients
2. Conclusion: in light of these studies, although it remains controversial, there is most likely an increased risk of lung cancer among HIV-infected individuals relative to non-HIV-infected individuals

C. Natural History

1. Data
 - a. many case-control studies (most with <20 patients)
 - b. Karp et al Chest 1993 n=7
Vaccher et al Annals of Onc 1996 n=19
Flores et al Am J Clin Onc 1995 n=19
Vyzula et al Lung Ca 1996 n=16
2. Conclusions
 - a. the natural history of lung cancer in the HIV population differs significantly from the non-HIV-infected population
 - b. compared to non-HIV-infected patients, HIV-infected patients with lung cancer:
 1. present at a younger age at diagnosis
 2. present with more advanced disease (higher stage)
 3. have a poorer mean survival
 4. have a higher likelihood of adenocarcinoma

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Emerging Infections in AIDS

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Goals and Objectives

1. To describe an overview of immune reconstitution due to potent antiretroviral therapy (ART).
2. To describe immune reconstitution lymphadenitis in AIDS patients on ART with mycobacterial and fungal infections.
3. To discuss the possibility that sarcoidosis may be a manifestation of an immune restoration disease.
4. To discuss the clinical and radiologic findings of a group of zoonoses including: bacillary angiomatosis, rhodococcus, pasteurella and bordetella pneumonia.

The natural history of HIV infection in the absence of treatment is characterized by progressive decline in CD4 count and immune competence. However, with potent antiretroviral therapy (ART), partial immune reconstitution occurs with a rise in CD4 cell count and a decrease in viral load and opportunistic infections. With increased longevity and partial immune reconstitution, we are currently recognizing new manifestations of previously described pulmonary infections. The association of some unusual pathogens with HIV infection is also increasingly recognized as HIV testing is performed more frequently in patients with unusual infections who may not have the traditional risk factors for HIV infection.

In this session I will discuss several diseases of immune restoration and then discuss a few specific uncommon zoonoses.

Diseases of Immune Restoration

Potent antiretroviral therapy has revolutionized the clinical course of HIV-infection. It is usually comprised of a three drug regimen with a combination of HIV protease inhibitors and nucleoside analog reverse transcriptase inhibitors. ART has been shown to prolong life in HIV-infected patients and is currently recommended in most HIV infected patients. It suppresses viral replication causing a marked decrease in the measured viral load and a consequent rise in the CD4 cell count, reflecting partial immune reconstitution. Various opportunistic infections and neoplasm have been shown to improve and occur with decreased prevalence in patients on ART. However, new manifestations of previously described diseases have recently been diag-

nosed in patients on ART and constitute a spectrum of immune restoration disease.

Tuberculosis

In HIV infection, presentations of tuberculosis other than upper lobe cavitory disease are common, including disseminated disease, cervical lymphadenitis and radiographically atypical pulmonary disease. The phenomenon of paradoxical response was originally described soon after the introduction of antituberculous chemotherapy and consists of a transient worsening of tuberculous symptoms and lesions in response to antituberculous therapy. The phenomenon of paradoxical response has reemerged as an important clinical entity in HIV infected patients with tuberculosis on antituberculosis medications in whom potent antiretroviral therapy (ART) is initiated. Such paradoxical reactions consist of fever and a marked worsening or the emergence of intrathoracic lymphadenopathy, pulmonary infiltrates or pleural effusions; or the worsening or new development of cervical lymphadenopathy; or the worsening or new development of other tuberculous lesions. Such paradoxical reactions appear to be immunologically mediated by a heightened immune response consequent to potent antiretroviral therapy. Cultures for *Mycobacterium tuberculosis* are invariably negative during this exuberant febrile inflammatory response. This phenomenon is self limited and may warrant corticosteroids for symptomatic treatment.

Mycobacterium Avium Complex (MAC)

Before the availability of potent antiretroviral therapy, MAC typically caused disease associated with infiltration of lymphoid organs but notably without inflammation. Typical disseminated MAC consisted of liver, spleen, and bone marrow infiltration associated with anemia and bacteremia occurring at a CD4 < 50/mm³. Now, focal inflammatory MAC lymphadenitis occurs without bacteremia soon after the initiation of potent ART in patients who had very low CD4 count before starting potent ART. Patients present with fever and marked cervical, intraabdominal or intrathoracic lymphadenopathy. Biopsy and culture reveal MAC. It is believed that such patients probably harbored subclinical MAC infection made



manifest by partial immune reconstitution consequent to ART. New lymphadenopathy, soon after starting ART in a patient with a very low CD4 count, should prompt a consideration of MAC in the right setting. Race et al propose screening for occult MAC infection in patients with advanced HIV who are initiating ART. Treatment for immune reconstitution MAC is with the usual antibiotics for MAC and may require adjunctive steroids.

Fungus

We have recently encountered several patients with late stage HIV infection and intrathoracic with fungal disease (histoplasmosis, cryptococcus). Their symptoms and radiographic findings were improving on antifungal therapy. Subsequently, they were started on ART and developed worsening intrathoracic disease including parenchymal infiltrate, nodules and lymphadenopathy concurrent with a decrease in their viral load. Biopsy in each case showed inflammation associated with the known fungal organisms and negative tissue cultures. This inflammatory reaction is likely a manifestation of immune restoration disease.

Sarcoidosis

The development of sarcoidosis is rare in AIDS patients. A number of cases have been described in the recent literature and we have recently encountered two cases of new onset sarcoidosis after initiation of potent antiretroviral therapy with rise in CD4 cell count. In each case, diagnostic material was available for pathological analysis that showed non-necrotizing granulomas with negative special stain for AFB and fungus. The radiographic findings were typical for sarcoidosis and included lung nodules often associated with lymphadenopathy. Work-up yielded no other infections or neoplasms that could be responsible for the radiographic and pathologic findings. Therefore, we believe that new onset sarcoidosis in HIV infected patients may be part of the spectrum of immune restoration disease.

Zoonoses

Zoonoses are infections that are transmitted from animals to humans. AIDS patients have been described to develop a variety of unusual zoonoses. I will briefly discuss bacillary angiomatosis, rhodococcosis, pasteurella and bordetella pneumonia.

Bacillary angiomatosis is a disease that is seen almost exclusively in AIDS patients. It is caused by two related organisms that cause different diseases in the non-AIDS population. *Bartonella henselae* and *Bartonella quintana* cause cat scratch fever. The house cat is the main reservoir for the organism and

the vector is the cat flea. *Bartonella quintana* causes trench fever. The main vector is the human body louse. In AIDS patients with bacillary angiomatosis, *Bartonella henselae* or *Bartonella quintana* infection causes vascular proliferation. The most common manifestation is subcutaneous disease with a purplish rash that superficially resembles Kaposi sarcoma. Other manifestations include peliosis hepatis and lytic bone lesions. In the chest, bacillary angiomatosis can have a varied presentation. Violaceous endobronchial lesions can mimic Kaposi sarcoma on bronchoscopic inspection of the airways. In the lung, parenchyma nodules are the most common manifestation. Additional findings include pleural effusions, lymphadenopathy and chest wall masses. Because of the vascular nature of these lesions, the lymphadenopathy and chest wall masses frequently densely enhance with intravenous contrast administration when imaged by CT. Because bacillary angiomatosis is a bacterial infection that responds well to antibiotic therapy, familiarity with its varied manifestations is important in leading to an early diagnosis.

Rhodococcus is a zoonosis caused by infection with *Rhodococcus equi*, an organism known to cause pneumonia in horse, pigs, and other farm animals. It can cause disease in immunocompromised people including AIDS patients with CD4 cell counts < 200 cells/mm³. The radiographic manifestations of Rhodococcus pneumonia include parenchymal consolidation, usually accompanied by cavitation. Pleural effusions and empyema frequently complicate Rhodococcal pneumonia. Lymphadenopathy may be present. Infections with *Rhodococcus equi* requires prolonged antibiotic therapy or surgical resection. Despite aggressive therapy, there is a high mortality for AIDS patients who develop Rhodococcal pneumonia.

Pasteurella multocida is a gram negative bacterium that is a normal component of the oral flora in dogs and cats. In patients with normal immunity and underlying lung disease, pasteurella may cause pneumonia after a dog or cat bite. In immunocompromised patients, pasteurella can cause pneumonia even in the absence of underlying lung disease. The radiographic findings include focal areas of consolidation which may be complicated by cavitation and pleural effusion.

Bordetella bronchiseptica is a gram negative coccobacillus that causes respiratory illness in dogs, cats and pigs. In HIV infected patients with CD4 counts of < 50/mm³, bordetella may cause pneumonia. The radiographic findings are usually bilateral interstitial opacities, although cavitation has been reported. History of contact with an infected dog or cat can often be elicited.





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Notes