Pulmonary Complications of Cancer Treatment

Objectives

- Develop awareness of the myriad pulmonary complications of cancer treatment and of challenge in making correct diagnosis
- Describe Radiation and Chemotherapy-Induced Complications
- Radiation-Induced Complications: Radiographic Patterns
  - Conventional wisdom
  - Challenges of current delivery techniques
- Chemotherapy-Induced Pulmonary Complications
  - Patterns of injury
  - Challenges of novel therapies

Pulmonary Complications of Cancer Treatment

- Radiation-Induced Pneumonopathy
- Chemotherapy-Induced Pneumonopathy
- Surgical
- Infectious: Community-acquired, Atypical, Aspiration
- Pulmonary emboli

Pulmonary Complications of Cancer Treatment

- Lung Cancer
- Other Cancers

Pulmonary Complications of Cancer Treatment

- Lung Cancer
- Other Cancers
**Elevated Risk in the Lung Cancer Patient**

- Primary neoplasm is pulmonary: lung surgery primary curative modality
- Underlying lung disease
- Mean age more advanced: ~70% diagnosed at 65 years of age or greater
  - Decreasing tissue mass
  - Impaired drug clearance
  - Greater number of co-morbidities


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**Cost of Better Treatments**

Aim to lengthen survival, improve palliation

Multimodality, multiregimen treatment now standard

- Surgery
- Chemotherapy
- Radiation therapy

Mounting Toxicity

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**New, escalating respiratory symptoms**

- Drug Toxicity
- Diagnosis Quandry
- Radiation Toxicity
- Infection

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**Radiation-Induced Toxicity**

Radiotherapy indicated in about 64% of NSCLC patients overall:

- ~46% initially, 18% later in illness

Radiotherapy indicated in about 54% of SCLC patients overall:

- 45% initially, 9% for recurrence or progression

Radiation Therapy Risks

- Irradiation of normal lung major dose-limiting factor
- Typical dose: 60 to 70 Gy to tumor and focal nodal metastases
- Invariably some damage to normal lung
- Threshold for pneumonitis ranges from 5 to 20 Gy
- 50-90% of patients undergoing lung irradiation develop radiographic or pulmonary function abnormalities.*
- Mechanism still not well understood


Factors Influencing Risk

- Volume of normal lung irradiated
- Cumulative dose
- Size of fractions delivered, schedule of delivery
- Comcomitant chemotherapy: certain agents in particular
- Previous Irradiation: lowers threshold
- Genetic factors?

Radiation Induced Lung Toxicity

- Improving geometric accuracy of delivery systems
  - conformal RT
  - intensity modulated RT
- Complications have not been eliminated. Ex: Pneumonitis reported in 5-15% of patients receiving external beam radiation therapy for lung cancer

Stages of Injury

- Acute, exudative stage: Radiation pneumonitis
  - 0-2 months after treatment
  - Steroid responsive
- Organizing, proliferative stage: Radiation pneumonitis
  - 2-9 mo after treatment
  - Steroid responsive
- Chronic, fibrotic phase: Radiation fibrosis
  - >9 mo after treatment, stable after 24 mo
  - Not steroid responsive, supportive therapy

Radiologic Manifestations: The Conventional Wisdom

**Conventional RT**

(Clinical Example Image Slide)

Geographic margins

Confined to the radiation portal

(Clinical Case Image slides)
Chemotherapy-Induced Complications

- Direct effects of therapy: Incidence ranges from 1 to 30%, depending on agent
- Overlap: Intercurrent infection, progression of tumor, fluid overload, pulmonary edema, pulmonary embolism
- Multidrug regimens: Difficult to ascribe to a particular agent
- Nonspecific radiologic findings, multiple patterns
- Less frequent than radiation toxicity, but can be florid and may have higher mortality rate
- Consult with referring clinician!

Agents (NSCLC and SCLC)

- Toxicity well described in certain established agents: mitomycin, bleomycin
- Novel chemotherapeutic agents
  - Antimetabolites: gemcitabine
  - Taxanes: paclitaxel, docetaxel
  - Topoisomerase I inhibitors: topotecan, irinotecan
  - Topoisomerase II inhibitors: etoposide
  - Tyrosine Kinase EGFR inhibitors: erlotinib, gefitinib
  - Vascular Endothelial Growth Factor Inhibitor: bevacizumab
- Combination regimens now the standard for both SCLC and NSCLC
- Clinical trials continue to reveal toxicity profiles of various combination regimens
- Higher response rates may be offset by greater toxicity
Class | Agents | Observed Pulmonary Toxicities
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Platinum Agents | Cisplatin, Carboplatin | Minor except when used in combination; various patterns in combination regimens
Taxanes | Paclitaxel, Docetaxel | NSIP, Interstitial Fibrosis, DAD, DAH, Veno-occlusive Disease
Antimetabolites | Gemcitabine | NSIP, Interstitial Fibrosis, DAD, DAH, Veno-occlusive Disease
Tyrosine kinase EGFR Inhibitors | Gefitinib, Erlotinib | DAD, DAH
Topoisomerase Inhibitors | Etoposide, Topotecan, Irinotecan | NSIP, Bronchiolitis Obliterans, DAD
Monoclonal Antibodies | Bevacizumab | DAH

Pulmonary Drug Toxicity: Treatment

- Remove offending agent
- Steroids
- Supportive treatment

Summary

- Long differential diagnosis in cancer patient with respiratory complaints, lung cancer patient in particular
- Radiation Therapy: continued challenge despite improvements in delivery techniques, confusing radiologic patterns
- Chemotherapy: wide spectrum of abnormalities, challenge posed by new agents and combination regimens
Key References


www.pneumotox.com