Bleomycin Induced Pulmonary Fibrosis

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Case presentation

- 43 year old female with dyspnea
- Dry cough x 5 days
- ROS Negative
- No other associated symptoms
Past Medical History

- HTN

- Recurrent Cystitis

- Granulosa Cell Tumor of Ovary
  - Hysterectomy with BSO
  - 3 Cycles of chemotherapy consisting of bleomycin, etoposide, and cisplatin
Physical Exam

- Vitals: BP 116/82, HR 127, RR 24, O2 sat 94% on 2L O2

- Physical Exam: No acute findings

- Labs: CBC – Hb 7.7; Lytes – normal

- ECG: Sinus Tachycardia
Hospital Course

- HD 1-2:
  - Minimal improvement
  - Increased oxygen demands
  - Pulmonary consult

- HD 3-10:
  - Pulmonary lowered oxygen flow
  - CPAP to maintain oxygenation
  - ID consult obtained
Hospital Course

- HD 11-17:
  - Worsening pulmonary status requiring intubation
  - Primary services transferred to pulmonary
  - Bronchoscopy performed and negative
  - Family conference held

- HD 18:
  - Family decides to withdraw care
  - Presumed cause of death ARDS secondary to presumed bleomycin toxicity
Bleomycin

- Isolated from *S. verticillus* in 1966
- Mechanism: Produces single and double stranded breaks in DNA
- Uses: Squamous cell Ca of head & neck, esophagus, cervix, Hodgkin & Non-Hodgkin lymphoma
- In 10% of cases causes varying degrees of pulmonary fibrosis
Pulmonary Fibrosis from Bleomycin

- Pathogenesis:
  - Oxidative damage
  - Deficiency of bleomycin hydrolase
  - Genetic susceptibility
  - Inflammatory cytokines

- Fibrosis incidence: Dose dependent
  - <270 mg: 0 – 2%
  - >360 mg: 6 – 18%
  - Standard dose, 270 or 360 mg: 0- 3%
Risk Factors

- Age
- Dose
- Renal dysfunction
- Concurrent use of cisplatin or gemcitabine
- Concurrent radiation therapy
Typical Presentation

- Symptoms generally appear within 1-6 months following last dose
- Subjective: Cough, chest discomfort, shortness of breath
- Objective: hypoxia, fever, tachycardia, and cyanosis
- Labs: eosinophilia, leukocytosis, widened A-a gradient
- Imaging: normal to diffuse fibrosis
  - CXR not representative of acuity/degree of fibrosis
Suggested Therapies

- Discontinuation of bleomycin when documented/strongly suspected lung toxicity (1A)

- Symptomatic with impaired PFTs: glucocorticoids (1B)
  - 0.75 – 1mg/kg prednisone

- Titrate down FiO2 to maintain sats 89 – 92% (2C)

- Use IV fluids sparingly

- Re-initiation contraindicated in patients with fibrosis
Questions?