Cryptogenic Organizing Pneumonia

Presented by: Eleni Martinez, Pharm.D.
PGY1 Pharmacy Resident
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Objectives

• Define cryptogenic organizing pneumonia (COP)
• Describe the pathogenesis and epidemiology for COP
• Explain symptoms and diagnostic tools for COP
• Discuss treatment and management strategies for COP
• Evaluate a treatment plan for a patient with COP based on a patient case
Background

• Bronchiolitis obliterans organizing pneumonia (BOOP) was first described by Gary Epler in 1985
• Characterized by
  • Sub-acute or chronic respiratory illness
  • Presence of granulation tissue in the bronchiolar lumen, alveolar ducts and some alveoli
• Number of known causes for BOOP
  • Idiopathic if the cause cannot be identified

BOOP: Bronchiolitis obliterans organizing pneumonia

Background

• Secondary causes for BOOP
  • Post-respiratory infection
  • Drug-related
  • Radiation therapy
  • Organ transplantation
  • Occupational/environmental
  • Miscellaneous causes

• Primary, idiopathic BOOP is now referred to as cryptogenic organizing pneumonia (COP)

Patient Case

- PG is a 54 year old female who had a complicated hospital stay from 2/15-3/10/15
- PMhx
  - Frequent pneumonia since childhood
- FMhx
  - (+) colon and bone cancer
- SChx
  - Quit smoking (smoked 1 pack per week for 10 years)
  - (-) alcohol, (-) illicit drug use
  - Works as an LPN for a local doctor’s office
- Home meds
  - Zolpidem CR 12.5mg orally at bedtime
Patient Case

• CC: Shortness of breath
• PE: Pleasant, well-developed, well-nourished, Caucasian female in no acute distress
• BP: 141/93, HR: 144, Temp: 97.9°F, O² sat: 92
• Ht: 5’2”, Wt: 52.6kg
• Chest X-ray: No acute cardiopulmonary process identified

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Patient Case

• Seen at Hamilton County Employee Clinic
  • Received corticosteroids and cough medicine
  • Returned in 5 days and received Clarithromycin course

• Admitted to Memorial Hixson on 2/15-2/21/15 with a 2-week history of cough and dyspnea
  • Unresponsive to outpatient antibiotics and corticosteroids
  • Admitting diagnosis: COPD exacerbation/acute bronchitis
  • Sent home on nebulizer treatment with albuterol, prednisone taper, and course of levaquin
Introduction

• COP is a rare inflammatory lung disorder
• Interstitial lung disease that affects the:
  • Distal bronchioles
  • Respiratory bronchioles
  • Alveolar ducts
  • Alveolar walls
• Organizing pneumonia refers to organized areas of inflammatory tissue that fill the bronchioles and alveoli
• Term “cryptogenic” means the cause is unknown
Symptoms

- Symptoms develop slowly over a few weeks or months
- Most common features include:
  - Persistent nonproductive cough
  - Dyspnea
  - Fever
  - Malaise
  - Weight loss of greater than 10 pounds

Pathogenesis

• Inflammation of lungs caused by series of events

  Leakage of plasma proteins
  ↓
  Recruitment of fibroblasts
  ↓
  Fibrin formation within the alveolar lumen
  ↓
  Alveolar epithelial injury

Epidemiology

- 1.1 to 7 cases per 100,000 hospital admissions annually
- Approximately 56 to 68 percent of cases have been deemed cryptogenic
- Most common in individuals ages 40 to 60
- 5-10 percent of chronic infiltrative lung disease in the U.S.
- Smoking ≠ precipitating factor

Physical Exam

- Physical exam
  - Inspiratory crackles or rales
- In rare cases patients may present with:
  - Wheezing
  - Arthralgia
  - Night sweats
- Lack of clinical response to empiric antibiotics along with physical exam may raise questions of COP

COP: Cryptogenic Organizing Pneumonia

Diagnostic Tools

- Chest x-ray
  - Bilateral, patchy or diffuse, consolidative or ground glass opacities in the presence of normal lung volumes
- CT scan
  - Triangular-shaped ground-glass opacities
- Pulmonary function testing
  - Decrease in vital capacity
- Bronchoalveolar lavage
  - May show high percentage of lymphocytes
- Transbronchoscopic or surgical lung biopsy
  - Rule out other differential diagnoses

Diagnostic Tools

Abnormal Chest CT (COP)  Normal Chest CT

COP: Cryptogenic Organizing Pneumonia
Diagnostic Tools

- Laboratory testing
  - CBC with diff, BUN, SCr, LFT, UA, ESR, CRP
    - Leukocytosis observed in around 50 percent of patients
    - Positive CRP observed in 70-80 percent
- Additional tests
  - Blood cultures, sputum gram stain, sputum enzyme immunoassay (EIA) or polymerase chain reaction (PCR)
- Tests for connective tissue disorders
  - Antinuclear antibody, rheumatoid factor, creatine kinase, anti-topoisomerase, and anti-double-stranded DNA
Treatment

- Treatment of COP has not been studied in randomized trials
- Therapy is initiated based on severity of disease

Treatment

- Corticosteroids are the current standard treatment
- Prednisolone is the preferred agent
  - 0.75 to 1mg/kg/day for 1 to 3 months
  - 0.75 to 0.5mg/kg/day for 3 months
  - 10 to 20 mg/day or every other day for a total of 1 year
- Patients should be followed with a chest x-ray and pulmonary function test every 2-3 months
- Adverse effects
  - Infection, hyperglycemia, weight gain, osteoporosis, adrenal suppression

Treatment

• Cytotoxic therapy can be added for patients who fail to improve with glucocorticoids
• Oral cyclophosphamide is commonly used
  • 1 to 2mg/kg/day up to a maximum of 150mg/day
  • Usually start at 50mg daily and increase over 2 to 4 weeks
  • Treatment is usually 6 months due to toxicity
• Adverse effects
  • Bone marrow suppression, increased susceptibility to infection, and gonadal toxicity,

Treatment

• Macrolides (3-month course)
  • Intolerant to steroid therapy or add-on agent
  • Azithromycin 250mg orally three times weekly
  • Clarithromycin 500mg orally twice daily

• Other immunosuppressive agents
  • Azathioprine 100-125mg orally daily
  • Mycophenolate mofetil 1,000mg orally twice daily
  • Cyclosporine A 75-100mg orally twice daily
Considerations for Fulminant Disease

• IV glucocorticoids
  • Methylprednisolone 125 to 250 mg every 6 hours
  • Methylprednisolone 750 to 1000 mg daily for 3 to 5 days

• Patients can be transitioned to oral prednisone once they show signs of improvement

• IV cyclophosphamide is often added to patients
  • Require mechanical ventilation
  • Do not respond rapidly to intravenous glucocorticoids

Prognosis

• Two-thirds of patients treated with glucocorticoids completely recover
  • Total clinical and physiologic improvement and normalization of the chest x-ray
• Most patients improve over several weeks to a few months
  • Symptomatic improvement may occur in 1 to 2 weeks

Patient Case

- Readmitted on 2/22/15
  - Persistent cough, fever, chills, hypoxemia and leukocytosis
  - Admitting diagnosis: COPD exacerbation/HCAP
  - Chest CT and chest x-ray abnormal
  - Sputum cultures obtained
  - Bronchial lavage on 2/27 shows aspergillus
  - Transferred for open lung biopsy
**Patient Case**

- BP: 119/57, HR: 127, Temp: 98.6°F, O² sat: 94
- Lungs: Slight inspiratory crackles
- Chest CT: Diffuse areas of groundglass attenuation throughout both lungs
- Chest X-ray: Asymmetric interstitial infiltrates

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Patient Case

• Transferred to Glenwood on 3/4/15
  • Treated with broad spectrum antibiotics
  • Lung biopsy showed acute interstitial lung process
  • Bronchial biopsy negative

• Imaging
  • Chest X-ray on 3/4/15
    • Mildly enlarging patchy infiltrates
  • Chest CT on 3/7/15
    • Diffuse hazy ground glass infiltrates throughout both lungs
Patient Case

• Pertinent Lab Trends

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• CRP and ESR are inflammatory markers
• Monitoring the progress of COP using these has been recommended but remains nonspecific and unreliable

CRP: C-Reactive Protein
ESR: Erythrocyte sedimentation rate
Patient Case

- Pathology Results 3/9
  - Multifocal organizing pneumonia with mild background interstitial fibrosis
- Treatment
  - Solu-Medrol IV 60mg every 6 hours for 3 days
  - Prednisone 40mg orally daily
  - Antibiotics were discontinued once prednisone was started
Patient Case

- Discharge on 3/10
  - Follow-up with PCP in 1 week
  - Follow-up with pulmonary in 4 weeks
- Pertinent Discharge Medications
  - Prednisone 40mg daily until pulmonary follow-up
  - Duonebs four times daily
- Pulmonary recommended discontinuation of antimicrobial therapy
  - All labs were within normal limits at discharge
Take Home Points

• COP is an idiopathic, inflammatory, non-infectious type of pneumonia
• Due to the similar clinical presentation, many patients are first misdiagnosed with CAP
• Gold Standard: long-term/high dose glucocorticoid therapy
• Pharmacists can play a vital role in making recommendations and counseling patients
References


Test Your Knowledge

A patient weighing 140kg is diagnosed with COP and the physician asks you for a prednisone dose recommendation, which dose do you recommend to start?

a. Prednisone 100mg daily
b. Prednisone 140mg daily
c. Prednisone 60mg daily
d. Prednisone 40mg daily
A patient weighing 140kg is diagnosed with COP and the physician asks you for a prednisone dose recommendation, which dose do you recommend to start?

a. Prednisone 100mg daily
b. Prednisone 140mg daily

c. **Prednisone 60mg daily**
d. Prednisone 40mg daily
Test Your Knowledge

True or False: All patients with COP must be treated with long-term/high dose steroids.
Test Your Knowledge

True or False: All patients with COP must be treated with long-term/high dose steroids.

FALSE
Questions
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