Cryptogenic Organizing Pneumonia: In the Setting of Staphylococcus aureus Endocarditis

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Abstract

Although COP is idiopathic by definition, it is important to investigate each diagnosed case for potential causes, such as iatrogenic from radiation or known causative medications [1], connective tissue diseases, inflammatory bowel disease, malignancies, history of lung transplant or bone marrow graft. OP may present weeks to months before other signs of connective tissue disorders and therefore the patient should undergo serologic testing for these diseases. [6] In the case presented, the specific etiology was unyielding and so remains cryptogenic in nature. This patient's symptoms quickly improved following the use of steroids and tolerated tapering off completely without relapse one year out from initial diagnosis.

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To the Editor,

Organizing pneumonia (OP) is a rare, diffuse lung disease process associated with nonspecific symptoms, radiologic abnormalities, and pulmonary function test (PFT) abnormalities. The histopathologic pattern is characterized by patchy filling of the lung alveoli and respiratory bronchioles with loose plugs of granulation tissue. Although formerly described in the context of pulmonary infection, the condition was recognized as an independent entity starting in the 1980s.[1] There are a variety of potential etiologies that culminate in the development of OP. However, when no cause is specifically identified, OP is classified as cryptogenic organizing pneumonia (COP), previously described as bronchiolitis obliterans with organizing pneumonia (BOOP).[2]

In COP, both genders are equally affected with the mean age of onset between 50 and 60 years old. The relative prevalence of COP is approximately twice as high in non-smoking individuals when compared to those that smoke.[3] Symptoms typically present as a mild flu-like illness with cough, fever, malaise, and dyspnea with risk for rapid progression requiring invasive ventilation[4] or even extracorporeal membrane oxygenation (ECMO)[2]. However, symptoms can regress quickly with steroid therapy. Chest radiologic findings can be variable and laboratory evaluations non-specific; a lung biopsy for histopathologic analysis is usually required to establish the definitive diagnosis.[4]

Discussed is a case of a 14-year-old female with no significant past medical history, who presented to the hospital for progressive dyspnea and worsening cough following a recent discharge related to methicillin-susceptible *Staphylococcus aureus* endocarditis. During her initial endocarditis hospital course, she required surgical procedures to repair and ultimately replace her mitral valve. A 6-week course of Nafcillin was initiated and she was discharged home a month later with documented complaints of a mild cough at time at discharge. Her chest X-ray at discharge revealed small bilateral pleural effusions and she was able maintained oxygen saturations above 90% without supplemental oxygen.

Upon re-admission one week after her initial discharge, she required high-flow nasal canula at 8 liters, 30% FiO2 with a chest X-ray revealing stable pleural effusions, but with progressive alveolar opacities involving the right middle and lower lung lobes with an interstitial component. Due to concern for infectious pneumonia, the patient was initiated on 24-hour broad spectrum antibiotics with linezolid and gentamicin, in addition to ongoing nafcillin course. Within the first 48 hours of admission, a large left ventricular pseudoaneurysm was identified that required urgent repair. Following repair, her antibiotic coverage was narrowed back to nafcillin as monotherapy. Unfortunately, she remained unable to wean off respiratory support. Repeated chest imaging showed progressive worsening of her right sided opacities.

Computed tomography (CT) angiography of the chest demonstrated evidence of severe right-sided airspace disease [Figure 1]. Right upper lobe segments showed patchy ground glass opacities intermixed with consolidations and mild interlobular septal thickening at the apex. There was near complete consolidation of the right middle lobe, as well as nonconfluent consolidative opacification with scattered ovoid lucencies throughout the right lower lobe. These findings were nonspecific, leaving a broad differential including: atelectasis, edema, or other airspace infiltrate, such as infectious pneumonia. Antibiotics were again broadened to include ceftriaxone. Despite this, a cavitary lesion developed on the standard radiograph one week after initial CT angiography. Repeat chest CT confirmed the presence of a cavitary lesion and demonstrated new development of left-sided ground glass opacities [Figure 1].

Bronchoscopy with BAL revealed a neutrophil (40%) and monocyte (42%) predominance. Her comprehensive infectious workup remained unremarkable. A wedge lung biopsy of her right upper and lower lobe was obtained via video-assisted thoracoscopic surgery (VATS). Histology showed extensive organizing pneumonia with extension into the bronchioles [Figure 1]. There were increases in intra-alveolar hemosiderin-laden macrophages and hyperplastic type II pneumocytes with organizing pleural fibrin. No evidence of vasculitis or capillaritis was visualized.

Upon confirmation of organizing pneumonia, the patient was started on intravenous methylprednisolone at a dose of 125 mg every 6 hours for 5 days, followed by a prolonged steroid taper. She received 2 doses of intravenous immunoglobulin (IVIG) after the initiation of steroids. In an effort to address the obliterative process of the airways, she was started on FAM therapy with inhaled fluticasone (110 mcg 2 puffs twice daily), azithromycin (500 mg MWF), and montelukast (10 mg nightly). The patient completed her 6-week course of nafcillin for her endocarditis and tolerated weaning off her respiratory support.

Prior to discharge, she was evaluated by Rheumatology and Immunology for potential causes of organizing pneumonia. Her laboratory workup included ANA, ANCA, PR3 antibodies, IgA, IgG, IgM, thyroid studies, and rheumatoid factor, with all results within normal limits. Genetic testing for connective tissue disease was negative. The patient was discharged home with close follow-up and ongoing steroid wean over 8-weeks. She participated in cardiopulmonary rehabilitation for 8 weeks and was weaned off steroids without difficulty. Pulmonary function testing (PFT) was obtained 4 months following the initial diagnosis and resulted in a forced expiratory volume in one second (FEV1) of 57% predicted with a total lung capacity (TLC) of 52% predicted. After one year of pharmacologic and mechanical therapies, the FEV1 improved to 73% predicted and the TLC to 78% predicted with a normal corrected diffusion capacity of the lung for carbon monoxide (DLCO) at 104% predicted. She resumed competitive tennis with reported excellent exercise endurance for 3 hours of continuous activity.

This unique case highlights a rare condition that is even rarer in the pediatric population. Clinical presentation can be severe. Radiologic findings tend to be diverse, but typically present with bilateral opacities that are patchy or diffuse and consolidative in the presence of normal lung volumes, often requiring high resolution CT scan to determine the extent and severity of disease.[6]Laboratory workup is often nonspecific, with frequent elevation of inflammatory markers such as C-reactive protein, erythrocyte sedimentation rate, and leukocyte count. Lung biopsy is often required to obtain the definitive diagnosis and initiate appropriate therapy. The delay in diagnosis and treatment may lead to clinical deterioration and permanent injury to the lungs.

The mainstay of COP therapy is corticosteroids, usually resulting in rapid clinical improvement and clearing of opacities on chest imaging. In adult patients, adjunctive FAM therapy may halt pulmonary decline of associated obliterative bronchiolitis.[5] The combined therapy may permit a reduction in steroid exposure, collectively leading to better health with an improved quality of life. Relapses are documented in less than 25% of cases. When occurring, they are usually within the first year of diagnosis and while tapering glucocorticoids. Patients respond well to resuming or increasing glucocorticoid treatment. However, for patients who are unable to discontinue steroids, glucocorticoid sparing agents, such as mycophenolate mofetil, can be considered.[6]

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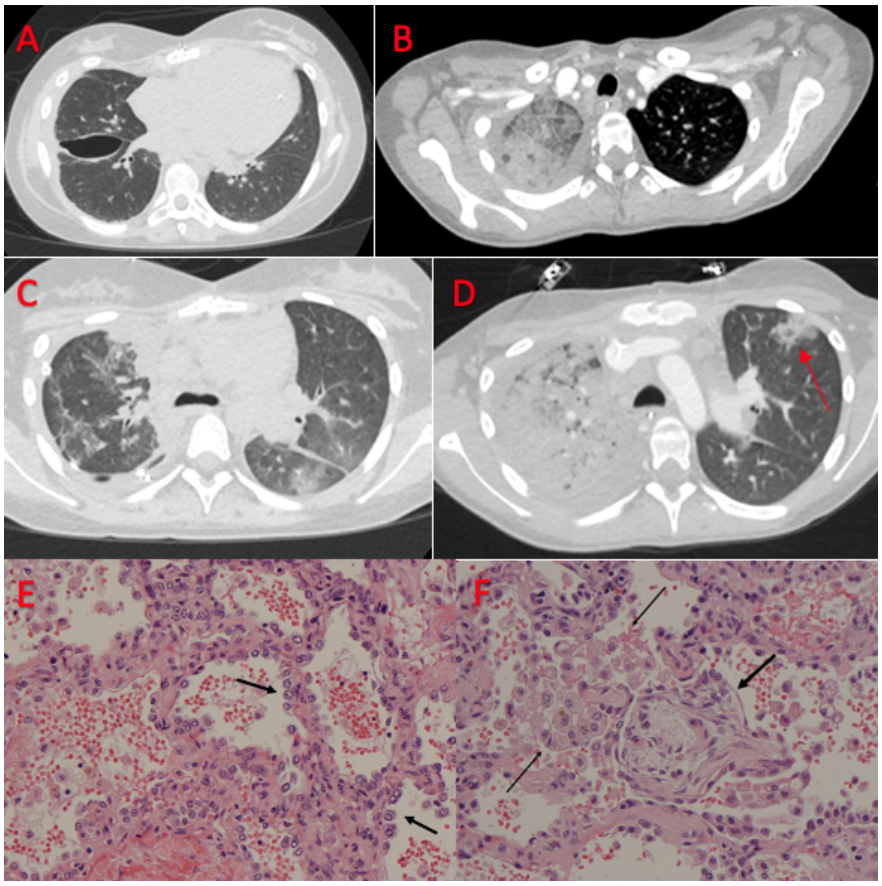

Figure 1: A) Cavity formation in the right lung B) Crazy paving pattern noted in the right upper lobe C) Areas of ground glass opacities and band-like opacities D) Reverse halo sign (arrow) E) H&E stain showing hyperplasia of type 2 pneumocytes (arrows), original magnification 200x F) H&E stain showing plug of organizing pneumonia (large arrow), increased foamy macrophages (between thin arrows) and pneumocyte hyperplasia, original magnification 200x