Case Report

High-resolution CT, histopathologic, and clinical features of granulomatous pneumocystis jiroveci pneumonia

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ABSTRACT

Although pneumocystis jiroveci pneumonia was historically associated with HIV/AIDS patients, there is a recent shift in demographics with increasing incidence in patients with hematologic malignancies and transplants. A granulomatous response to pneumocystis jiroveci infection is uncommon and most commonly presents as multiple randomly distributed nodules on chest imaging. Granulomatous pneumocystis jiroveci pneumonia presents with similar clinical manifestations as typical pneumocystis pneumonia but is usually not detected by bronchoalveolar lavage and may require biopsy for a definitive diagnosis. For this reason, the radiologist may be the first provider to suggest this diagnosis and guide management.

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Introduction

Pneumocystis jiroveci pneumonia (PJP), formerly known as Pneumocystis Carinii Pneumonia, is a significant cause of infection in immunocompromised patients. Initially brought to light during the AIDS epidemic, it has also shown to be associated with the use of cytotoxic and immunosuppressive therapies [1]. At risk individuals are immunocompromised such as those with HIV, primary immunodeficiency, hematologic malignancies, solid tumors, and transplant recipients [1]. Non-HIV immunocompromised hosts now make up the majority of patients with pneumocystis pneumonia in industrialized countries [2] with the incidence shown to be on the rise in this population [3].

Classically, PJP pneumonia presents as ground glass opacities with or without cyst formation on HRCT imaging [4]. A smaller subset of patients with PJP have atypical imaging manifestations such as masses and nodular opacities which have been shown to represent granulomatous response to the
PJP infection, known as granulomatous PJP (GPJP) [5]. Recognition of these atypical imaging manifestations is important as diagnostic considerations for pulmonary nodules and masses in immunocompromised patients often first include infectious etiology such as fungi, lung cancer, metastatic disease, hematological malignancy, and lymphoproliferative disorders [6]. Herein we report a case of GPJP as the heralding event in a patient subsequently diagnosed with peripheral T-cell lymphoma.

**Case report**

A forty-nine-year-old female with a history of recurrent pneumonia and asthma developed worsening dyspnea for 6 months before presenting to the emergency department for shortness of breath, dry cough, and wheezing. An initial chest x-ray was reported as negative. She was diagnosed with an acute asthma exacerbation and was discharged home on prednisone. The patient was seen in an outpatient facility 5 days later for persistence of symptoms despite adherence to therapy as well as interval development of a rash on the face and arms. She was subsequently found to have new chest x-ray infiltrates. A HRCT revealed airway inflammatory changes, ground glass opacities, and consolidation (Fig. 1). At this time, the primary consideration was an atypical infection.

The patient was subsequently admitted to the hospital due to worsening respiratory distress and further history revealed a 30 lbs weight lost in the preceding 3 months. Laboratory testing revealed new onset leukopenia and HIV tests were negative. A bronchoalveolar lavage was performed which showed abundant pneumocystis jiroveci organisms. The patient received a 2-week course of TMP-SMX and followed by a 1-week course of atovaquone, both of which did not result in any significant clinical improvement. Video-assisted thoracoscopic surgery wedge lung biopsies were then obtained and showed well-formed granulomas with pneumocystis jiroveci within the granulomas (Fig. 2). No lymphomatous infiltrates or other organisms were found. A CT obtained shortly thereafter and approximately 1 month after initial CT imaging demonstrated multiple new nodules in her lungs, most in the 1 cm range, which were correlated with the pathologic results of granulomatous PJP infection (Fig. 1).

A third line therapy consisting of 3 weeks of clindamycin and primaquine was initiated which eventually led to symptomatic improvement. An MRI of the left forearm performed due to swelling revealed extensive edema and enlargement of the extensor muscle group involving predominately the extensor carpi radialis longus. A biopsy of the area confirmed a diagnosis of peripheral T-cell lymphoma. She was eventually discharged in stable condition. She received 1 cycle of CHOEP (Cyclophosphamide, Adriamycin, Vincristine, Etoposide, and Dexamethasone) and subsequent salvage chemotherapy with Romidepsin for new lesions.

**Discussion**

Patients with GPJP present with symptoms similar to that of typical PJP infection, most commonly dyspnea, cough, and fever. Rarely patients present with unique clinical findings including chest pain from chest wall and pleural involvement [7,8] as well as hypercalcemia related to the numerous granulomas [9]. A stronger association of GPJP with hematologic malignancy compared to HIV/AIDS has been reported [10]. A multicenter retrospective study comparing the presentation of PJP in patient with AIDS vs malignancy demonstrated nodular lesions in 1 out the seventeen (6%) patients with AIDS and 5 out of twenty-one (24%) patients with malignancy [11]. Most
of the malignancies reported in that study were hematologic (16/21) [11]. On average, GPJP developed 2 weeks to 2 months after stopping corticosteroids and 3-8 weeks after initiating HAART [12].

It has been reported that up to 81% of GPJP cases show pulmonary nodules on imaging [10]. When present, they are often multiple and randomly distributed [5,12]; however, solitary pulmonary nodules [13,14] and masses [15] have been reported. Nodules can range from a few millimeters to greater than 1 cm [4], although there have been reports of masses as large as 7 cm [15,16]. A significant minority (17%) have diffuse infiltrates without nodules [10]. Two studies have reported the appearance of nodules on radiographs and CT scans a few days after a negative study, showing that these granulomas can develop quickly [13,17]. Enlarging nodules over weeks to months was a consistent finding in multiple studies in patients who were not being treated adequately [18–20]. The nodules have been shown to demonstrate new caviation over a period of days [13]. In some studies, the nodules shrank or persisted on imaging even after treatment and resolution of symptoms [21–23].

It is also important to note that nodular opacities particularly in immunocompromised patients are not specific to GPJP. A retrospective analysis of 39 patients with PJP showed 7 patients (18%) to have nodules and nodular components [24]. In 6 of the 7 patients (86%), a second disease process affecting the lungs was discovered upon biopsy. These included mycobacterial and fungal infections, leukemic nodules, Kaposi’s sarcoma, lymphoma, and bronchogenic carcinoma [24]. This underscores the need to biopsy pulmonary nodules in an immunocompromised patient as more than one process may be present [24]. Additional atypical parenchymal features of PJP infection include lobar consolidation and airway abnormalities including bronchiectasis, bronchiolitis, bronchiolitis obliterans, and rarely an endobronchial lesion [25]. Associated atypical extrapulmonary findings include regional lymphadenopathy and pleural effusions [25].

Histologically, nodules and masses have been demonstrated to represent a granulomatous response to PJP [5,12]. The characteristic feature of GPJP is pneumocystis organisms within granulomas on homatoxylin and eosin (H&E) stain (A). These were confirmed to represent Pneumocystis Jiroveci (arrows) on Gomori methenamine silver (GMS) stain (B).

Fig. 2 – Histologic images from Video-assisted thoracoscopic surgery biopsy of right middle and lower lobes nodules performed about one month after the initial CT demonstrates diffuse granulomas (arrows) containing micro-organisms on hematoxylin and eosin (H&E) stain (A). These were confirmed to represent Pneumocystis Jiroveci (arrows) on homatoxylin and eosin (H&E) stain (B).
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