Case Report

Multimodality imaging in a case of multiple pulmonary hyalinizing granulomas - A decade follow-up

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ABSTRACT

A 44-year-old male was referred to our clinic (2015) to evaluate multiple lung nodules with increasing fatigue, dyspnea, and weight loss. He was being assessed to an outside hospital for the same since 2010. The X-ray and computed-tomography (CT)-chest showed numerous pulmonary nodules and bilateral hilar adenopathy. Imaging workup at our institute (2015) redemonstrated extensive calcified pulmonary nodules. 18fluoro-2-deoxy-d-glucose positron emission tomographyCT showed widespread pulmonary nodules with low-grade uptake. Video-assisted thoracic surgery lung biopsy revealed pulmonary hyalinizing granuloma (PHG). Recently because of increasing symptoms, he is being evaluated for a lung transplant. This case represents a rare diagnosis of PHG with a decade follow-up.

KEY WORDS: Fluoro-2-deoxy-d-glucose, multiple pulmonary nodules, positron emission tomography/computed-tomography, pulmonary hyalinizing granuloma

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INTRODUCTION

Pulmonary hyalinizing granuloma (PHG) is a rare benign condition, which usually manifests as solitary or multiple pulmonary nodules. The etiology of PHG remains unclear. Accurate diagnosis of PHG may require an excisional biopsy to differentiate from other entities. Chest imaging shows solitary or multiple randomly distributed nodules. A patient with a single lesion remains stable, and resection is often curative. Patients with multiple lesions may show progressive enlargement of nodules with increasing dyspnea. There is no definitive treatment for multiple nodules, although the successful resolution with glucocorticoid administration has been reported.

CASE REPORT

A 44-year-old male was evaluated for fatigue and dyspnea for a few months in 2010. His X-ray and CT scan demonstrated multiple well defined pulmonary nodules. Laboratories test for autoimmune, fungal serologies, and tuberculosis revealed no significant abnormalities. Histoplasma antibody was positive

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by complement fixation, while urinary antigen was negative. Given multiple nodules, Midwest location, positive Histoplasma antibody (Ab), a possible diagnosis of chronic smoldering pulmonary histoplasmosis was considered and started on antifungal therapy. The patient was kept on conservative management with a pulmonologist from 2010 to 2015.

He was referred to our institute because of increasing fatigue, dyspnea, and weight loss. Imaging workup at our institute in 2015 redemonstrated extensive calcified pulmonary nodules on X-ray and CT scan [Figure 1]. The patient was investigated for infectious diseases. Serology panel for HIV, antinuclear Ab, antineutrophil cytoplasmic Ab, rheumatoid factor, anti-(ds)-DNA Ab, Sm Ab, SS-A/SS-B Ab, ribonucleoprotein Ab, Scl-70 Ab, Jo 1 Ab, P-ANCA, SSA/SSB was negative. He had negative fungal antibodies for aspergillus, Blastomyces, and coccidiosis. Histoplasma capsulatum Ab screen was positive; however, urine Histoplasma antigen was negative.

His fluoro-2-deoxy-d-glucose (FDG)-PET/CT showed mildly FDG avid multiple lung nodules [Figure 2]. The stability of nodules and the absence of significant uptake on PET argued against the pulmonary process being an active component of systemic illness. Bronchoscopy with

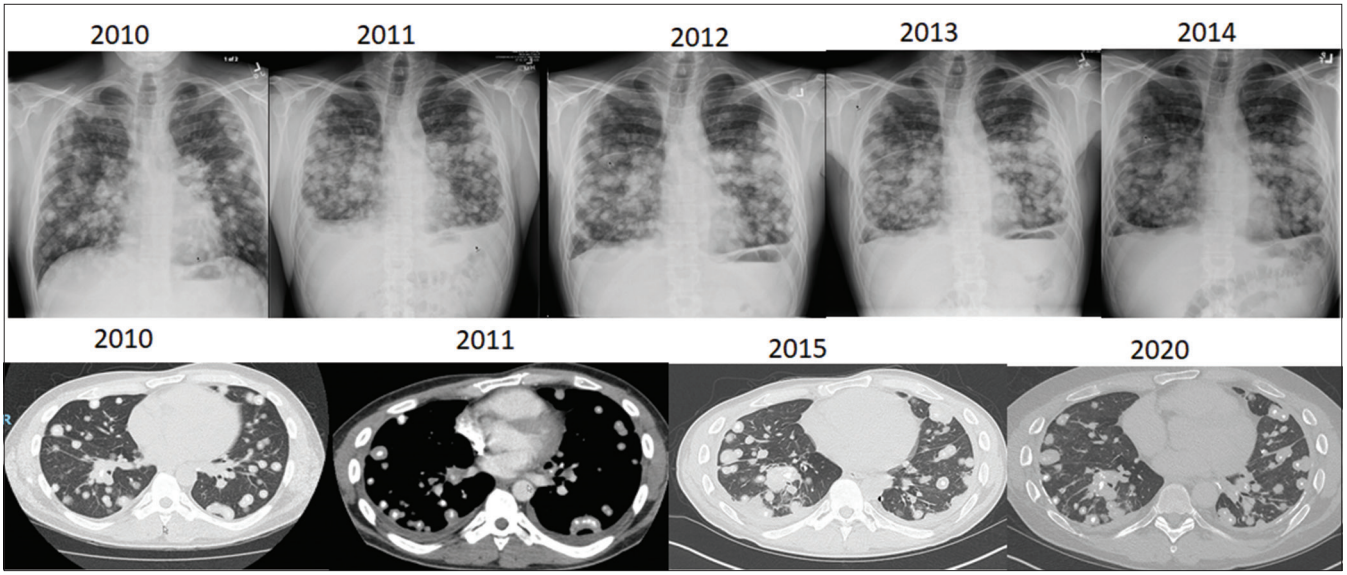

Figure 1: Upper row chest X-ray images (2010–2014) and lower row computed Tomography-chest (2010, 2011) images showed multiple slowly progressive pulmonary nodules

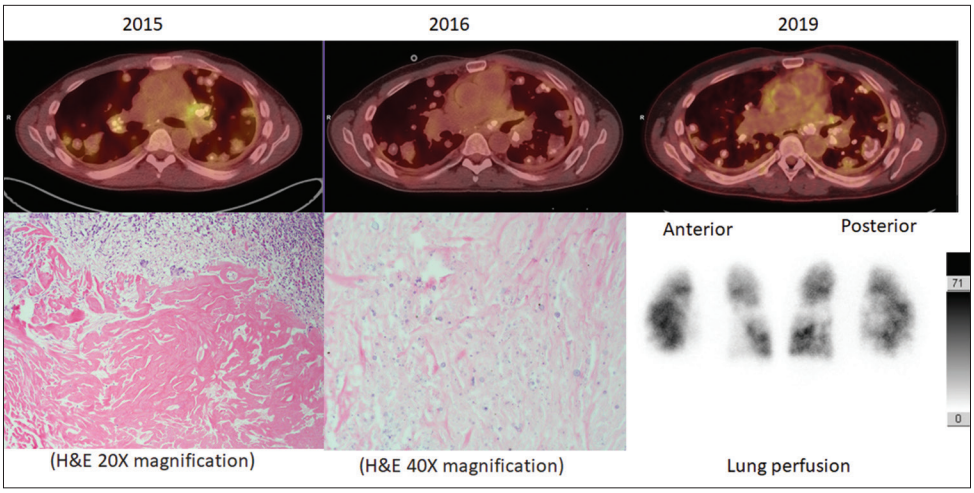

Figure 2: Fluoro-2-deoxy-d-glucose-positron emission tomography/computed-tomography of a 44-year old male for evaluation of multiple lung nodules. Fused positron emission tomography/computed-tomography (top left image, 2015) showed widespread pulmonary nodules, bilateral hilar, and mediastinal lymph nodes with amorphous central calcifications and low-grade fluoro-2-deoxy-d-glucose uptake. Follow-up positron emission tomography/computed-tomography (upper-middle 2016 and top right 2019 images) showed almost similar findings with mild progression. H and E-stained image (lower left × 20) showed a well-circumscribed nodule of thick collagen fibers with peripheral dense lymphoplasmacytic infiltrate and central focal calcifications. The lower middle image showed central calcifications (H and E, ×40). Recently, he was also evaluated for lung transplant. Tc-99 m macroaggregated albumin lung perfusion (lower right) showed heterogeneous distributions of activity

bronchial lavage was done, which was negative for bacterial, fungal, AFB cultures with negative AFB and fungal smears. Bronchial biopsy showed chronic inflammation that was negative for granulomas or malignancy. Video-assisted thoracic surgery biopsy of a nodule revealed a Pulmonary hyalinizing granuloma (PHG) diagnosis. H and E stain showed well-circumscribed nodules of thick collagen fibers with peripheral dense lymphoplasmacytic infiltrate and central focal calcifications [Figure 2]. A rituximab and prednisone trial was started based on the IgG4/IgG ratio of 12% (≥40%).

On follow-up, his energy level and weight improved significantly, without significant improvement in hypoxemia. Over the past 5 years, his oxygen requirement was increasing. Echocardiogram in 2018 showed decreased ejection fraction (40%) and pulmonary arterial hypertension. Serial chest CT scan and FDG PET-CT scan showed similar findings with slow progression [Figures 1 and 2] of the pulmonary nodules. On his recent visit (2020), he showed signs of severe end-stage lung disease with severe obstructive and restrictive pulmonary disease. He had chronic hypoxic, hypercarbia respiratory failure, and pulmonary hypertension. He is currently on Rituxan, Prednisone, and oxygen supplementation appears to be responding to the therapy. Because of end-stage lung disease, he was being evaluated for a lung transplant. Tc-99 m macro aggregated albumin lung perfusion (lower right) showed heterogeneous distributions of activity in both lungs [Figure 2].

DISCUSSION

PHG is a rare benign fibrosing nodular pulmonary disease that usually manifests as single or multiple nodules mimicking metastatic lung cancer with unclear pathophysiology and no definite treatment. It affects adults between the ages of 15 and 83 (mean age at the diagnosis 44.6) years.[1] There is no sex predilection or race predominance. The clinical symptoms of PHG are mild and nonspecific and may include cough, fever, fatigue, dyspnea, pleuritic chest pain, sinusitis, and pharyngitis. Several patients are entirely asymptomatic, with lesions only found through routine screening examinations.[1-3]

The etiology of PHG remains unclear. It has been proposed that the nodules may represent an abnormal immune response to infectious agents, such as tuberculous bacilli and Histoplasma, or autoimmune processes.[1,4-7] Patients presenting with autoimmune disease such as Sclerosing mediastinitis, retroperitoneal fibrosis, rheumatoid arthritis, posterior uveitis, Sjogren's syndrome, hemolytic anemia are sometimes associated with PHG.[4] Associations of PHG with lymphoproliferative disorders, such as Castleman's disease lymphoma, have been described.[8] The identification of these associated pathologies is essential for the outcome, prognosis, and therapy.

The differential diagnosis of PHG includes fungal infections, mycobacteria, rheumatoid arthritis, Wegener granulomatosis, sarcoidosis, amyloidosis, sclerosing mediastinitis, idiopathic systemic fibrosis, and IgG4-related sclerosing disease.[1,9-12] Accurate diagnosis of PHG may require an excisional biopsy to differentiate from the entities mentioned above. Microscopically, the lesions are well-circumscribed and are characterized by a dense network of concentric hyalinized collagen bronchovascular bundles with perivascular lymphoplasmacytic infiltrate. It rarifies in the center of the nodule.[1,9] The collagen is deposited in ropy, whorled collagen bundles separated by clear spaces.[13]

Chest radiography and CT findings show solitary or, more often, multiple randomly distributed, unilateral or bilateral nodules and masses with well-defined borders and without calcification.[9] Rarely nodules may show cavitation.[9,10] Mediastinal lymphadenopathy is usually not associated.[4] FDG-PET/CT is a valuable study for an indeterminate pulmonary nodule with significant overlaps between benign and malignant lesions.[14] It can reveal increased metabolic activity in PHG lesions.[15] It may help to guide biopsy and to identifying extrapulmonary lesions to rule out secondary causes. FDG-PET/CT may demonstrate a decrease in metabolic activity after corticosteroid treatment.[15]

The prognosis for patients with PHG is generally excellent, with no significant impact on longevity.[1] A patient with a single lesion remains stable, and resection is often curative. As in our cases, some patients with multiple lesions may show progressive enlargement of nodules and increased dyspnoea.[1,4] There is no definitive treatment for multiple nodules, although the successful resolution with glucocorticoid administration has been reported.[1,4,15,16] PHG should be included in the differential diagnosis of multiple pulmonary nodules. Excisional biopsy is required to make a diagnosis and rule out other malignant pathologies.

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Conflicts of interest
There are no conflicts of interest.

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