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Non-neoplastic Pulmonary Hyalinising Granuloma

R. Paluri[1*], N. Paranjape[1] and A. Manne[1]

[1]University of Alabama at Birmingham, USA.

Authors' contributions

This work was carried out in collaboration between all authors. Author RP collected the data wrote the first draft of the manuscript. Author NP reviewed the draft and wrote abstract section and author AM managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Pulmonary hyalinising granuloma (PHG) is a rare, benign and non-infectious pulmonary fibrosing lesion with unknown etiology. Fewer than 100 cases have been reported thus far. PHG can mimick advanced lung carcinoma and should therefore be a part of differential diagnosis for pulmonary nodule. It is characterized by whorled deposits of collagen and hyaline. Here we report the case of a 43 years old female who presented with dyspnea and constitutive symptoms. Imaging studies revealed bilateral pulmonary nodue and the histopathology consistent with PHG.

Keywords: Pulmonary hyalinising granuloma; lung nodules; non-neoplastic hyalinizing granuloma; pulmonary granuloma.

1. INTRODUCTION

Pulmonary Hyalinizing Granuloma (PHG) is an uncommon, benign nodular fibrosing lung disease and histopathologically characterized by whorled deposits of collagen and hyaline[1]. PHG was reported for the first time by Engleman et al in 1977[2]. The exact etiology and pathogenesis of PHG remain unclear. Fewer than 100cases have been reported thus far. We present a case of PHG who was managed conservatively.

**Corresponding author: E-mail: rpaluri@uabmc.edu;*

2. CASE PRESENTATION

A 43 year-old female with a past medical history of asthma, chronic smoking for more than 20 pack years came to the emergency room with complaints of shortness of breath, non productive cough, generalized weakness and subjective fever. She was diagnosed with influenza A at an outside medical facility. No other co-morbidities were noted and no abnormalities were identified on physical examination. Plain chest roentgenograms during this admission (Fig. 1) revealed two large homogeneous circumscribed nodular lesions in the upper and lower lobes on the right and another lesion in the left mid chest laterally along with a lingular infiltrate. CT scan of chest without contrast (Fig. 2) was obtained and axial sections demonstrated multiple large lobulated masses bilaterally suspicious for metastatic disease. Percutaneous left lung core needle biopsy identified rare non-neoplastic fibrosclerosing inflammatory lung lesion. Histopathological examination revealed thick hyalinized lamellae and collagenized fibrosclerosing material along with chronic inflammatory cells consisting of lymphocytes and plasma cells (Fig. 3). These features were hightly suggestive of PHG. GMS stain was negative for fungal organisms. Pan-keratin Immunohistochemical analysis showed no

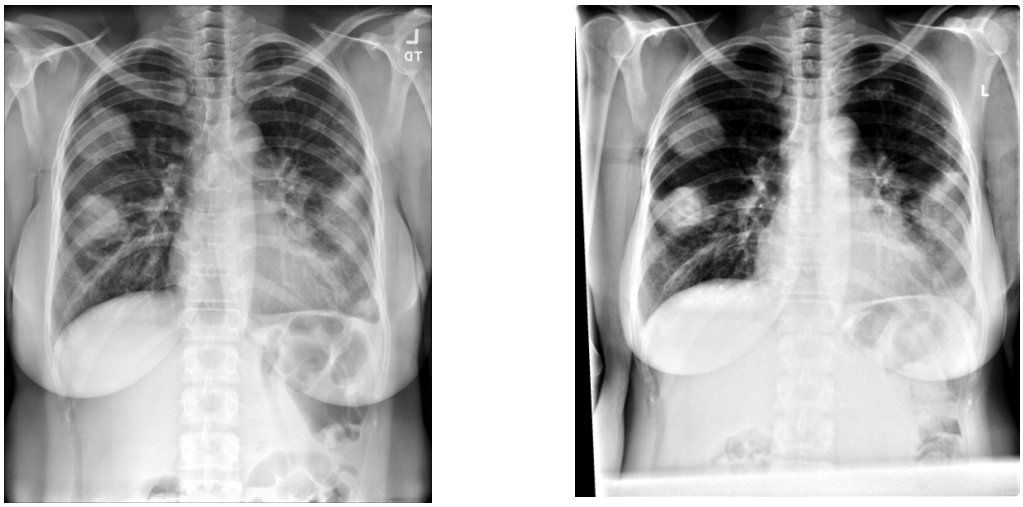

Fig. 1. Initial X-ray of chest PA views (left) and repeat X-ray after 6 months (Right)

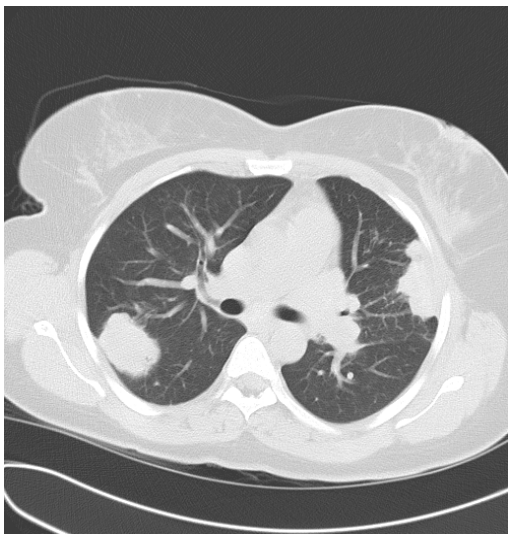

Fig. 2. CT scan of the chest demonstrating circumscribed nodules

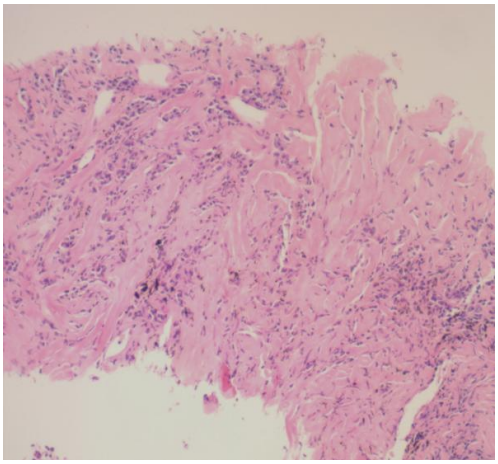

Fig. 3 A. H&E 100x- chronic inflammation and hyalinized fibrous tissue

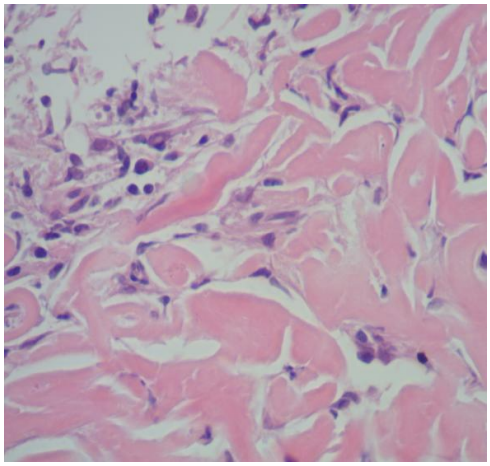

Fig. 3 B. H&E 400x- Acellular, dense, hyalinized collagen bundles and chronic inflammatory cells

evidence for underlying neoplasm. Further workup included fungal serologies for histoplasmosis, blastomycosis, coccidiodomycosis, and aspergillosis all of which were negative. HIV antibody was negative, as was tuberculin skin test, antinuclear antibody and Rheumatoid factor. ESR was slightly elevated at 53. Serum immunoglobulins showed slightly elevated IgG at 2160 (normal: 700-1600) and IgM at 307 (42 -230).

Pulmonary function tests demonstrated restrictive defectat 85%. She was treated for community acquired pneumonia and influenza A during her hospitalization. She had two subsequent follow-up visits at three month interval and reports improvement in her respiratory symptoms. The nodular lesions in chest x ray have been stable over last 6 months with no active interventions.

3. DISCUSSION

The exact etiology of PHG remains obscure. It was reported in adults between 19 and 77 yrs with no sex or racial predilection [1]. It has been postulated that it is a chronic exaggerated immune response to antigenic stimuli possibly by chronic granulomatous infections such as tuberculosis or histoplasmosis or autoimmune process [3,4]. Autoantibodies such as Rheumatoid factor and anti-nuclear antibody, coombs positive hemolytic anemia as well as circulating immunocomplexes were demonstrated in a limited number of patients in the absence of primary autoimmune condition [5,6]. Previous exposure to fungal or mycobacterial diseases have been reported to be associated with PHG [7]. A case of PHG has also been reported in a HIV/AIDS patient suggesting that it could represent noninfectious immune reconstitution inflammatory syndrome (IRIS) [8]. Associations with lymphoproliferative diseases such as Castleman's disease, lymphomas also have been reported, hypothesizing possible role of immunological reactive process [3,9]. Recent study also reported possible association with tuberculosis, autoimmune and malignant disease process [10]. Our patient likely had sporadic presentation.

Occassionally these cases are identified as incidental finding in asymptomatic patients who commonly present with unilateral or bilateral nodules[11] that are typically focal, irregular and uncalcified [12]. Cavitation has been reported rarely [13]. Positron emmistion tomography (PET scan) can show increased metabolic activity in these lesions [14]. Its presentation as bilateral nodules, as in the present case, is uncommon, a reason why many times it is misinterpreted as metastatic tumor [15]. Differential diagnosis includes but not limited to primary or metastatic malignancy such as pulmonary MALT lymphoma [16], infections such as tuberculosis, histoplasmosis or septic emboli, amyloidosis, immune disorders such as rheumatoid nodules, wegener's granulomatosis, sarcoidosis, lymphomatoid granulomatosis and plasma cell granuloma [3,5,7,17]. Final diagnosis is based on clinical and histo-pathological assessment.

Clinically, patients have nonspecific symptoms such as fever, chills, productive or nonproductive

cough, fatigue, dyspnea, pleuritic chest pain and sinusitis. Occasionally, the lesions can be incidental findings on routine chest roentgenograms. Chest radiography and CT scan usually demonstrate unilateral or bilateral, solitary or multiple well circumscribed nodular lesions and with or without amorphous calcifications [18]. Histopathology of pulmonary nodule is the gold standard for diagnosis of PHG [5]. On light microscopy, PHG consists of dense central whorled deposits of hyalinized eosinophilic lamellar collagen surrounded by perivascular lymphoplasmacytic infiltrate [19]. On electron microscopy, the hyaline lamella is characterized by amorphous, dense and compact material [20]. Typical cells within nodules include multinucleated histiocytic giant cells, plasma cells and lymphocytes. Granulomas and special stains for acid-fast bacilli and fungi are usually negative [4]. Congo red stain with polarization of light and crystal violet stain may be positive and is differentiated from amyloid by electron microscopy of hyaline lamellae which is dense, compact and amorphous in PHG and fibrillar in amyloid [5].

The clinical course of PHG is usually benign with favorable prognosis [20]. Single lesions tend to be stable and multiple lesions may be enlarged progressively over several years. Spontaneous regression was also described although it may take several years [5]. However, three patients with PHG were preveiously reported to have progressed to sclerosing mediastinitis and retroperitonitis [2]. Single lesions are often curable by resection. Recurrence was noted in few cases previously [21]. However, there is no definitive treatment for multiple nodules. Some studies reported glucocorticoids for resolution [22]. Management includes symptomatic treatment and monitoring every three to six months for disease progression.

4. CONCLUSION

PHG is relatively an uncommon disease presentation with non specific respiratory symptoms and has benign clinical course. It should be a part of differential diagnosis for nodular or cavitary pulmonary lesions.

CONSENT

As per international standard or university standard written patient consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical permission has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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