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Case Report

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Pulmonary Hyalinizing Granuloma with Negative IgG4 In Serum and Tissue: A Case Report

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Abstract

Pulmonary hyalinizing granuloma (PHG) is defined as IgG4 related sclerosing disease, which typically presents with fibrosclerotic inflammatory and lymphocytic infiltration and characterizes by IgG4+ plasma cells in serum and histopathology. Here, we report a case of a 46-year-old-man with a history of cough, dry eye and asbestos exposure for twenty years. Nodular lesions were detected accidentally in the right lung. The serological and bronchoalveolar lavage fluid tests showed no clinically detectable aetiology. The lesions had a maximum standardized uptake value (SUVmax) ranging from 2.5 to 4.2 by 18-fluorodeoxyglucose positron emission tomography (FDG-PET) and suspected pulmonary malignancy on computed tomography (CT) imaging. Eventually, the patient underwent thoracoscopic surgery. The pathology indicated hyalid granuloma surrounded by interstitial lymphocyte proliferation with negative IgG4 staining in tissue. It is different from previous reports showing the histologic characterizes of PHG with serum and tissue IgG4-positive plasma cells. This case presents a patient with PHG mimicking malignancy on CT imaging and displays the current manifestation of dual-negative serum and tissue IgG4 plasma cells in PHG.

Keywords: *Pulmonary Hyalinizing Granuloma, lung cancer, IgG4, CT imaging.*

Introduction

Pulmonary Hyalinizing Granuloma (PHG) is a rare benign tumor, characterized by frequently asymptomatic manifestation and slightly more multiple nodules with no preferential sites. It is no apparent differences in gender and age at onset [1, 2]. The clinical symptoms of PHG are atypical and easily missed, such as fever, cough, fatigue, dyspnea, chest pain, sinusitis. In previous reports, abnormality of an immune response, such as antigenic infection [1] and autoimmune disease [3], might be involved in the pathogenesis of PHG. The PHG usually overlap with IgG4-related sclerosing disease, both serum and tissue IgG4 positive staining [4]. It is associated with sclerosing mediastinitis and retroperitoneal fibrosis, both of which may suggest a similar fibrotic response to infectious triggers. However, the critical pathogenesis of PHG is unclear. Disturbingly, it is indeed a tricky bug for clinics to establish the condition because of the bewildering malignant features on radiographic images, namely malignant masquerade, especially accompanying signs of the vascular cluster, lobulation and multiple nodules. Here, we report a case of PHG presenting with negative IgG4-plasma cells in local lesions and serological IgG4- tests.

Case report

A 46-year-old man, a non-smoker with a history of gouty arthritis treated with uric acid-lowering drugs, was presented to the clinic to evaluate and treat multiple slow-growing lung nodules, especially in the right upper lobe. Unfortunately, he lost the radiographic imaging a year ago. He has been exposed to asbestos for twenty years. He denied fever, night sweats, chest pain, blood-tinged sputum or weight loss, except irritating cough and dry eye. The chest CT scan showed lesions in the right lung were characterized by vascular cluster and small burrs on the edges. The size was 20.5×14.8 mm, 9.0×9.8 mm and 11.8×11.0mm, respectively, and no mediastinal and hilar lymphadenopathy and pleural thickening or effusion as well (Fig. 1A). He was taken antibiotic treatment for two weeks. In Jun. 2020, Scan with 18-fluorodeoxyglucose positron emission tomography and computed tomography (18-FDG-PET/CT) outside our hospital showed nodules in

the right lobe was slightly enlarged. The size was 21.5×15.0 mm, 16.2×12.2mm and 12.3×12.0mm, respectively, and the SUVmax were 4.2, 3.0 and 2.5, respectively (Fig. 1B).

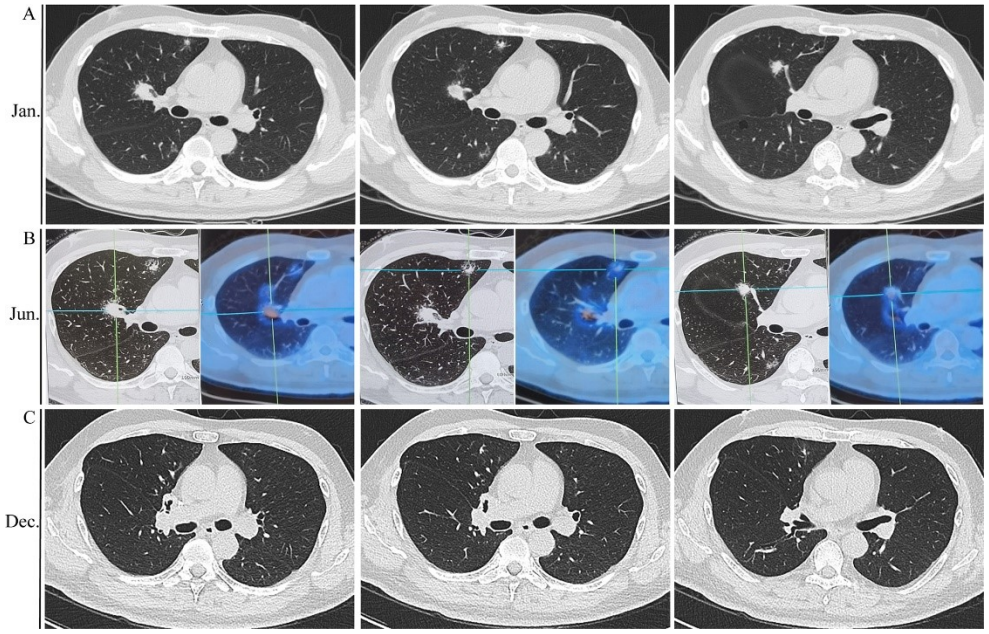

Figure 1: Thoracic CT images. A. Chest CT scan showing three nodular lesions with vascular cluster and small burrs on the edges on Jan. 2020. B. PET/CT showing slightly growing lesions on Jun.2020, before the surgery. C. Chest CT scan showing no local recurrence on Dec.2020, after the surgery.

The blood tests showed an elevated level of alanine aminotransferase (ALT), aspartate transaminase (AST) and uric acid (UA), ALT was 84 (normal 9~50U/L), and AST was 50 (normal 15~40U/L), UA was 0.524 (normal 0.100~0.420 mmol/L), WBC, RBC, PLT, creatinine level was normal. The erythrocyte sedimentation rate (ESR) was 31 (normal ≤15mm/h). The results of serology panels were as follows: Antinuclear antibody 1:100 (normal＜1:100), anti-SSA 153 (normal≤25), other biomarkers including serum IgG4, rheumatoid factor, anti-dsDNA, anti-Sm, anti-SS-B, anti-nRNP, anti-Ro52, anti-Scl-70, anti-Jo1, ANCA, MPO/PR3 were negative or normal. Serum immunoglobulins showed normal total IgG of 15.80 (normal, 7 to 16 g/L), IgG4 of 0.956 (normal, 0.03 to 2.01 g/L). Classification of Lymphocyte type was normal. Etiological tests, such as Aspergillus, Cryptococcus, Candida, Tuberculosis, HIV, Syphilis, and Hepatitis B virus, were also negative. A pulmonary function showed no signs of obstruction or restriction and diffusion dysfunction.

The patient underwent right upper lobectomy along with hilar lymph node dissection because of suspected malignancy clinically. Microscopically (Figure 2), the nodules indicated proliferative collagen fibres with polyclonal lymphocytic infiltrate and occasional formation of lymphoid follicles plasma cells. The hyaline lesion in the center was interspersed with the macrophages. No epithelioid cells were seen. Immunohistochemical results showed negative tissue IgG4 staining. Elastic fibres, acid-fast, and Periodic Acid-Schiff staining were negative. Because of the manifestation of dry eye and positive anti-SSA, we also underwent labial gland biopsy. The biopsy showed no evidence of Sjogren's syndrome. Thus, the patient received no subsequent particular drugs and followed up regularly. Six months after the pulmonary resection, the chest CT scan showed no increased nodules or local recurrence (Figure 1C).

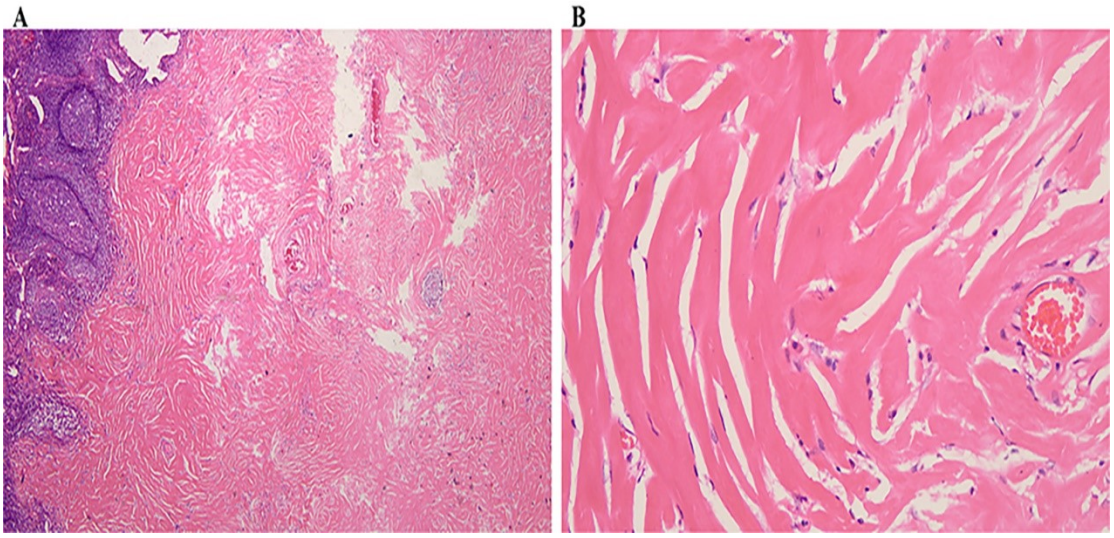

Figure 2: Histopathology of the biopsy on the right lung. It shows that a mass composes of dense, lamellar bands of collagen around small blood cessels in association with scattered lymphoplasmacytic infiltrates at the margin of the nodules. No epithelioid cells were found. (Hematoxylin and Eosin staining, A: × 20, B: × 200).

Discussion

It presents primary PHG with a history of asbestos inhalation and exposure for twenty years. The level of IgG4 expression in serum and tissues were negative, which is different from the previous report [4]. PHG was first reported in 1977 by Engleman [2]. Pathologically, it manifests as a nodular hyalinizing fibrotic reaction with dense, thickened, collagenous bundles. In these established twenty cases, 5/20 patients showed a history of tuberculosis infection or response to PPD tests, and 4/20 had sclerosing mediastinitis with 2/4 positive cutaneous response to Histoplasma, and 2/20 had a 'vasculitis'. The histological features share a twin-like resemblance to sclerosing mediastinitis [5]. The aetiology infection (such as Tuberculosis, Histoplasma) and immune imbalance reaction to endogenous or exogenous antigen played an essential role in the pathogenesis of PHG. D.C. Schlosnagle found that autoantibodies and circulating immune complexes in PHG patients [3]. It has been drawn attention that people with Sclerosing mediastinitis, Sjogren's syndrome, rheumatoid arthritis and other autoimmune diseases prone to suffer PHG [6].

In this case, we also examined some elevated serological biomarkers, including antinuclear antibody, anti-SSA. It indicates the abnormality of an immune response. Microscopically, no epithelioid cells or granulomas were found in the lesion; however, scattered plasma cells and polyclonal cells infiltrate in the periphery. The hyaline lesion in the centre was interspersed with the macrophages. Because of long-term inhalation and exposure to asbestos, we should consider the potential triggering or pathogenic factors of asbestos in the development of PHG.

It has been reported that PHGs manifests as multiple or solitary pulmonary nodules with well-defined borders and multiple lesions measuring 2~4cm on radiologic imaging [1]. Cavity formation and calcification have been described. Reported hyalinizing granuloma in extrapulmonary organs includes mediastinum, lymph nodes [7]. The differential diagnostic considerations include primary or metastatic neoplasia, granulomatous disease, vasculitis, and infection [8, 9]. FDG-PET is commonly used to distinguish benign and malignant lung tumor with more than 90% sensitivity and specificity [10, 11]. SUV uptake in lung neoplasm is associated with high tumor proliferation and activation, and a high SUV forebodes poor prognosis [10-12]. It has been reported that 6/15 cases of PHG have an increased uptake of FDG ranging from 2.2 to 9.6[1]. This patient has a SUVmax of 4.2 in concordance with other benign tumor mimicking malignancy [9]. Thus, comprehensive clinical, laboratory and metagenomic analysis of the patients' samples are an integral part of verifying the diagnosis of PHG.

There is no definitive treatment for PHG, although the successful resolution of PHG with the usage of glucocorticoids has been reported [13, 14]. Because of inter-lobar parenchymal infiltration and irregular or indistinct borders on chest X-ray representing the characteristic features of lung cancer, most patients underwent thoracoscopic surgery, as in this case. One postoperative point with autoimmune thyroiditis relapsed after two years of follow-up [15]. The patients in this case also follow up regularly after surgery. Until now, there are no signs of recurrence after ten months. More data toward the period of follow-up and points of postoperative precautions need to be established. PHG patient prognosis is generally excellent with non-fatality except for multiple nodules and complication with other diseases.

In summary, we reported an unusual case of PHG without other diseases, except that the pulmonary nodule has apparent signs of suspected malignancy on chest radiologic imaging. No exact infection and rheumatic-immune illness were beginning to emerge. As the abnormality of serological immune biomarkers existed, we speculate that an imbalance of immunity plays a role in this disease. We should consider the PHG as a differential diagnosis of pulmonary lesions, especially the slow-growing nodules or mass.

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Availability of data and materials
These data collected and analyzed during this study are included in this published article.

Authors' contributions
RYY, DBZ and NZ conceived and led the preparation of the manuscript and performed the literature search. PZ collected the data, organized and analyzed the figures. ZWZ prepared the immunohistochemical analysis. SQL designed the study and edited the manuscript. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate
Not applicable.

Patient consent for publication
Informed consent for all data and clinical history was obtained from the patient.

Competing interests
The authors declare that they have no competing interests.

References

1. Lhote R, Haroche J, Duron L, Girard N, Lafourcade MP, Martin M, Begueret H, Taytard A, Capron F, Grenier P, Piette JC, Cohen-Aubart F, Amoura Z. Pulmonary hyalinizing granuloma: a multicenter study of 5 new cases and review of the 135 cases of the literature. Immunol Res 2017, 65(1): 375-385.
2. Engleman P, Liebow AA, Gmelich J, Friedman PJ. Pulmonary hyalinizing granuloma. Am Rev Respir Dis 1977, 115(6): 997-1008.
3. Schlosnagle DC, Check IJ, Sewell CW, Plummer A, York RM, Hunter RL. Immunologic abnormalities in two patients with pulmonary hyalinizing granuloma. Am J Clin Pathol 1982, 78(2): 231-235.
4. Chapman EM, Gown A, Mazziotta R, Churg A. Pulmonary hyalinizing granuloma with associated elevation in serum and tissue IgG4 occurring in a patient with a history of sarcoidosis. Am J Surg Pathol 2012, 36(5): 774-778.
5. Chalaoui J, Gregoire P, Sylvestre J, Lefebvre R, Amyot R. Pulmonary hyalinizing granuloma: a cause of pulmonary nodules. Radiology 1984, 152(1): 23-26.
6. Winger DI, Spiegler P, Trow TK, Goyal A, Yu H, Yung E, Katz DS. Radiology-Pathology Conference: pulmonary hyalinizing granuloma associated with lupus-like anticoagulant and Morvan's Syndrome. Clin Imaging 2007, 31(4): 264-268.
7. Kamona A, Al Lawati F, Kamona A, Al Busaidi N, Al Mahrooqi Y, Al-Tai S, Al Lawati N, Al-Umairi RS. Pulmonary Hyalinising Granuloma: A report of two cases. Sultan Qaboos Univ Med J 2019, 19(2): e157-e160.
8. Long NM, Smith CS. Causes and imaging features of false positives and false negatives on F-PET/CT in oncologic imaging. Insights Imaging 2011, 2(6): 679-698.
9. Zhou D, Xing X, Fan J, Zhang Y, Liu J, Gong Y. PD-1/PD-L1 negative schwannoma mimicking obstructive bronchial malignancy: A case report. Thorac Cancer 2020, 11(8): 2335-2338.
10. Kandathil A, Kay FU, Butt YM, Wachsmann JW, Subramaniam RM. Role of FDG PET/CT in the Eighth Edition of TNM Staging of Non-Small Cell Lung Cancer. Radiographics 2018, 38(7): 2134-2149.
11. Budak E, Çok G, Akgün A. The Contribution of Fluorine 18F-FDG PET/CT to Lung Cancer Diagnosis, Staging and Treatment Planning. Malecular Imaging and Radionuclide Therapy 2018, 27(2): 73-80.
12. Pleitz JL, Sinha P, Dressler EV, Aouad RK. Correlation of Positron Emission Tomography/Computed Tomography Scan with Smoking, Tumor Size, Stage and Differentiation in Head and Neck Cancer Patients. World J Nucl Med 2017, 16(1): 51-55.
13. Shinohara T, Kaneko T, Miyazawa N, Nakatani Y, Nishiyama H, Shoji A, Ishigatsubo Y. Pulmonary hyalinizing granuloma with laryngeal and subcutaneous involvement: report of a case successfully treated with glucocorticoids. Intern Med 2004, 43(1): 69-73.
14. Cunha AD, Melo N, Guimaraes S, Moura CS, Pereira JM, Morais A. Pulmonary hyalinizing granuloma: Atypical presentation. Pulmonology 2020.
15. Fidan A, Ocal Z, Caglayan B, Dogusoy I, Gumrukcu G. An unusual cause of pulmonary nodules: Pulmonary hyalinizing granuloma with recurrence. Respiratory Medicine Extra 2006, 2(4): 112-115.