A Case of Pulmonary Hyalinizing Granuloma Associated with Posterior Uveitis

HIDIR ESME, SITKI SAMET ERMIS,1 FATMA FIDAN,2 MEHMET UNLU2 and FATMA HUSNIYE DILEK3

Departments of Thoracic Surgery, 1Ophthalmology, 2Chest Disease, and 3Pathology, Afyon Kocatepe University, Faculty of Medicine, Afyon, Turkey

ESME, H., ERMIS, S.S., FIDAN, F., UNLU, M. and DILEK, F.H. A Case of Pulmonary Hyalinizing Granuloma Associated with Posterior Uveitis. Tohoku J. Exp. Med., 2004, 204 (1), 93-97 — A 48-year-old male was admitted to our hospital because of abnormal pulmonary shadows and a decrease in visual acuity. He had a history of tuberculosis 20 years ago. The chest roentgenogram showed multiple pulmonary nodules throughout both lung fields. No definitive diagnosis was established either by brushing cytology or biopsy through bronchoscopy or percutaneous needle biopsy. Pathological examination of open lung biopsy specimen revealed that extensive, hyalinized lamellar collagen bundles arranged in whorls, parallel arrays. Plasma cells and lymphocytes were found between the collagen bands and germinal centers were seen at the periphery of the lesion. A definitive diagnosis of pulmonary hyalinizing granuloma was made on the basis of these histopathological findings. Although there is no established treatment for pulmonary hyalinizing granuloma, during 1 month of follow-up, posterior uveitis mildly resolved with glucocorticoid treatment and there had been a slight increase in visual acuity. pulmonary hyalinizing granuloma; open lung biopsy; posterior uveitis © 2004 Tohoku University Medical Press

Pulmonary hyalinizing granuloma (PHG) was described by Engleman et al. (1977). It is a rare disease characterized by multiple bilateral pulmonary nodules. The nodule is usually 2 to 4 cm in diameter, although larger lesions have been reported, and some are cavitary. In many cases, multiple lesions are present, simulating metastatic tumors. The nodules are typically benign in histology and clinical course, but slowly grow in size and number. Because of their behavior and to rule out a malignancy, biopsy is required to establish the primary diagnosis of PHG (Ren et al. 2001).

Although PHG has occurred with tuberculo-
sis (Engleman et al. 1977), aspergillus infection (Pinckard et al. 2003), rheumatoid arthritis (Kalifa et al. 1976), multiple sclerosis (John et al. 1995), pulmonary small lymphocytic lymphoma (Ren et al. 2001), and various other diseases, we have not found the association of PHG with posterior uveitis described in the medical literature. We present the first case of PHG and concomitant posterior uveitis of the eye.

**CASE REPORT**

A 48-year-old-white man consulted to Ophthalmology department of our hospital with at least 2 years history of posterior uveitis, multiple bilateral pulmonary nodules and without respiratory symptoms. He had no fever, malaise or weight loss. He had a history of tuberculosis 20 years ago and had been treated with antituberculosis therapy and received right upper lobectomy because of a thick-walled cavity. He admitted to a 22 pack-year history of cigarette smoking but denied any inhalational occupational or recreational exposures.

On physical examination, the patient’s blood pressure was 110/70 mmHg, pulse rate 88/minute, and respiratory rate was 20/minute. Best corrected visual acuity was bilaterally 0.6. Intraocular pressure was measured 14 mmHg in the right eye, and 16 mmHg in the left eye. Examination of vitreous revealed a moderate degree of vitreous cells bilaterally. A cotton-wool spot and half optic-disc sized retinal hemorrhage were observed in the posterior pole of the right eye. Vasculitis was observed in the macula of the left eye. Retinal periphery and optic disc examinations using a Goldmann triple mirror contact lens appeared normal. The ears, nose, and throat appeared normal, and chest, cardiovascular, and general physical examinations were unremarkable.

Laboratory studies, including a complete blood count and serum chemistry profile, yielded normal values. Antinuclear antibody and rheumatoid factor antibody testing was positive, and the patient’s angiotensin-converting enzyme level was normal. Pulmonary function tests performed at our institution revealed FVC of 2.84 liter (67% predicted), FEV1 of 2.26 liter (63% predicted), and FEV1/FVC ratio of 76% (89% predicted).

Chest roentgenograms and computed tomography (CT) scans showed pulmonary nodules throughout both lung fields (Fig. 1). Flexible fiberoptic bronchoscopy showed edematous airways but no endobronchial lesions, and transbronchial biopsy showed mild bronchial inflammation.

![Fig. 1. Pulmonary multiple nodules.](image)
Microbiologic studies of the broncho-alveolar lavage specimen were negative for acid-fast bacilli, bacteria, and fungus. All culture findings were negative. No aberrant or malignant cells were present in the bronchial washings. Transthoracic biopsy was negative. Via limited mini-thoracotomy, a tan nodule measuring 2.0 to 3.0 cm in diameter was excised by wedge resection from right lower lobe, which grossly consisted of normal lung parenchyma containing white, firm, well-circumscribed nodule, 2.5 cm in diameter. Microscopically, nodular lesion was surrounded by massive lymphoid cells which formed germinal centers. It consists of thick hyalinizing collagen bands arranged in whorls, parallel arrays, or vague storiform pattern (Fig. 2). There were plasma cells and lymphocytes between the collagen bands. A few bronchiolar and vessel walls and lymphoid nodules were observed in the lesion. The histological findings are consistent with PHG.

The postoperative course was uneventful. The patient was discharged 5 days after surgery. Vitreous cells decreased after surgery with 1 month use of glucocorticoid treatment (Oral fluorocortolone 1 mg/kg/day) and there had been a slight increase in visual acuity, but there had been no reduction in the size of the pulmonary lesions.

**DISCUSSION**

PHG is a rare lung disease of unknown etiology and pathogenesis. Both sexes are equally affected, ages ranging from twenties to eighties. More than half of the patients have autoimmune phenomena or previous exposures to mycobacterial or fungal antigens (Yousem and Hochholzer 1997; Ren et al. 2001). Clinically, the condition may be asymptomatic, but most of the patients complain of cough, chest pain, and shortness of breath. Our patient did not present respiratory symptoms and had a history of tuberculosis 20 years ago.

Chest radiographs show homogeneous round nodules, 2 to 4 cm in diameter, but in rare instances they can be much larger. The nodules are often multiple and bilateral. Occasionally calcification or cavitation is present (Patel et al. 1991). The CT scan of our patient’s chest documented multiple parenchymal and subpleural nodules without cavitations and calcification.
The etiology of PHG is unknown. There is theoretical consideration of a possible strong antigenic challenge that produces a chronic immune response, which provokes the development of PHG nodules. Up to 60% of patients with PHG reported have serologic evidence of an autoimmune disorder including antinuclear, antismooth muscle antimicrosomal or antithyroglobulin antibodies and rheumatoid factor (Schlosnagle et al. 1982; Ren et al. 2001). However, it remains unclear whether autoimmunity is a predisposing factor or a consequence of PHG. Since sclerosing mediastinitis and retroperitoneal fibrosis are frequently associated with PHG, it has been hypothesized that all of these conditions may present essentially the same reactive response of an immunologic mechanism triggered by histoplasma organisms, tuberculosis bacilli, or other infectious agents (Engleman et al. 1977; Chalaoui et al. 1984). Nevertheless, no consistent relationship has been found to exist between PHG and any particular infection or immune process. Ultrastructural studies have not shown any specific features or provided clues to the aetiology and pathogenesis of this disease.

The differential diagnosis includes infective chronic granulomatous disease, including tuberculosis and histoplasmosis, inflammatory pseudotumours, nodular amyloidosis, rheumatoid nodule, solitary fibrous tumor of pleura, nodular sclerosing Hodgkin’s disease, sclerosing non-Hodgkin’s lymphoma and Wegener’s granulomatosis. The patient was diagnosed with posterior uveitis. In the differential diagnosis, tuberculosis was not likely since the pulmonary infection was successfully treated 20 years ago and the posterior uveitis improved with the use of corticosteroids. Other causes of posterior uveitis were eliminated by clinical examinations and hematological tests.

Diagnosis of PHG requires histological examination of an adequate specimen, usually obtained by open lung biopsy. Macroscopically, hyalinizing granuloma appears as a sharply circumscribed white-tan rubbery mass. With light microscopy, PHG contains lamellae of homogenous hyaline material, with interspersed plasma cells, lymphocytes, and giant cells. In early active lesions, the cellular components predominate, while the collagenous lamellar bands are more prominent in old chronic lesions (Ren et al. 2001). Although lamellar hyaline collagen arrayed in a disorderly, whorled, storiform pattern is characteristic of PHG, the histopathologic differential diagnosis includes a number of reactive and inflammatory lesions. Pulmonary nodular amyloidosis can present with multiple nodules, but microscopically the nodules are composed of globular eosinophilic material without lamellar collagen bundles. Involuting plasma cell granuloma and intrapulmonary fibrous tumor are clinically solitary lesions, but both microscopically lack the lamellar collagen bundles typical of PHG. The lesions of Wegener’s granulomatosis and histoplasmosis, as well as rheumatoid nodules, typically contain a central necrotic core surrounded by a rim of palisading histiocytes, features not associated with PHG (Ren et al. 2001; Pinckard et al. 2003).

Prognosis generally considered benign, but 30% of patients with PHG may have progressive disease manifested by enlarging nodules and increasing dyspnea (Yousem and Hochholzer 1997). Engleman et al. (1977) reported sclerosing mediastinitis developed in 4 of the 20 patients.

Shinohara et al. (2004) reported that although there is no established treatment for PHG, the laryngeal tumor diminished and all other lesions disappeared with glucocorticoid treatment. During 1 months of follow-up in our patient, the posterior uveitis mildly resolved with glucocorticoid treatment.

In summary, pulmonary hyalinizing granuloma itself is a rare benign disease and is important in the differential diagnosis of lung diseases showing multiple pulmonary nodules. The extrapulmonary involvement is seen in about 20% of the reported cases of PHG. The association of pulmonary hyalinizing granuloma with posterior uveitis could be coincidental, but since there is a possibility of immune reaction in the pathogenesis
of both diseases, the association is of particular significant.

References


