Pulmonary Hyalinizing Granuloma with Laryngeal and Subcutaneous Involvement: Report of a Case Successfully Treated with Glucocorticoids

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Abstract

We report a case of pulmonary hyalinizing granuloma (PHG) with laryngeal and subcutaneous involvement. A 43-year-old man was admitted to our hospital for assessment of hoarseness. Cervical and chest computed tomography, respectively, revealed a laryngeal tumor and two pulmonary masses. Specimens obtained from the pulmonary masses were compatible with PHG. The histopathology of biopsy specimens from both the laryngeal tumor and a subcutaneous tumor resembled that of the resected lung masses. Although there is no established treatment for PHG, the laryngeal tumor was diminished and all other lesions disappeared with glucocorticoid treatment.

Key words: pulmonary hyalinizing granuloma, inflammatory pseudotumor, human herpesvirus-8, systemic idiopathic fibrosis, mediastinal fibrosis

Introduction

Pulmonary hyalinizing granuloma (PHG) is a very rare disease with a distinct fibrosing lesion of the lung characterized by central whorled deposits of lamellar collagen. It is a histopathologic syndrome of unknown etiology for which there is no established treatment (1). PHG is sometimes accompanied by extrapulmonary fibrous lesions at other sites, including kidney, tonsil, and thyroid glands (2). However, the coexistence of laryngeal and subcutaneous involvement in PHG has not been reported. To our knowledge, this is the first encounter with a case of PHG accompanied by laryngeal and subcutaneous involvement.

Case Report

A 43-year-old man was referred to the department of otorhinology of our hospital in June 1999 with a 3-month history of hoarseness. He had an unremarkable disease history and was on no medication. He had smoked half a pack of cigarettes a day for 20 years. Cervical computed tomography (CT) revealed a laryngeal tumor, which was biopsied under laryngoscopy (Fig. 1). Microscopically, the tumor was composed of fibrous tissue with infiltration of chronic inflammatory cells. No malignant cells were found. A chest radiograph on admission showed two masses in the left middle lung field. On chest CT, one mass was located in the left S3 and the other in the left S5 (Fig. 2). Gallium scan showed gallium uptake at the middle neck and 2 areas of uptake in the lung (Fig. 3). Abnormality was not found on abdominal CT. Although transbronchial and percutaneous lung biopsies were performed, no definitive diagnosis could be made. Since the possibility of lung cancer could not be excluded, left upper lobectomy was performed in January 2000. Histopathologically, the masses were composed of bundles of dense lamellar hyalinized tissue aligned in whorls and streams without central necrosis or calcification. Along with hyalinizing fibrosis, dense infiltrates of lymphocytes, plasma cells with frequent lymph follicle formation, and spindle-shaped stromal cells were seen (Fig. 4A, B). The inflammatory cells and spindle-shaped stromal cells showed no atypia. There were no granulomatous lesions. Special stains for fungi and acid-fast bacilli were negative. Congo red stain for amyloid was negative. On immunohistochemical analysis, the plasma cells showed the polyclonal pattern for lambda and kappa light chains.

The laryngeal tumor gradually grew after lung resection,
and tracheal stenosis increased. Tracheostomy and biopsy of the laryngeal tumor were therefore performed in July 2000. Pyrexia over 38°C appeared after the tracheostomy and lasted about 1 month. Histopathologically, the laryngeal tumor showed hyalinizing fibrosis with scattered plasma cells, resembling the resected lung masses (Fig. 5A, B). A short while after the biopsy, a soft tissue density lesion attached to the left chest wall, together with cardiac effusion and pleural effusion, was observed on chest CT. There was also a high density area in the adipose tissue of the anterior mediastinum on chest CT. This lesion was compatible with mediastinal fibrosis (Fig. 6). A subcutaneous tumor also appeared in the left forearm; this tumor was also biopsied. The microscopic features of the subcutaneous tumor also resembled those of the resected lung masses. A final diagnosis of PHG with laryngeal and subcutaneous involvement was made on the basis of the histopathology of the resected lung masses and the laryngeal and subcutaneous tumors, as well as the clinical manifestations.

Steroid pulse therapy (methylprednisolone 1 g/day for 3 days) was initiated in mid-August 2000, followed by a supplement of prednisolone (PSL) (60 mg/day). The dose of PSL was then gradually tapered. One month later, the laryngeal tumor had diminished and all other lesions including the subcutaneous tumor, the lesion attached to the left chest wall, the high density area in the anterior mediastinum, the cardiac effusion and pleural effusion observed on CT had disappeared. The patient was discharged in November 2000 on oral PSL at a dose of 25 mg/day. Two years after initiation of steroid therapy, the patient is taking PSL at a dose of 7.5 mg/day.

Figure 1. Cervical CT showing a tumor in left side of the larynx. Laryngoscope revealed the submucous tumor lesion in the arytenoid cartilage.

Figure 2. A chest radiograph on first admission disclosing 2 dense infiltrations in the left middle lung field. On chest CT, these infiltrations were recognized as 2 masses, 1 in the left S3 and the other in the left S5.
mg/day, with no evidence of recurrence.

**Discussion**

The patient was diagnosed as PHG with laryngeal and subcutaneous involvement, on the basis of both the histopathologic findings and clinical features. With regard to the intrapulmonary lesions, inflammatory pseudotumor (IPT) should be considered as a differential diagnosis because the healing stage of IPT sometimes resembles that of PHG. It has been reported that in the larger lesions of IPT there may be hyalinized fibrosis, which is characteristic of PHG (2). Clinically, IPT most often produces a solitary lesion (1), but PHG usually produces multiple intrapulmonary lesions (3). IPT patients rarely have both extrapulmonary and intrapulmonary lesions (4). In contrast, about 20% of PHG patients sometimes have mediastinal or retroperitoneal fibrosis (2). It has also been reported that PHG is accompanied by fibrous lesions at other sites, including the kidney, tonsil, and thyroid glands (2). Recently, the presence of human herpesvirus-8 (HHV-8) DNA sequences in a patient with IPT has been reported (5). In the present patient, the serum antibody titer against HHV-8 and gene expression of HHV-8 in the resected lung were negative. By combining all of this evidence, we were able to diagnose our patient with PHG.

Regarding extrapulmonary lesions, the case encompassed a variety of fibrous lesions including mediastinal, laryngeal and subcutaneous fibrosis. It is well known that idiopathic retroperitoneal fibrosis may be accompanied by similar fibrotic lesions in other sites, including the mediastinum, thyroid, orbit and extrahepatic biliary tree (6, 7). Such accompanying lesions are regarded as systemic idiopathic fibrosis (2, 6, 7). Although the pathogenesis of systemic idiopathic fibrosis is obscure, several case reports of idiopathic fibrosis include hypersensitivity reaction to insoluble

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**Figure 3.** Gallium scan revealing gallium uptake at larynx and 2 gallium uptake in the lung (arrows).

**Figure 4.** Histopathology of the pulmonary mass in the left S3. Dense infiltrates of lymphocytes with frequent formation of lymph follicles, plasma cells, and spindle-shaped cells were seen in association with hyalinizing fibrosis (A; HE stain, ×16). Bundles of lamellar hyalinized fibrosis were remarkable (B; HE stain, ×40).
lipids, immune complex glomerulonephritis, circulating immune complexes, and vasculitis (8, 9). This supports the possibility that systemic idiopathic fibrosis is under autoimmune disorders. Since the presence of the retroperitoneal fibrosis was not confirmed and such autoimmune disorders were not found in this case, this case was not diagnosed as systemic idiopathic fibrosis. However, Kuramochi et al recently suggested that PHG may be a condition belonging to systemic idiopathic fibrosis (2). It thus seems reasonable to recognize that the fibrous lesions in the present case including larynx, skin, mediastinum and lung are manifestations of the same disease like systemic idiopathic fibrosis.

It has been reported that the prognosis of PHG with a single lesion is curable if the lesion is completely resected (10). In contrast, cases with multiple lesions may be progressive (10). Although the effectiveness of glucocorticoids in PHG has not been fully established, all of the present patient’s lesions, including both the intrapulmonary and extrapulmonary manifestations, responded to glucocorticoid treatment. This strongly supports that the intrapulmonary and extrapulmonary lesions were multi-organ expressions of the same systemic immunological abnormality.

In summary, the present patient was diagnosed as PHG accompanied by laryngeal and subcutaneous involvement. To our knowledge, this is the first report of PHG with laryngeal and subcutaneous fibrosis. Both the intrapulmonary and extrapulmonary multiple lesions were successfully treated with glucocorticoids. It remains to be elucidated whether glucocorticoids are equally effective for the treatment of PHG in general.

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References

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