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CASE REPORT

Pulmonary and thymic lymphoid hyperplasia in primary Sjögren's syndrome

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Abstract Pulmonary and thymic lymphoid hyperplasia with characteristic clinicoradiological manifestations were seen in a 71-year-old woman who was diagnosed with primary Sjögren's syndrome. A hazy opacity 12 mm in diameter and an anterior mediastinal nodule 20 mm in diameter were incidentally detected on computed tomography. Thoracoscopic biopsy revealed lymphoid hyperplasia in the lung accompanying thymic lymphoid hyperplasia. Immunohistochemically, the pulmonary lesion was considered to be nodular lymphoid hyperplasia (NLH), not lymphoma. A previously undescribed finding in the NLH was the hazy opacity containing an air bronchiologram, not a solid nodule. This finding might suggest a common causal relation for NLH, thymic hyperplasia, and primary Sjögren's syndrome.

Key words Bronchiolocentric distribution · Ground-glass opacity · Nodular lymphoid hyperplasia · Sjögren's syndrome · Thymic lymphoid hyperplasia

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Introduction

Abbondanzo et al. summarized the pathological properties of nodular lymphoid hyperplasia (NLH) and clarified the entity and associated terminology.[1] However, the clinicoradiological features of NLH are not fully understood, as fewer than 20 cases have been accumulated in the literature. We present herein a case of NLH displaying computed tomographic (CT) characteristics not previously mentioned. Moreover, the patient displayed concomitant lesions of thymic lymphoid hyperplasia and primary Sjögren's syndrome.

Case

Nodular lesions were detected incidentally on CT scans during a health checkup of a 71-year-old woman. Chest radiographs could not identify the problem. She complained of a slightly dry mouth but no respiratory symptoms. The Schirmer test, salivary scintigraphy, and antibodies to Ro (SSA) and La (SSB) antigens all showed abnormalities. Primary Sjögren's syndrome was diagnosed.[2] Lip biopsy demonstrated polyclonal lymphocytic infiltration. Neither dysproteinemia nor antibody to human immunodeficiency virus or Epstein-Barr virus was detected.

High-resolution CT (2 mm collimation, original field of view 12 cm) of the chest demonstrated localized ground-glass attenuation in the right lower lobe with a diameter of 12 mm, containing an air bronchiologram (Fig. 1). The lesion showed a slightly irregular contour and had a CT appearance similar to that of nonmucinous bronchioloalveolar carcinoma but distributed around a bronchiole. Moreover, an anterior mediastinal

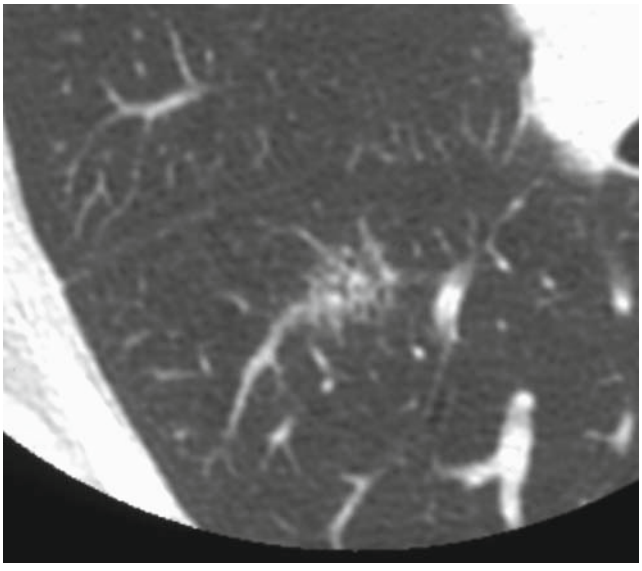

Fig. 1. Targeted high-resolution computed tomography (CT) of the right lower lobe with a slice thickness of 2 mm. Localized ground-glass opacity with a diameter of 12 mm containing an air bronchiologram and irregular contour. Original field of view was 12 cm

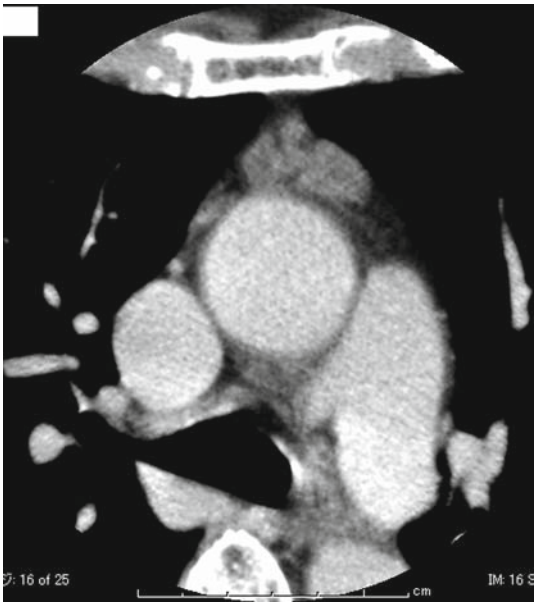

Fig. 2. Enhanced CT of the mediastinum showing an anterior mediastinal nodule ($20 \times 8 \times 14$ mm) with an irregular multilobular rim. After administration of 50 ml of contrast material infused during 30 min, the lesion attenuation was elevated from 35 HU to 81 HU. The thymus was thought to be included in the nodule

nodule with a $20 \times 8 \times 14$ mm and irregular multilobular rim showing inhomogeneous internal intensity was located between the sternum and ascending aorta (Fig. 2). No hilar lymphadenopathy was apparent. The presence of primary Sjögren's syndrome suggested that both the pulmonary and mediastinal lesions were related to lymphoproliferative disorders.

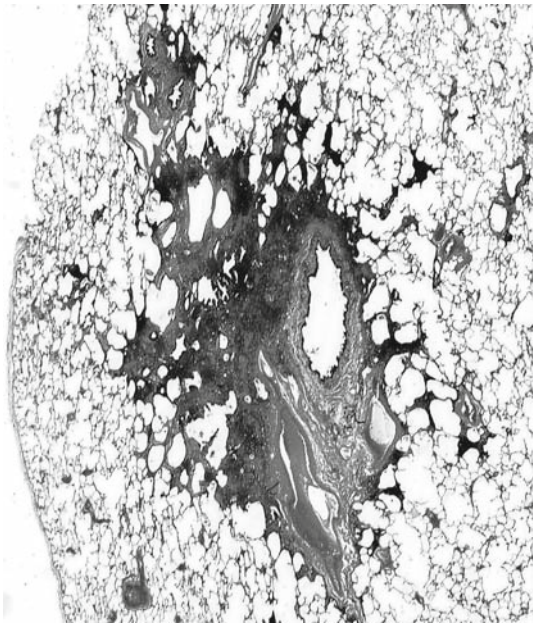

Fig. 3. Histological findings in the specimen resected from the right lower lobe. There was localized dense lymphoplasmacytic infiltration in one bronchiole and surrounding alveoli. On a close-up view of the resected bronchiole, abundant mature lymphoid proliferation was seen to have infiltrated the bronchiole, with formation of a reactive germinal center and mantle zone. Immunohistochemical studies proved that these lymphoplasmacytes were polyclonal. Bronchiolectasis was not apparent. (H&E, ×4)

Bronchoalveolar lavage (BAL) was performed with the following results: total cell count, 1.7×10^5/ml; lymphocyte fraction, 14%; CD20-positive lymphocytes, 4.8%; and CD4/CD8 ratio, 1.79. Lymphocytosis and monoclonal lymphocytic proliferation were absent from the BAL fluid.

Thoracoscopic thymectomy and pulmonary segmental resection were performed. The solitary parenchymal lesion showed abundant mature lymphoid proliferation infiltrating the bronchiolar wall with the formation of a reactive germinal center and mantle zone (Fig. 3). Lymphocytic infiltration was not limited to the bronchiolar wall; it extended to alveoli attached to the affected bronchiole. The lesion spreading to the alveoli resembled follicular bronchiolitis but was limited to alveoli neighboring the diseased bronchiole. No lymphoepithelial lesion was detected, and the bronchiolar lumen was preserved. Immunohistochemically, infiltrating plasma cells were positive for both kappa and lambda light chains, immunoglobulin G (IgG), IgA, and IgM. In addition, lymphocytes were positive for B cells (CD 20), T cells (CD3), and Bcl-2. These immunohistochemical results indicated the polyclonal nature of infiltrating lympho-

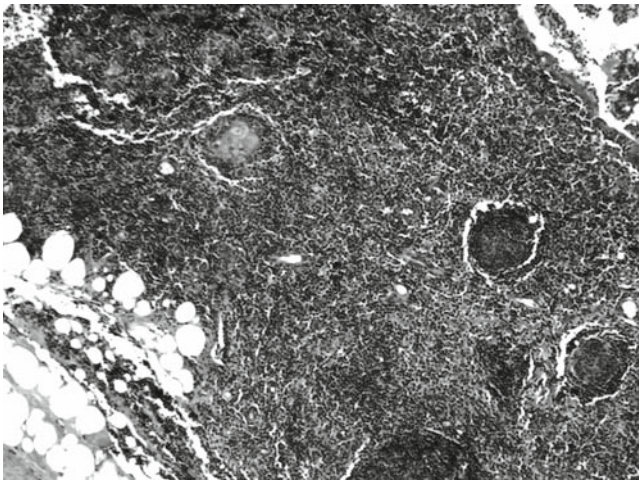

Fig. 4. Histologic findings in the thymus. There was well-defined lymphoid hyperplasia containing germinal centers and thymic epithelium. (H&E, ×40)

plasmacytes. Immunoglobulin heavy chain rearrangement analysis was attempted but failed. The histological appearance was that of NLH limited to a single bronchiole. The histological appearance of the anterior mediastinal nodule revealed reactive lymphoid hyperplasia of the thymus (Fig. 4), similar to that of NLH. Neither NLH nor thymic hyperplasia recurred after resection. There was no additional treatment.

We obtained informed consent from the patient and institutional review board approval (National Defense Medical College).

Discussion

Previous reports have described the rarity of NLH, and the clinicoradiological findings of this disease are not completely understood at present.[1] Histological manifestations of NLH, which include localized polyclonal lymphoid proliferation, are distinct from those of lymphocytic interstitial pneumonia and follicular bronchiolitis owing to the limited area affected.[1] As all lymphoproliferative disorders in the lung would originate in bronchus-associated lymphoid tissue (BALT), some overlap might exist between these three pulmonary lymphoproliferative disorders.[3]

Common radiological features of NLH include a well-demarcated solid nodule, whereas hazy contours and concomitant thymic hyperplasia were demonstrated by CT in this patient. Histologically, the rim of the lesion also displayed a shaggy appearance, with lymphoplasmacytic infiltration extending into the alveolar walls in a manner similar to that of follicular bronchiolitis or lymphocytic interstitial pneumonia. Follicular bronchiolitis is diffuse, multicentric disease, whereas the radiological and histological findings in this patient indicated that it was limited to one bronchiole.[3] Furthermore, an air bronchiologram was detected by CT in the patient, a finding that has not been described in NLH previously. The lesion in this patient clearly demonstrated a bronchiolocentric distribution, and the affected bronchiolar lumen was not obliterated.

Based on these observations, we concluded that NLH, follicular bronchiolitis, and lymphocytic interstitial pneumonia may represent aspects of a continuous clinicoradiological spectrum.[1] NLH combined with autoimmune disease has been reported in only one other case.[4] However, follicular bronchiolitis and lymphocytic interstitial pneumonia occasionally accompany autoimmune diseases, particularly primary Sjögren's syndrome. Primary Sjögren's syndrome is frequently accompanied by various pulmonary diseases.[5–7] These facts suggest that primary Sjögren's syndrome should be intensively investigated in cases of NLH.[2]

A small thymic nodule that was incidentally detected was a challenging diagnostic problem. Thymoma is the most frequent disorder in the thymus, but excluding thymic hyperplasia is difficult.[8] Thymic lymphoid follicular hyperplasia is a histological reaction that frequently accompanies myasthenia gravis,[9] whereas true thymic hyperplasia is a nonspecific pathologically enlarging process. There is no established imaging disparity that distinguishes the two types of thymic hyperplasia. The combined lymphoid hyperplasia in this case might be the result of a common lymphoproliferative pathogenesis in the lung and thymus.

Conclusion

We encountered a patient with NLH demonstrating a ground-glass opacity and an air bronchiologram, thymic lymphoid hyperplasia, and primary Sjögren's syndrome. Lymphoproliferative disorders, including NLH, should be discussed when a pure ground-glass opacity is detected by CT.[10]

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