Korean J Thorac Cardiovasc Surg 2018;51:133-137 □ CASE REPORT □
ISSN: 2233-601X (Print) ISSN: 2093-6516 (Online) https://doi.org/10.5090/kjtcs.2018.51.2.133

Pulmonary Nodular Lymphoid Hyperplasia in a 33-Year-Old Woman

Ji Ye Park, M.D.[1], Seong Yong Park, M.D., Ph.D.[2], Seokjin Haam, M.D., Ph.D.[1], Joonho Jung, M.D.[1], Young Wha Koh, M.D.[3]

[1]*Department of Thoracic and Cardiovascular Surgery, Ajou University School of Medicine,*
[2]*Department of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine,*
[3]*Department of Pathology, Ajou University School of Medicine*

Pulmonary nodular lymphoid hyperplasia is a reactive lymphoproliferative disease. It is very rare, which means that many aspects of the disease are unknown or have not been proven. Pulmonary nodular lymphoid hyperplasia can be symptomatic or asymptomatic, progressive or not, and solitary or multiple, and a surgical approach is the current treatment of choice. We present a case of pulmonary nodular lymphoid hyperplasia that was visualized as multiple ground glass opacities on a computed tomography (CT) scan, and observed for 1 year because the patient was pregnant. Over this period, the number and extent of the opacities progressed, but no symptoms were reported. A surgical biopsy was done and some remaining lesions regressed on follow-up CT scans, while others progressed, without any appearance of symptoms.

Key words: 1. Respiratory tract diseases
2. Lung, benign or congenital lesions
3. Thoracoscopy
4. Video-assisted thoracic surgery
5. Lung, pathology

Case report

A 33-year-old woman was referred from a local hospital with incidental abnormal chest computed tomography (CT) scan findings in 2014. She had no remarkable symptoms, and was healthy, without any prior clinical history except for having been diagnosed with a benign thyroid nodule.

The initial chest CT scan performed in June 2014 revealed several bilateral ground glass opacities (GGOs) measuring up to 1 cm and 1 right apical lesion measuring 1.2 cm, which was an aggregated calcified granuloma with fibrotic changes (Fig. 1A, B). The GGOs were multifocal and showed a nodular pattern, suggesting that they were likely to be chronic lesions, and the initially proposed differential diagnosis included atypical adenomatous hyperplasia (AAH), adenocarcinoma *in situ*, or organizing pneumonia. The calcified granuloma in the right apex was thought to be most likely a post-inflammatory change.

A follow-up chest CT scan was done 3 months later, and no interval change was found. The complete blood count and routine laboratory results were within the normal range, except for the serum total immunoglobulin E level, which was slightly elevated (115 kU/L). A video-assisted thoracic surgery biopsy

Received: August 8, 2017, Revised: November 14, 2017, Accepted: November 14, 2017, Published online: April 5, 2018
Corresponding author: Seong Yong Park, Department of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
(Tel) 82-2-2228-2140 (Fax) 82-2-393-6012 (E-mail) psy1117@hanmail.net

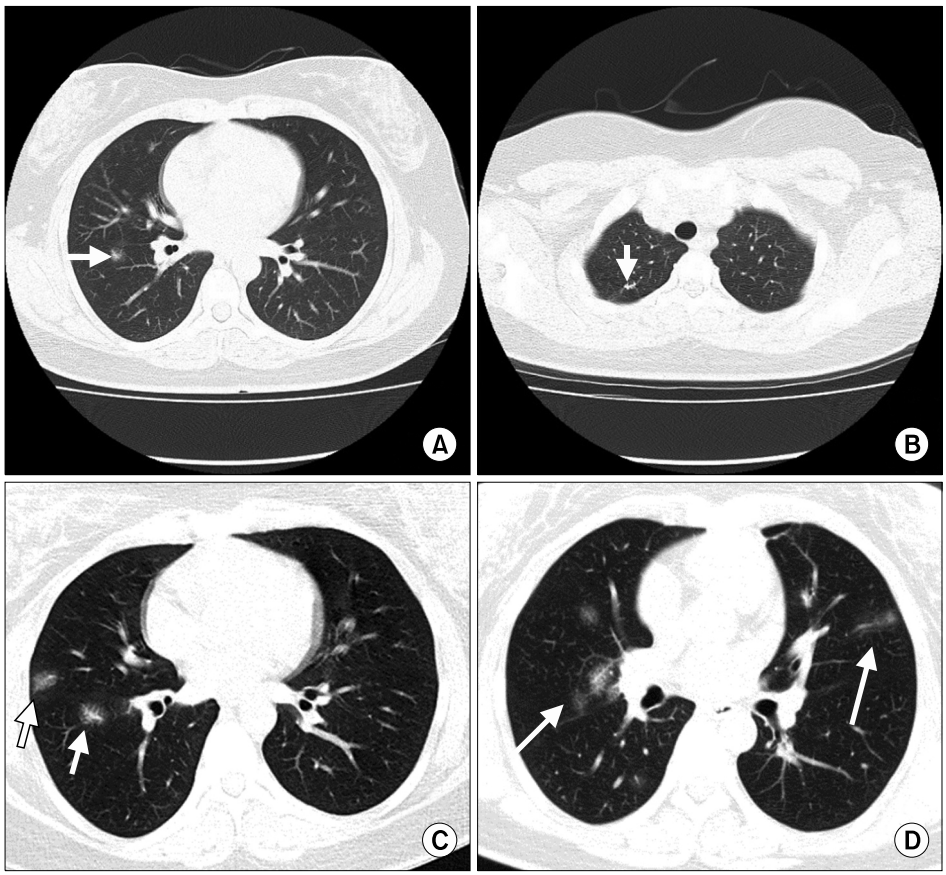

Fig. 1. Initial chest computed tomography scan in 2014. (A) The ground glass opacities was 1.0 cm at right upper lobe apex (arrow). (B) Calcified granuloma in the right apex of the lung (arrow). (C, D) Final chest computed tomography scan before the surgical biopsy in September 2015, showing an increased number and extent of multifocal peribronchovascular distributed nodular ground glass opacities in both lungs (arrows).

was thought to be the most appropriate choice for evaluating the GGO nodules, but before the biopsy was performed, it was found that the patient had an intrauterine pregnancy and was 3 weeks pregnant. The surgical biopsy was postponed until September 2015, after she gave birth.

A year later, another follow-up CT scan was done in August 2015, finding an increased number and extent of multifocal peribronchovascular GGOs in both lungs compared with the previous study (Fig. 1C, D). Adenocarcinoma with multiple AAH seemed to be the most likely diagnosis, followed by mucosa-associated lymphoid tissue (MALT) lymphoma.

A video-assisted thoracic surgical biopsy was done in September 2015. After wedge resection of left upper lobe using 2 endostaplers, 2 nodules were palpable in the specimen. The specimen consisted of resected lung tissue, measuring 6×4×1.7 cm. The cut sections revealed 2 ill-defined whitish solid nodules, measuring 1.3×1.3 cm and 0.7×0.5 cm, respectively.

She was discharged 2 days after surgery without any complications, and the pathologic results were received 1 week later. The histopathologic examination showed follicular lymphoid hyperplasia with interfollicular lymphoplasmacytosis, consistent with nodular lymphoid hyperplasia (Fig. 2). The immunohistochemical results showed CD3 and CD20 positivity, focal positivity of the kappa and lambda light chains, and Bcl-2 negativity.

The patient has been followed up with annual chest CT scans subsequently. A follow-up chest CT in June 2016 showed that some GGOs had progressed, while others had regressed spontaneously (Fig. 3A, B). She has visited our outpatient clinic every 3 months, and has shown no symptoms for the past 22 months.

Discussion

Pulmonary nodular lymphoid hyperplasia (PNLH) is a reactive lymphoproliferative disease. It was first described in 1983 by Kradin and Mark [1] and only

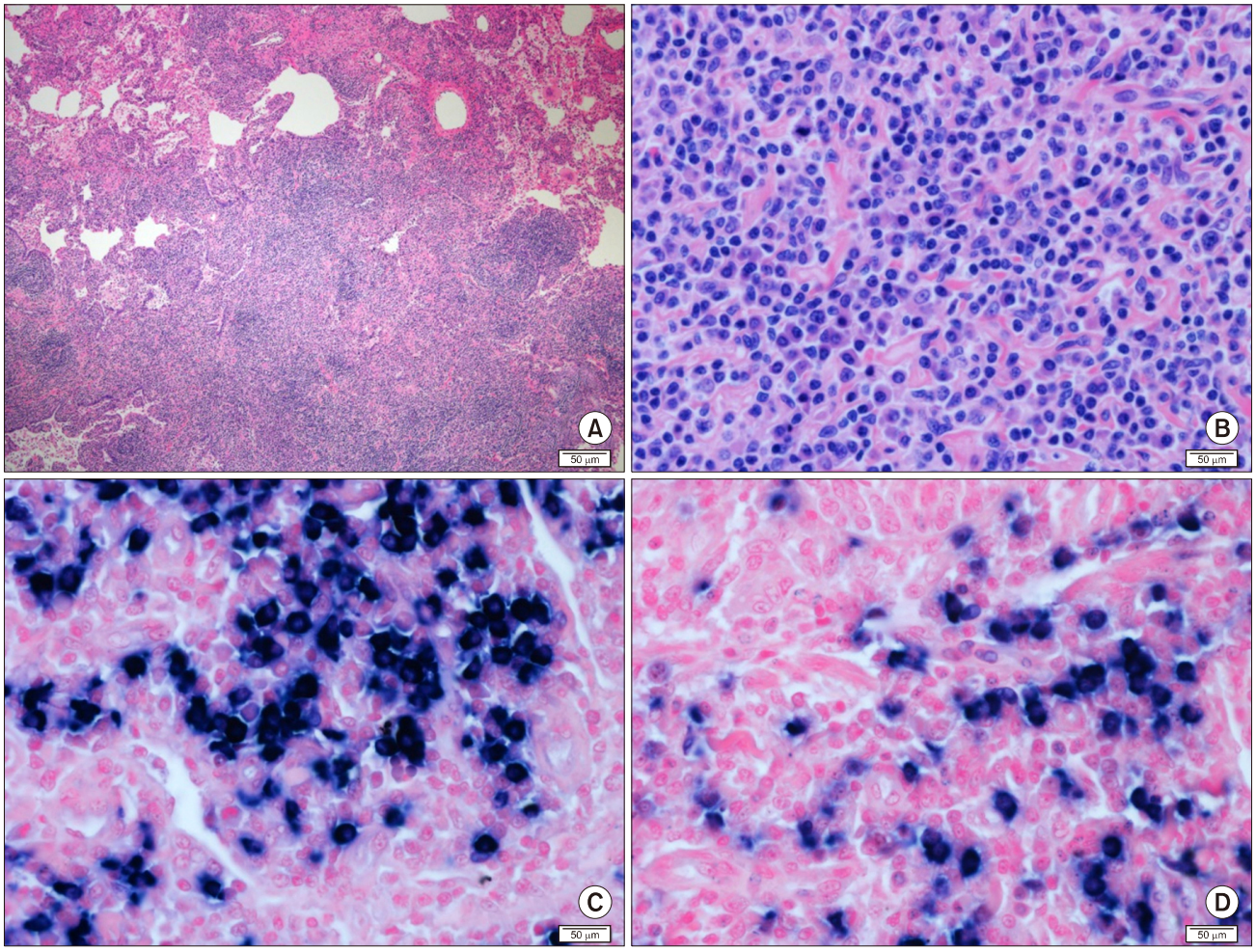

Fig. 2. (A) Diffuse nodular effacement of the lung parenchymal structure by lymphoid infiltration (H&E, ×100). (B) Aggregation of polymorphic lymphocytes and plasma (H&E, ×400). (C) Polytypic pattern of kappa light chain expression (dark blue). (D) Polytypic pattern of lambda light chain expression (dark blue).

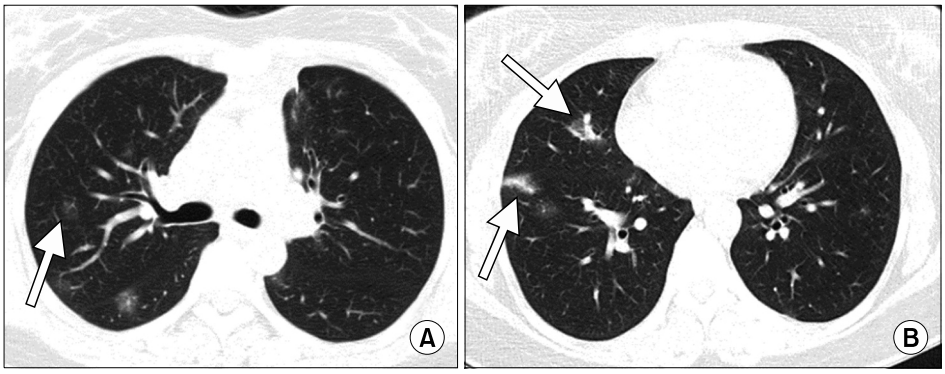

Fig. 3. Follow-up computed tomography scan obtained 1 year after the surgical biopsy, in September 2016. (A) The ground glass opacities in the right lower lobe had become smaller than observed in the computed tomography scan from September 2015 (arrow). (B) The solid portion of some lesions progressed and new lesions emerged (arrows).

dozens of cases have been reported since then. Before Abbondanzo et al. [2] reviewed 14 cases of PNLH, proposed it as a disease entity, and suggested a treatment strategy, it was often referred to as pseudolymphoma, and many authors believed that it corresponded to MALT lymphoma [3]. PNLH has no

disease-specific symptoms, characteristics, or radiologic findings, and its prognosis has also been found to vary.

At first, PNLH was suggested as a term to describe the presence of 1 or more nodules or infiltrates composed of reactive lymphoid cells. It is now diagnosed histologically or immunohistochemically. Histologically, PNLH is composed of well-defined lymphoid tissue masses with numerous reactive germinal centers, interfollicular lymphocytes, and plasma cells. Immunohistochemical findings show a mixture of T and B cells with germinal centers expressing CD20 antigens and interfollicular lymphocytes expressing CD3, CD43, and CD5 [4]. Focal positivity of the lambda and kappa light chains is also found in PNLH. This case showed the characteristic features of follicular lymphoid hyperplasia with interfollicular lymphoplasmacytosis, and immunostaining showed CD3 and CD20 positivity with focal positivity of the lambda and kappa light chains.

This case presented 2 characteristic features. One was the radiologic feature of multiple and bilateral GGOs, because of which the differential diagnosis included malignancy. The differential diagnosis included adenocarcinoma (minimally invasive or invasive) with multiple AAH, multifocal lymphoma (MALT lymphoma), and multiple focal fibrosis. The GGOs were multiple and could not be completely resected, so only a surgical biopsy was done to confirm the diagnosis and to determine the proper course of treatment. Several cases of multiple GGOs in PNLH have been found since Kajiwara et al. [5] first reported this feature in 2005. Most of the previously reported cases of PNLH have been solitary pulmonary nodules.

Second, the patient did not receive any treatment for PNLH for nearly a year because of her pregnancy, and only 2 lesions were resected for the purpose of pathologic confirmation. Therefore, this case provides useful information on the natural course of PNLH. Until surgery, the number and extent of the lesions on radiography progressed without symptom aggravation. Future long-term follow-up of this patient might yield more insights into the long-term natural course of the remaining lesions and the prognosis of this disease.

The treatment of choice for PNLH has been surgical resection since Abbondanzo et al. [2] reported 14 cases of PNLH in 2000. Most of the previously described cases had single pulmonary nodules, and every patient received complete surgical resection, with no recurrence observed. However, in 2005, Kajiwara et al. [5] reported a case of PNLH with multiple GGOs; only a surgical biopsy was done and the remaining lesions spontaneously regressed during the follow-up period. Miyoshi et al. [6] reported a similar case of a 50-year-old male patient with small multiple nodular lung lesions, in whom a surgical biopsy was performed and the remaining lesions regressed spontaneously after 6 years.

These 2 cases imply that surgical resection may not be the only answer for the treatment of PNLH. However, it is very difficult to decide whether to remove the nodule(s), because the clinicopathology of the disease is poorly understood. More information and cases should be gathered to understand why some patients show progression and others experience regression.

In our case, only a surgical biopsy was performed, and the patient has been followed up for 22 months so far. Some progression and regression have been found simultaneously in follow-up CT scans, but no symptoms have been reported. Long-term follow-up will clarify the natural course of the remaining lesions and yield further insights into the prognosis of PNLH.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

References

1. Kradin RL, Mark EJ. *Benign lymphoid disorders of the lung, with a theory regarding their development*. Hum Pathol 1983;14:857-67.
2. Abbondanzo SL, Rush W, Bijwaard KE, Koss MN. *Nodular lymphoid hyperplasia of the lung: a clinicopathologic study of 14 cases*. Am J Surg Pathol 2000;24:587-97.
3. Addis BJ, Hyjek E, Isaacson PG. *Primary pulmonary lymphoma: a re-appraisal of its histogenesis and its relationship to pseudolymphoma and lymphoid interstitial pneumonia*. Histopathology 1988;13:1-17.
4. Carrillo J, Restrepo CS, Rosado de Christenson M, Ojeda Leon P, Lucia Rivera A, Koss MN. *Lymphoproliferative lung disorders: a radiologic-pathologic overview: part I: re-*

active disorders. Semin Ultrasound CT MR 2013;34:525-34.
5. Kajiwara S, Sakai S, Soeda H, et al. *Multifocal nodular lymphoid hyperplasia of the lung.* J Thorac Imaging 2005;20:239-41.
6. Miyoshi S, Hamada H, Katayama H, et al. *A case of pulmonary nodular lymphoid hyperplasia with a resected cavity, followed by spontaneous regression of the remaining lesions.* Intern Med 2010;49:1617-21.