PULMONARY PUZZLE

Bilateral pulmonary nodules in a patient with extensive autoimmune disease

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CLINICAL PRESENTATION

A 64-year-old woman presented to our hospital complaining of generalised fatigue and history of mechanical fall with rib fractures while in Africa. Chest X-ray (CXR) incidentally discovered multiple bilateral pulmonary nodules. She has a history of rheumatoid arthritis on methotrexate, Hashimoto's thyroiditis, Sjögren's syndrome (SS) and psoriatic arthritis on immunotherapy. She denied symptoms of cough, chest pain, dyspnoea, weight loss, night sweats, fever or haemoptysis. She denied smoking, alcohol consumption, illicit drug use and environmental exposures. She had a family history of lymphoma in sister but no personal/family history of arteriovenous malformations, hamartomas or vasculitis. CXR conducted 3 years prior showed no lesions. She was up-to-date with breast screening but refused colonoscopy. Physical exam was unremarkable.

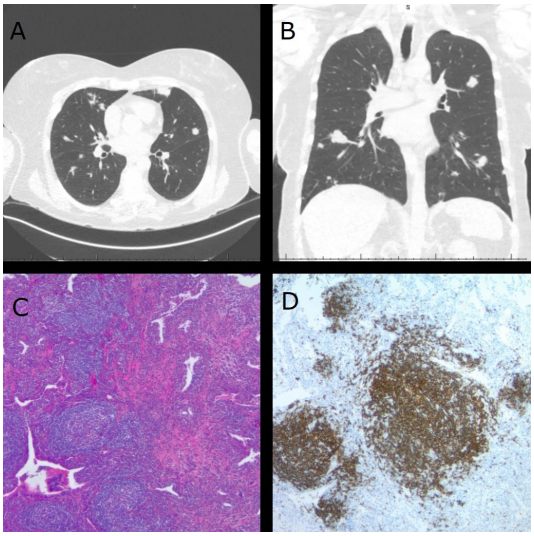

Figure 1 Chest CT, axial view (A) and coronal view (B). Bilateral, multiple pulmonary nodules with random distribution, varying sizes and smooth contours. Anterior left upper lung nodule shows surrounding ground-glass changes. Lesions are not distributed in any particular pattern, that is, not following lymphatics or vasculature. Microscopy: ×40 magnification, H&E staining (C). Dense, monotonous population of centrocyte-like cells with plasmacytoid differentiation, with residual germinal centres and lymphoepithelial lesions. Microscopy with ×40 magnification, CD20+ immunohistochemical staining (D), highlights the extensive B-cell infiltration.

On arrival to USA, chest CT confirmed bilateral nodules with lower lung predominance (figure 1) and positron emission tomography scan demonstrated hypermetabolic activity of the nodules. Lab work—blood count, metabolic profile, urinalysis, immunoglobulins, HIV, serum/urine protein electrophoresis and vasculitis panel—was normal. Infectious workup—for tuberculosis, histoplasmosis, coccidiomycosis, pneumocystis, and bacterial and viral pneumonia—were also negative. She was positive for SS-A and SS-B antibodies, negative for rheumatoid factor, anti-Scl-70 and anti-Jo-1 antibodies, and had normal antinuclear antibodies. Bone marrow biopsy and flow cytometry were normal. She underwent bronchoscopic transbronchial biopsy of nodules and endobronchial ultrasound-guided transbronchial needle aspiration of lymphadenopathy; these were non-diagnostic. Then, the patient underwent CT-guided biopsy, which showed dense lymphoplasmacytic inflammatory infiltration but was negative for malignancy. Finally, surgical thoracoscopy was performed with wedge resection.

QUESTION

What is the diagnosis?

ANSWER

This patient, with a significant history of autoimmune disease, underwent wedge resection—pathology showed mucosa-associated lymphoid tissue (MALT) lymphoma of the lung. MALT lymphoma is a rare, indolent, extranodal lymphoma constituting 0.5% of primary lung neoplasms. While MALT lymphoma most commonly occurs in the gastrointestinal tract in association with *Helicobacter pylori* infections, other potential origins are salivary glands, orbits, thyroid and lungs.[1] The suspected pathogenesis is chronic antigenic stimulation of lymphoid tissue by infection, inflammation and autoimmune stimuli. The most common gene defect is translocation t(11;18)/BIRC3-MALT1 with activation of NF-κB pathway triggering neoplastic transformation. Among the autoimmune disorders, SS is most strongly associated with the development of MALT lymphoma. Interestingly, *Achromobacter xylosoxidans* has been linked to pulmonary MALT lymphomas. The disease has no specific signs and symptoms; 36% of patients are asymptomatic at diagnosis.[2]

Radiographic imaging shows variable presentation.[3] Diagnosis requires a surgical biopsy, usually

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wedge resection, during video-assisted thoracoscopy or thoracotomy, as the yield from bronchoscopic transbronchial and CT-guided biopsies is very low.[4] Immunohistochemical staining is crucial to assess the architecture of the lymphoid infiltrate and to exclude other lymphomas.[1] Pulmonary MALT lymphoma has an excellent 5-year overall survival rate (>80%). Optimal management is controversial due to the lack of evidence-based guidelines. Patients with systemic disease (stage III/IV—Ann Arbor Classification) receive a chemotherapeutic agent (bendamustine, fludarabine or chlorambucil) combined with anti-CD20 antibody (rituximab).[5] Our patient received bendamustine and rituximab therapy due to the progression of her lymphoma; 3 months later, she is making a remarkable recovery and shows radiographic improvement.

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REFERENCES

1 Bacon CM, Du M-Q, Dogan A. Mucosa-Associated lymphoid tissue (MALT) lymphoma: a practical guide for pathologists. *J Clin Pathol* 2007;60:361–72.
2 Schreuder MI, van den Brand M, Hebeda KM, *et al*. Novel developments in the pathogenesis and diagnosis of extranodal marginal zone lymphoma. *J Hematop* 2017;10:91–107.
3 Bae YA, Lee KS, Han J, *et al*. Marginal zone B-cell lymphoma of bronchus-associated lymphoid tissue. *Chest* 2008;133:433–40.
4 Muñoz-Largacha JA, O'Hara CJ, Sloan JM, *et al*. Surgical management of pulmonary mucosa-associated lymphoid tissue lymphoma associated with light-chain deposition disease. *Ann Thorac Surg* 2016;101:e207–10.
5 Kiesewetter B, Ferreri AJM, Raderer M. Chemoimmunotherapy for mucosa-associated lymphoid tissue-type lymphoma: a review of the literature. *Oncologist* 2015;20:915–25.