

From Sjögren's Syndrome (Autoimmune Epithelitis) to MALT Lymphoma and κ Light-Chain Amyloidosis: A Rare Case

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Abstract

Sjögren's syndrome/Autoimmune epithelitis (SS/AE) is associated with persistent B-cell activation and an increased risk of B-cell lymphoproliferative disorders, particularly mucosa-associated lymphoid tissue (MALT) lymphoma. Localized pulmonary amyloid light-chain (AL) amyloidosis is a rare manifestation that may occur in association with indolent lymphoproliferative disease. We present a 57-year-old woman with SS/AE and IgM κ -positive MALT lymphoma involving the salivary glands. Ten years later, she developed a solitary 2-cm pulmonary nodule. Thorascopic biopsy demonstrated κ light-chain amyloid deposition, consistent with localized pulmonary AL κ amyloidosis. Extensive evaluation revealed no evidence of systemic amyloidosis or disseminated lymphoma. The lesion remained stable during two years of follow-up. This case illustrates the complex relationship between SS-associated B-cell dysregulation, MALT lymphoma, and localized AL amyloidosis. New pulmonary lesions in patients with SS and previous lymphoproliferative disease warrant thorough histopathological evaluation and assessment for systemic involvement.

Keywords: Sjögren's syndrome; MALT lymphoma; Pulmonary amyloidosis; AL amyloidosis; κ light chain; B-cell lymphoproliferative disorders.

Introduction

Amyloidosis is characterized by the extracellular deposition of misfolded proteins that aggregate into amyloid fibrils. Amyloid diseases are classified according to the biochemical nature of the precursor protein, the distribution of amyloid deposits (localized or systemic), and whether the condition is acquired or hereditary. These disorders can manifest with a broad spectrum of clinical presentations, depending on the type and distribution of amyloid deposition. Amyloid light-chain (AL) amyloidosis results from the deposition of amyloid fibrils derived from monoclonal immunoglobulin light chains produced by clonal plasma cells or B cells. It is associated with plasma cell dyscrasias, including multiple myeloma, and certain B-cell lymphoproliferative disorders, including lymphoma [1].

Pulmonary amyloidosis may be localized or occur as part of systemic disease. It is generally classified into three patterns: nodular parenchymal, diffuse alveolar-septal, and tracheobronchial amyloidosis. Pulmonary involvement is most commonly associated with systemic AL amyloidosis, although localized pulmonary amyloidosis is also well recognized. Localized disease typically affects the tracheobronchial tree or pulmonary parenchyma and may present as solitary or multiple pulmonary nodules [2]. Nodular pulmonary amyloidosis is often asymptomatic and incidentally detected, and its clinical course is generally indolent, allowing conservative management in appropriately selected patients [3].

Case Report

A 57-year-old woman was diagnosed with Sjögren's syndrome/autoimmune epithelitis (SS/AE) in 2015. The diagnosis was based on xerophthalmia, xerostomia, arthralgias, leukopenia (white blood cell count: 3.300/ μ L), positive anti-Ro52/Ro60 and anti-La autoantibodies, elevated rheumatoid factor (713 IU/mL; reference range: <14 IU/mL), reduced complement levels (C3: 65 mg/dL, reference range:

90-180 mg/dL; C4: 7 mg/dL, reference range: 20-50 mg/dL), and IgM κ monoclonal gammopathy. A minor labial salivary gland biopsy revealed dense lymphocytic infiltrates (Tarpley score: 4+) composed of cells with slightly irregular nuclei and relatively abundant pale cytoplasm, resembling centrocytes. Lymphocytes invaded, infiltrated, and distorted the surrounding salivary ductal epithelium. The ducts were hyperplastic and formed solid islands of cells packed with infiltrating lymphocytes. Lymphocytes invaded the pre-existing, reactive germinal centers, completely taking over or altering the native architecture of the minor salivary gland. Immunohistochemistry revealed strong positivity for the pan-B-cell markers CD20, CD19, and CD79a, as well as BCL-2, and an IgM κ monoclonal B-cell population; these findings were compatible with marginal-zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) [4].

Three years later, the patient developed persistent, painful, right parotid gland enlargement. A parotidectomy was performed, and histopathological examination confirmed again the diagnosis of IgM κ -positive MALT lymphoma again, showing a dense, sheet-like infiltrate of small- to medium-sized centrocyte-like lymphocytes with irregular, cleaved nuclei and pale cytoplasm. Salivary acini were destroyed, and the residual ducts showed prominent lymphoepithelial lesions with epithelial distortion and focal luminal obliteration. Scattered plasma cells and immunoblasts were also present. The neoplastic cells expressed CD19, CD20, CD22, CD79a, BCL-2, and IgM κ . The Ki-67 proliferation index was low. Further lymphoma staging with upper and lower gastrointestinal endoscopy, bone marrow biopsy, and whole-body ¹⁸F-FDG PET/CT did not reveal any additional sites of involvement. The patient was treated with hydroxychloroquine (200 mg once daily) and pilocarpine (5 mg three times daily) and underwent clinical follow-up every six months.

Ten years after the initial diagnosis (in 2025), the patient developed

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Citation: Ilir I Cinoku*, From Sjögren's Syndrome (Autoimmune Epithelitis) to MALT Lymphoma and κ Light-Chain Amyloidosis: A Rare Case. Jour of Clin & Med Case Rep, Imag 2026; 7(1): 1256.

a persistent dry cough. Thorough clinical examination was unremarkable. A chest computed tomography (CT) revealed a solitary pulmonary nodule measuring 2 cm in diameter in the right lower lobe (Figure 1A). Whole-body ^{18}F -FDG PET/CT demonstrated FDG uptake confined to this lesion, with a standardized uptake value (SUV) of 2.7 (Figure 1B). The patient subsequently underwent thoracoscopic lung biopsy. Histopathological examination demonstrated pulmonary κ light-chain amyloid deposition, consistent with localized AL κ amyloidosis (Figure 2). An extensive evaluation for systemic amyloidosis,

including complete blood count, comprehensive metabolic panel, thyroid function tests, urinalysis, and echocardiogram, revealed no significant abnormalities.

After two years of follow-up, the pulmonary nodule remains stable, and the patient has not developed any features of systemic amyloidosis.

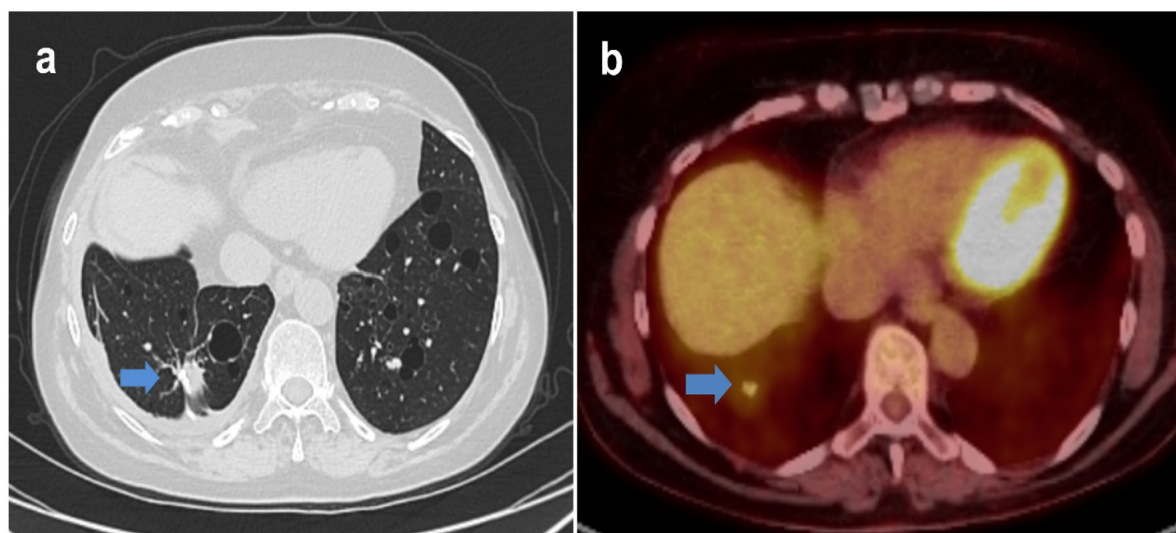


Figure 1: (a) Chest CT revealing a nodular lesion in the right lower lobe of the lung (b) FDG-PET/CT revealed FDG uptake by the lung lesion with a standardized uptake value of 2.7.

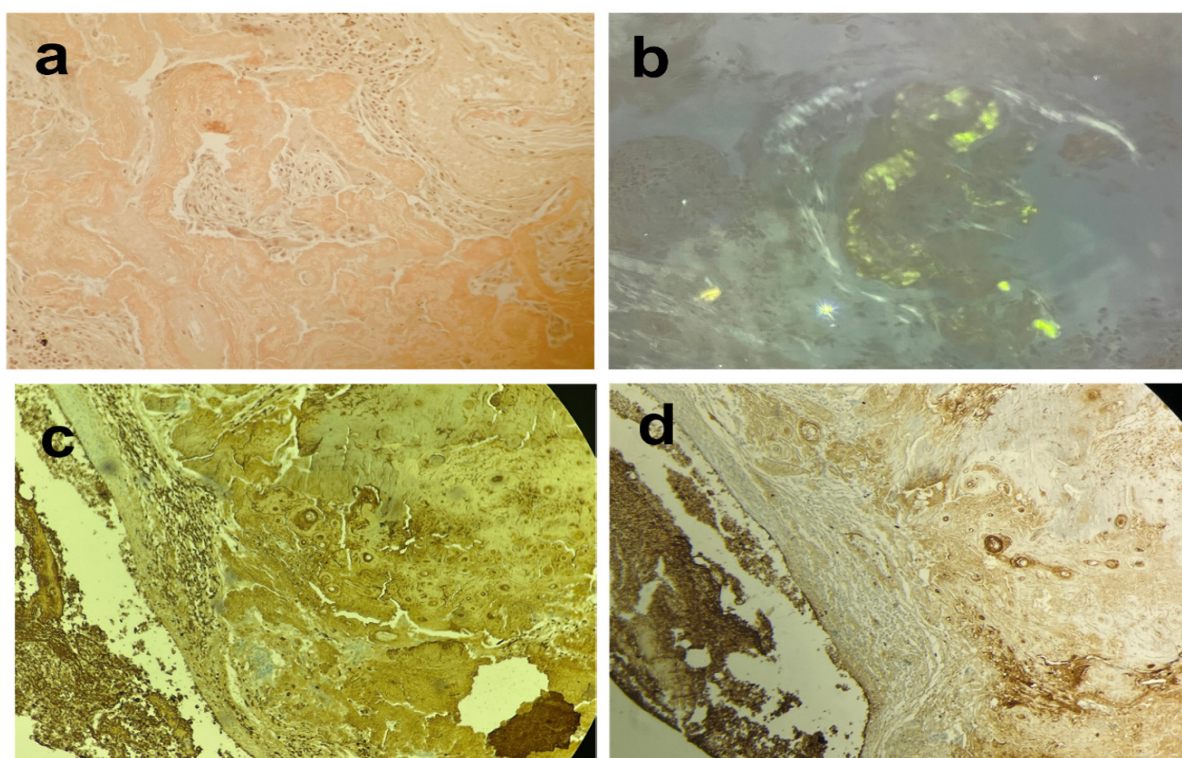


Figure 2: Histopathological confirmation of pulmonary amyloidosis. (a) Congo red staining demonstrating extensive extracellular deposition of amorphous amyloid material. (b) Under polarized light microscopy, the deposits display characteristic apple-green birefringence, confirming amyloid deposition. (c) Immunohistochemical staining positive for κ light chains. (d) Immunohistochemical staining for λ light chains didn't stain the amyloid fibrils.

Discussion

SS/AE is an autoimmune disorder with unique features. Its clinical spectrum extends from an exocrinopathy to systemic disease, affecting the lungs, kidneys, liver, and vessels, and in a tenth of patients it evolves into lymphoid malignancy [5]. In this report, we present an SS/AE patient with characteristic clinical and serologic findings, and

IgAk monoclonal gammopathy, evolving to salivary gland IgM κ MALT lymphoma and finally developing a nodular κ light chain amyloidosis. The κ amyloid proteins most probably arose from the IgM κ -positive MALT lymphoma. The possibility that the κ amyloidosis arose from the benign IgAk monoclonal gammopathy is minuscule. Solitary nodular pulmonary amyloidosis, as seen in our patient, has been de-

scribed in patients with indolent B-cell lymphoproliferative disorders, including lesions within the MALT lymphoma spectrum with or without an associated autoimmune disease [6]. Monoclonal immunoglobulin abnormalities are well documented in SS/AE and reflect, at least in part, persistent B-cell activation and clonal expansion. These abnormalities are clinically relevant because SS/AE is associated with an increased risk of B-cell lymphoproliferative disorders, particularly MALT lymphoma [7,8].

Management of nodular pulmonary amyloidosis depends on the extent of disease, associated symptoms, evidence of progression, and the presence of an underlying lymphoproliferative disorder or systemic amyloidosis. For selected patients with localized, asymptomatic disease and no evidence of an associated aggressive malignancy (e.g., diffuse large B-cell lymphoma) or systemic amyloidosis, observation with clinical and radiological surveillance may be appropriate because the disease often follows an indolent course [10]. A key diagnostic challenge is distinguishing nodular pulmonary amyloidosis from systemic AL amyloidosis and pulmonary lymphoma involvement. Although imaging may reveal solitary or multiple nodules, sometimes with calcifications or cysts, histopathological examination

is essential to confirm amyloid deposition and assess for an associated lymphoproliferative disorder [11].

Conclusion

This case highlights the complex relationship between SS/AE-associated B-cell dysregulation, MALT lymphoma, and immunoglobulin light-chain amyloid deposition. It also underscores the importance of distinguishing localized pulmonary amyloidosis from systemic AL amyloidosis and pulmonary lymphoma involvement. In patients with SS/AE and a history of B-cell lymphoproliferative disease, new pulmonary lesions warrant careful investigation, including histopathological assessment and appropriate evaluation for systemic involvement. Long-term clinical surveillance is essential to monitor disease progression or the emergence of additional lymphoproliferative manifestations.

Conflicts of Interest/Competing Interests: The authors declare that there are no conflicts of interest.

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