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Case Report

CT-guided biopsy in the differential diagnosis of Sjogren syndrome associated cystic lung disease: A case of lung nodular AL-*k* amyloidosis ☆,☆☆

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ABSTRACT

Pulmonary involvement in Sjogren syndrome (SS) could manifest as cystic lung disease (CLD). CLD in SS includes lymphocytic interstitial pneumonia (LIP) and pulmonary amyloidosis. Differential diagnosis usually requires surgical lung biopsy, whereas CT-guided percutaneous fine needle aspiration biopsy (CT-FNAB) has not yet explored. We describe the case of a 63-year-old never smoker Caucasian female with a SS diagnosis who displayed a newly detected diffuse CLD at high-resolution computed tomography, though totally asymptomatic. Given the favorable location of one big lesion at the superior left lobe, a CT-FNAB was proposed instead of a more invasive SLB. At histology examination a diagnosis of pulmonary nodular AL kappa amyloidosis in the context of SS was established. In conclusion, CT-FNAB might represent an alternative and less invasive diagnostic procedure than SLB

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in the differential diagnosis of CLD, even if further research is needed. Moreover, this case presents an unusual association between SS and pulmonary nodular AL kappa amyloidosis, with pulmonary nodules and cysts without systemic manifestations.

Introduction

Pulmonary involvement in Sjogren syndrome (SS) could manifest as cystic lung disease (CLD), typically represented by lymphocytic interstitial pneumonia (LIP) [1]. Nonetheless CLD in SS can also be expression of pulmonary amyloidosis [2]. Differential diagnosis of CLD usually requires surgical lung biopsy (SLB), whereas diagnostic potential of less invasive methods, as CT-guided percutaneous fine needle aspiration biopsy (CT-FNAB) has not yet explored [3]. We describe a rare case of pulmonary nodular AL kappa amyloidosis in a patient with SS-associated CLD, diagnosed through a novel mini-invasive approach, namely CT-FNAB instead of SLB.

Case presentation

In November 2019, a 63-year-old never smoker Caucasian female with a SS diagnosis who displayed a newly detected diffuse CLD at high-resolution computed tomography (HRCT), though totally asymptomatic, was referred to the Pulmonology-Rheumatology Multidisciplinary-Outpatient-Clinic of San Matteo University Hospital (Pavia-Italy), a reference center for the diagnosis and treatment of connective tissue disease's (CTD)'s pulmonary manifestations. SS was diagnosed in 1997 (*sicca syndrome*, antiSSA/Ro52+ and relapsing parotidean adenomegalies). Although asymptomatic for pulmonary involvement, yearly spirometry and chest X-ray were performed, without signs of SS localization. Also, a previous chest HRCT performed in 2015 was negative. On physical examination, rare bilateral crackles could be heard, without signs of active arthritis or lymphadenopathies. Autoimmunity test with myositis antibodies panel confirmed anti SSA/Ro52+; Schirmer test and sialometry were positive. Spirometry (FVC 151%, FEV1 139%), diffusion capacity for carbon-monoxide (DLCO 6.5, 100%) and 6-minute-walking-test were negative. HRCT showed multiple bilateral nodules and cysts of various diameters ranging from millimeters to 2 centimeters, with a defined but irregular wall, partially filled with coarse calcifications (Fig. 1a). Therapy with prednisone (2.5 mg/day) and hydroxychloroquine (400 mg/day) was initially confirmed. The case was discussed in the Pavia Multidisciplinary Group for Interstitial Lung Disease which involves Pulmonologists, Rheumatologists, Radiologists, and Pathologists [4]. HRCT was reviewed by 2 thoracic radiologists who suspected nodular amyloidosis, a condition associated with SS in 6% of cases [1,5]. Given the favorable location of one big lesion at the superior left lobe, a CT-FNAB was proposed instead of a more invasive SLB (Fig. 1b). Histology excluded lymphoproliferative disorder but revealed Congo-red-staining positivity, along with apple-green birefringence on polarized microscopy, findings consistent with amyloidosis. Electron microscopy immunohistochemistry (immunogold postembedding) for amyloid typing showed immunoreactivity for anti-kappa light chain polyclonal antibodies. No clinical or instrumental signs of systemic amyloidosis were found. A diagnosis of pulmonary nodular AL kappa amyloidosis in the context of SS was established. Treatment with azathioprine and hydroxychloroquine 200 mg/day was suggested and the patient is currently followed-up for monitoring disease course.

Discussion

SS is an autoimmune inflammatory connective tissue disease characterized by lymphocytic infiltration of exocrine glands (*sicca syndrome*) and other organs damage, including the lung. Typical lung involvement in SS is represented by LIP, nonetheless SS has also been associated with pulmonary amyloidosis, generally diagnosed by SLB [2]. Amyloidosis is caused by abnormal extracellular deposits of misfolded proteins and is classified in systemic and localized forms basing on amyloid deposition in a single or multiple organs. Three forms of pulmonary amyloidosis have been described: nodular, diffuse-interstitial and tracheobronchial amyloidosis. Nodular localized amyloidosis is a benign entity, that does not evolve to systemic disease, although local progression is possible. Association with SS has been reported with nodular amyloidosis of the skin, lungs, and breast [6–8].

Both LIP and amyloidosis could manifest as CLD, although in the differential diagnosis of CLD lymphoproliferative disease must always be excluded. LIP is characterized by coexistence of separate thin-walled cysts and nodules, without calcifications. Cysts have typically size from 1 to 30 mm and are randomly distributed, with a basal, perivascular prevalence [9]. On the contrary, in amyloidosis nodules are associated to cysts and can present coarse calcifications as in the present case. Cysts are usually thin-walled, round or lobulated, with size ranging from 1 to 2 cm. Distribution is usually subpleural and peribronchovascular [10].

Although cystic patterns in LIP and amyloidosis are enough characteristic to be discriminated at HRCT without biopsy, tissue sampling for diagnosis confirmation is often required, mainly to exclude the presence of lymphoproliferative disease, as mucosal-associated lymphoid tissue lymphoma (MALT-lymphoma) [3]. Indeed, immunohistochemistry and flow-cytometry on sampled lung tissue allow the identification of polyclonal or monoclonal lymphocytic populations, respectively seen in LIP or MALT-lymphoma [11]. Tissue sampling is usually obtained through SLB, which still represents

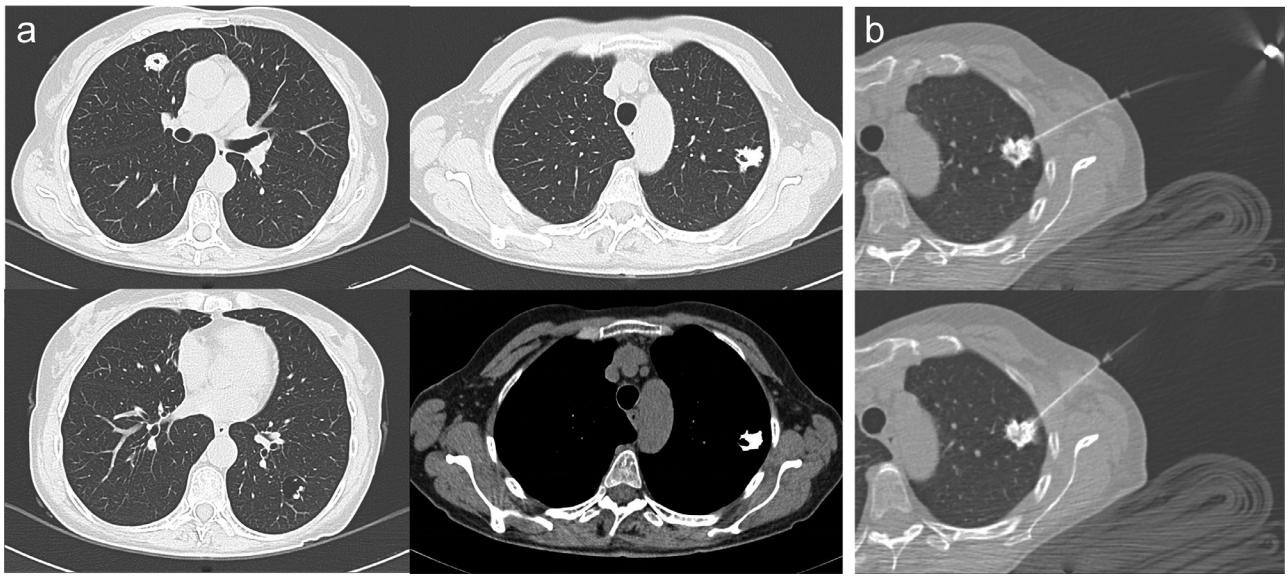

Fig. 1 – Cystic lung disease at chest HRCT and CT-FNAB of the target lesion: (a) HRCT of the chest showing multiple bilateral nodules and cysts of various diameters ranging from millimeters to 2 centimeters, with a defined but irregular wall, partially filled with coarse calcifications; (b) CT-FNAB of a target lesion in the superior left lobe. Specimens collected through this mini-invasive method were diagnostic for pulmonary nodular AL kappa amyloidosis. HRCT, high resolution computed tomography; CT-FNAB, CT-guided percutaneous fine needle aspiration biopsy.

the procedure of choice, with a superior diagnostic yield than transbronchial biopsy [12]. CT-FNAB might represent an alternative and less invasive diagnostic procedure than SLB in the differential diagnosis of CLD, as in the present case, but further research with dedicated studies is needed to explore CT-FNAB diagnostic potential; since now, only single case reports can be found in the literature [13,14].

Conclusion

We reported a novel potential application of CT-FNAB in the differential diagnosis of CLD. In particular, this case presents an unusual association between SS and pulmonary nodular AL kappa amyloidosis, with pulmonary nodules and cysts without systemic manifestations.

Key message: CT-FNAB could help in the differential diagnosis of CLD as SS pulmonary involvement.

Author contributions

All the authors conceived the study; CT, GZ, AV, GP, FMe, LC drafted the manuscript; CT, GZ, AV, RD, ZK, FMa, VC, PMi, GP, FMe, LC collected the data and collaborated to the critical review of the literature; CB performed CT biopsy; PMo performed histological analysis; CT, GZ, EB, VC, GP, FMe, LC clinically managed the patient; AV, RD critically revised HRCT images; CT, GZ, AV, FMe, LC revised the manuscript critically for important intellectual content; all the authors approved final version of the manuscript.

Ethics

All procedures were in accordance with the declaration of Helsinki and approved by the local ethics committees.

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