

## Letter to the Editor (Case report)

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### Mediastinal mass in a patient with rheumatoid arthritis: lymphoid cystic thymic hyperplasia

#### Key Message

- Thymic hyperplasia and other thymic anomalies should be listed as a differential diagnosis in RA patients presenting with a mediastinal mass.

DEAR EDITOR, Rheumatoid arthritis (RA) is a chronic inflammatory disorder that can have both articular and extra-articular involvement. Autoimmunity caused by the interaction of environmental and genetic factors is the principal driving force of the pathogenesis [1]. Thymic hyperplasia, which can accompany various rheumatic disorders, can be seen in two morphologies: true thymic hyperplasia or lymphofollicular hyperplasia, which can be associated with autoimmunity characterized by an increase in the size and weight of the thymus gland [2]. We report an RA patient with lymphoid cystic thymic hyperplasia and review the current literature focusing on the thymic abnormalities in RA. A 31-year-old man was admitted to our clinic with arthralgia and morning stiffness lasting 2–3 h in both hands and dyspnoea. He had lost 7 kg in the last 5 months. He had been using SSZ and NSAIDs, with a diagnosis of RA for 1 year. He had a 6-pack-year smoking history. His medical history was unremarkable, and he denied using any illicit drugs. Joint examination revealed arthritis of bilateral second and third PIP joints, bilateral third and fourth MCP joints and bilateral wrists, pain, and limited movement of the left hip. Systemic examination revealed no further abnormalities.

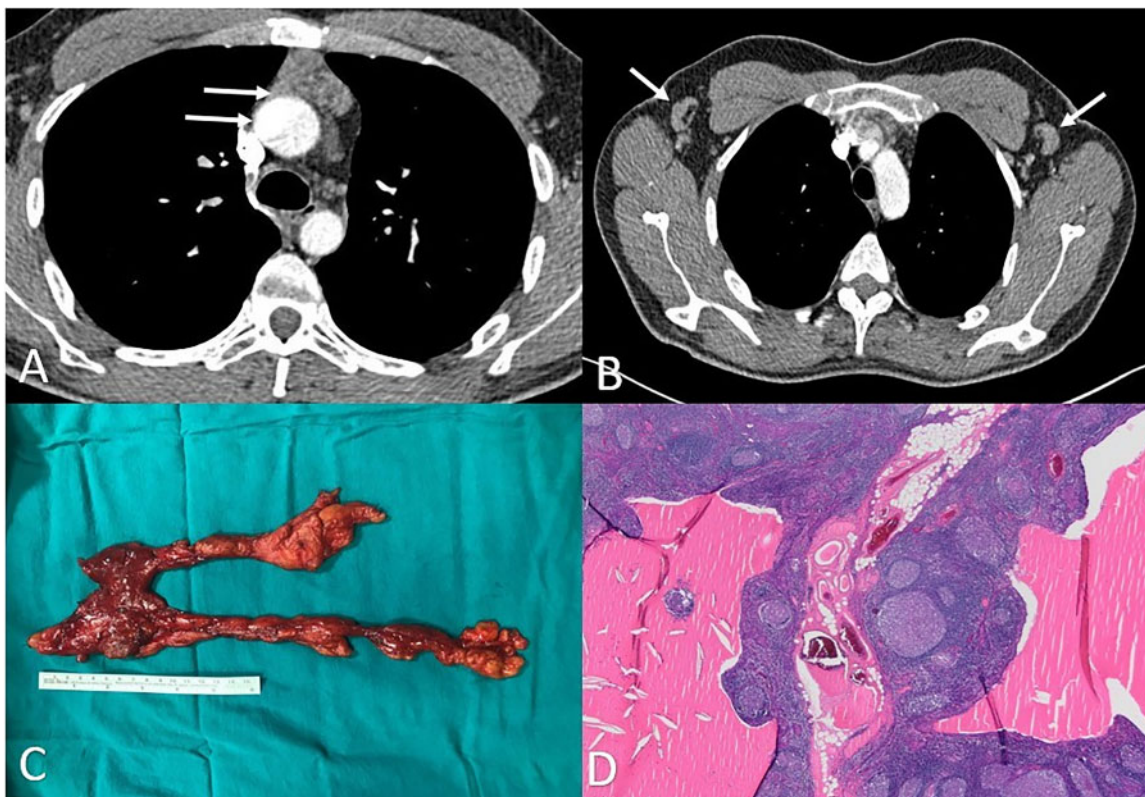
In laboratory investigations, anaemia (haemoglobin 11.5 g/dl), elevated ESR (104 mm/h), elevated CRP (20.7 mg/dl), positive RF (105 IU/ml) and positive anti-CCP (98.5 RU/ml) were found. Routine biochemistry, ANCA and ANA were all within normal limits. In addition, the Quantiferon-TB test was negative. In the chest radiograph, there was a radiodense mass-lesion appearance around the trachea. Thorax CT was ordered to rule out malignancy because of the suspicious mass-lesion appearance on chest radiography, weight loss and dyspnoea complaints.

Thorax CT revealed a homogeneous thymus gland with soft tissue density 2.6 cm × 4.5 cm × 8.4 cm in size in the anterior mediastinum, with axillary lymphadenopathies (Fig. 1A and B). Its density was higher than expected for his age, but there was no sign of a cystic or solid mass in it. Trans-sternal extended thymectomy was performed by an experienced thoracic surgeon, and the thymectomy

material was 20 cm × 10 cm × 1.5 cm in size and weighed 118 g (Fig. 1C). On macroscopic examination, multilocular cysts were found on the cut surface, many of which were filled with colloid-like material. Histopathological examination of the thymus revealed multiple cysts, hyperplastic lymphoid tissue with germinal centres, and Hassall corpuscles. The cysts were lined with thymic epithelium (Fig. 1D). Immunohistochemically, cytokeratin AE1/AE3 and p40 highlighted the epithelium of the cysts and Hassall corpuscles. Lymphoid markers revealed the mixed distribution of CD3<sup>+</sup> and CD20<sup>+</sup> cells and did not show monoclonal proliferation of B cells or T cells. Both CD20<sup>+</sup> B cells and CD3<sup>+</sup> T cells attacked the epithelium. Acquired multicystic thymic tissue with lymphoid hyperplasia was the pathological diagnosis.

After the operation, MTX 15 mg/week and HCQ 2 × 200 mg/day were started, and SSZ was discontinued because the DAS-28 was 5.1. After 3 months, adalimumab 40 mg every 2 weeks was added to the treatment regimen owing to inadequate response (DAS-28 of 5.1). At the last control visit, there was one tender joint and no swollen joints. ESR was 20 mm/h and CRP 2 mg/dl. The DAS-28 score was 2.8, and a major clinical response was observed. However, owing to severe limitation of the left hip, left hip replacement was done 2 months later.

The thymus, which is the main lymphoid organ responsible for the primary education of T cells, has a close relationship with autoimmune disorders. Dysregulation in thymic involution and T cell education process are proposed mechanisms for the pathogenesis of RA [3]. Another key structure, Hassall's corpuscles in the thymus gland, is thought to play a role via regulatory T cells in the pathogenesis of autoimmune diseases, such as RA [4]. Apart from thymic epithelial neoplasms, thymic enlargement and absence of thymic involution were present in ~20% of RA patients, and this rate was significantly higher in RA patients [5]. However, according to our literature review (with the following keywords in PubMed: arthritis and thymoma, arthritis and TH, arthritis and thymic cyst, RA and thymoma, RA and TH, RA and thymic cyst), we found that the coexistence of RA and thymic epithelial neoplasms was reported extremely rarely; three patients had thymoma, two had multilocular thymic cyst, one had mucosa-associated lymphoid tissue (MALT) lymphoma of the thymus and two had follicular hyperplasia of the thymus [6, 7]. Although we cannot confirm the link between the cystic thymic hyperplasia in our patient and the RA diagnosis, it would nevertheless be interesting to explore the association between thymic neoplasms and autoimmune rheumatic diseases further, based on the above findings. Besides, a recent study by Murata *et al.* [5] reported that prescription of biologic DMARDs was significantly higher in RA patients with thymic enlargement, similar to a former study by Meunier *et al.* [8]. Although there are no available data to suggest that RA patients with

**Fig. 1** Radiological, macroscopic and microscopic views of thymic hyperplasia

(A) CT obtained after i.v. administration of contrast showed a homogeneous thymus with soft tissue density in the anterior mediastinum (arrows). (B) There was reactive hyperplasia in the axillary lymph nodes on both sides (arrows). (C) The thymectomy material was macroscopically 20 cm × 10 cm × 1.5 cm in size and weighed 118 g. (D) A low-power view shows multiple cysts and hyperplastic lymphoid tissue (×20; Haematoxylin and Eosin staining).

thymic neoplasms have higher disease activity and progressive disease, our case suggests that patients with thymic enlargement and cystic thymic hyperplasia might have a more progressive disease course (our patient needed a hip replacement by 1 year).

In conclusion, clinicians should keep in mind thymic hyperplasia and other thymic anomalies in cases of clinical or radiographic suspicion in patients with RA.

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