A rare case of IgG4-related disease involving the uterus

Sr., IgG4-related disease is a disorder of uncertain aetiology characterized by tumour-like lesions at multiple sites, increased serum IgG4 and a rapid response to corticosteroid treatment [1, 2]. It can involve almost any organ, but uterine involvement has not been reported to the best of our knowledge. In the present report we describe a case of IgG4-related disease that involved the uterus.

A 68-year-old woman with no history of allergic disease had been prescribed oral antihistamines and low-dose betamethasone (0.25 mg/day) at a local clinic for persisting cough, erythema on bilateral forearms and peripheral blood eosinophilia (540/mm$^3$). The cough initially improved, but later returned, whereas the erythema and eosinophilia resolved. After 2 months the patient was referred to our hospital due to shortness of breath and bilateral pleural effusions. Vital signs were unremarkable; percutaneous oxygen saturation was 94% while breathing room air. No adventitious breath sounds were audible and dull percuSSIONs were noted on both sides of the chest. There was no evidence of erythema or oedema. Blood examination revealed normal serum CRP levels. Thoracentesis demonstrated bilateral exudative pleural effusions, but microbiological analyses of these fluids yielded negative results. The pleural effusion cytology showed neutrophils, lymphocytes and macrophages, but no malignant cells. Tests for serum tumour markers, IL-6 and autoantibodies were all negative. Tuberculosis infection was excluded on the basis of a negative IFN-γ release assay.

Contrast-enhanced whole-body CT performed as a screening study showed bilateral pleural effusions, thickening of the soft tissue around the descending aorta (Fig. 1A) and an enlarged heterogeneously enhancing uterus (Fig. 1B). Left thoracoscopic pleural biopsy was performed under local anaesthesia. Histopathological examination revealed pleuritis with plasma cell infiltration, but the aetiology was not determined. CT-guided needle biopsy from the paraaortic lesion was not performed to avoid risk. Gynaecological referral was made due to the uterine enlargement in this post-menopausal woman. Transvaginal endometrial cytology revealed atypical cells, but subsequent endometrial biopsy specimens did not contribute to the diagnosis. Uptake of $^{18}$Ffluorodeoxyglucose as measured by PET was observed in the bilateral pleura, paraaortic region and uterus (Fig. 1C). The patient agreed to a total hysterectomy for definitive diagnosis, of which differential diagnoses included malignancy, particularly lymphoma and sarcoma. Histopathologically the muscle layer of the uterine corpus showed fibrosis with lymphoid follicles that consisted of lymphocytes, plasma cells and eosinophils (Fig. 1D), accompanied by focal obstructive phlebitis. On immunostaining, plasma cells were positive for IgG and IgG4 (Fig. 1E), and the IgG4:IgG ratio was >60%. Furthermore, immunostaining with κ and λ antibodies supported no evidence of lymphoma.

Serum IgG4 was elevated [307 mg/dl (normal <135 mg/dl)], leading to a diagnosis of IgG4-related disease. Re-evaluation of the previously obtained pleural specimens revealed numerous IgG4-positive plasma cells. Treatment was initiated with prednisolone at a dose of 0.6 mg/kg/day. Repeat CT after 2 months, while taking a prednisolone dose of 0.2 mg/kg/day, revealed marked resolution of pleural effusions and paraaortic lesions. At the latest follow-up after 2 years, the patient remained well.

To the best of our knowledge, this is the first report of IgG4-related disease involving the uterus diagnosed based on consistent clinical and pathological features. Pleural involvement of IgG4-related disease is also rare, but we are aware of >10 published cases of IgG4-related disease with pleural involvement [1, 3, 4]. Non-infectious periaortitis is known to be a subtype of this disease [1]. Nonetheless, the simultaneous and isolated presentation of involvement of pleurae, paraaortic lesions and uterus may be rare.

In the present case, the muscle layer of the uterus showed fibrosis and infiltration of lymphocytes, eosinophils and IgG4-positive plasma cells. These pathological findings are consistent with previously described characteristics of IgG4-related disease [1, 2]. Uterine pseudotumours may be important differential diagnoses [5], including epithelial and stromal metaplasia, pseudolymphoma, inflammatory myofibroblastic tumour, adenomyosis and post-therapy surgical changes. Of these, inflammatory myofibroblastic tumour is frequently associated with IgG4-related disease in other organs such as the liver [6] and lung [4]. The pathological characteristics of inflammatory myofibroblastic tumours resemble those of IgG4-related disease, hence it is assumed that some past cases of uterine IgG4-related disease were diagnosed as uterine inflammatory myofibroblastic tumour.

Transvaginal endometrial cytology and biopsy did not yield the diagnosis in the present case. For the diagnosis of IgG4-related disease of the pancreas, the usefulness of endoscopic US-guided fine-needle aspiration has been increasingly recognized for obtaining adequate tissue samples [7]. Thus it is possible that transvaginal US-guided needle aspiration may be useful for diagnosing IgG4-related disease involving the uterus.
In conclusion, we demonstrate that IgG4-related disease can involve the uterus. Additional case descriptions are required to better characterize the pathological and clinical features of uterine IgG4-related disease.

**Rheumatology key message**

- It is important to recognize that IgG4-related disease can involve the uterus.

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**References**