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### Arthropathy with infiltrate IgG4-positive plasma cells in synovium

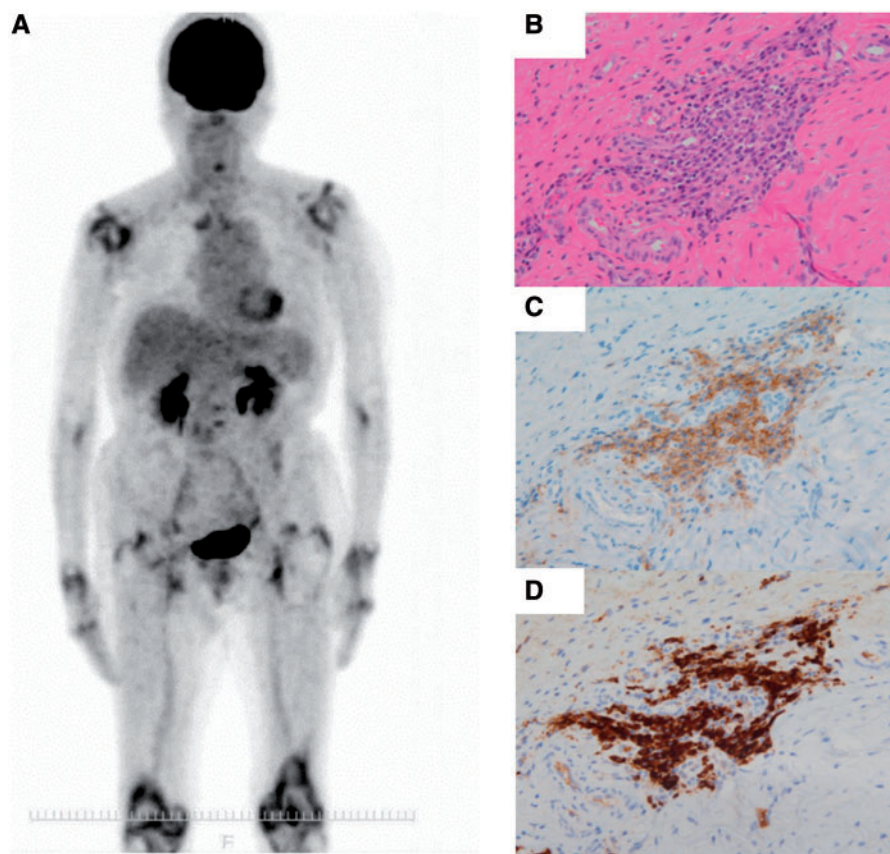
SIR, Recent reports of IgG4-related disease have described various organ involvement [1, 2]. Chronic inflammation can affect lacrimal glands, salivary glands, the thyroid, lung, pancreas, kidney and prostate. The concept includes Mikulicz's disease, Riedel's thyroiditis, pulmonary fibrosis, pulmonary pseudotumour, autoimmune pancreatitis, a part of tubulointerstitial nephritis and chronic prostatitis. It is important to note that these lesions can occur at different times and sites. The disease is clinically characterized by elevated serum IgG4 concentration and infiltration of abundant IgG4-positive plasma cells in the various tissues, mainly exocrine tissue [3, 4]. Mikulicz's disease presents with enlargement of the lacrimal or salivary glands with infiltrate IgG4-positive plasma cells. Numerous IgG4-positive plasma cells were characteristically observed in pancreatic tissue with autoimmune pancreatitis. In IgG4-related disease, mass-forming lesions (pseudotumours) that consist of lymphoplasmacytic infiltrates and sclerosis, such as retroperitoneal sclerosis, are observed [5]. Fluorodeoxyglucose PET (FDG-PET)/CT is a very useful tool for evaluation of multiple organ involvement in IgG4-related disease [6, 7]. Here, we would like to report a case of arthropathy with infiltration of IgG4-positive plasma cells in synovial tissue without any other organ involvement. In the present case, we have not detected any organ involvement or mass-forming lesion on FDG-PET/CT except for the joints.

A 74-year-old female, who had been diagnosed with OA, was admitted because of polyarthralgia and body weight loss (–15 kg/year). She was negative for fever and swelling of symmetrical submandibular glands.

Superficial lymph nodes were not palpable. Swelling of the joints of the hands, knees and shoulders without deformities were observed. CRP levels, serum IgG, serum IgE and IgG4 were elevated to 80, 36, 150 mg/l, 755 IU/ml and 2170 mg/l (normal range 700 mg/l), respectively. RF, anti-CCP antibody, anti-DNA and anti-Sm antibodies were negative except for ANA in a homogeneous pattern (1:80). Serum MMP-3 level was high (>800 ng/ml). Multi-centric Castleman's disease (MCD) and Crow-Fukase syndrome were initially considered because serum IL-6 and VEGF levels were elevated at 41.3 and 1870 pg/ml, respectively. The patient was negative for ascites, oedema in the extremities, splenomegaly and polyneuropathy. Polyclonal hypergammaglobulinaemia existed, but M-band was not found in immunoelectrophoresis. No mass lesions were observed in thoracic or abdominal organs on ultrasonographic examination and contrast CT imaging. FDG-PET/CT showed abnormal accumulation in multiple joints without organ involvement, including spleen or lymph nodes (Fig. 1A). Therefore, MCD, Crow-Fukase syndrome or SLE were unlikely in this patient. Right knee MRI revealed osteophytes, joint space narrowing and gadolinium enhancement of synovial tissue, and no bone destruction was observed. She was diagnosed with OA, and right total knee arthroplasty was performed. Histological examination of the synovium of the right knee showed papillary proliferation with marked infiltrate IgG4/CD138 double-positive plasma cells without lymphoid follicles or fibrosis (Fig. 1B–D). However, hyperplasia of the synovial lining cells, the hallmark of RA [8], was not observed in this case. Furthermore, a high concentration of serum IgG4 and abundant infiltration of IgG4-positive plasma cells in the synovium were observed. This contrasts greatly with RA, in which a high concentration of serum IgG1 and dominant IgG1-positive plasma cells in the synovium are common [9]. Lip biopsy was performed to rule out Mikulicz's disease and histopathological examination of minor salivary glands revealed no infiltrate IgG4-positive plasma cells. Based on these findings, she was diagnosed with IgG4-related arthropathy and low-dose prednisolone (15 mg/day) was administered for 12 weeks. Polyarthralgia disappeared, and CRP, serum IgG, IgE, IgG4, IL-6, VEGF and MMP-3 were decreased to 0.1, 13 320 mg/l, 600 IU/ml, 1520 mg/l, 11.2, 147 pg/ml and 300 ng/ml, respectively.

Arthritis is reported to occur in 10% of patients with IgG4-related systemic disease [4]. Recently, Shinoda *et al.* [10] reported a case of Mikulicz's disease with destructive arthritis in which histopathological examination of the synovium showed infiltrate IgG4-positive plasma cells. However, arthropathy without infiltration of IgG4-positive plasma cells in the various tissues has not been reported. Whole-body FDG-PET/CT scan can detect the active lesions in systemic IgG4-related diseases and active systemic lesions. In the present case, FDG-PET/CT scan showed abnormal accumulation of FDG only in multiple joints

**Fig. 1** FDG-PET/ CT and histological findings of the synovium of the right knee. FDG accumulation was observed only in multiple joints (A). Synovial tissue of haematoxylin and eosin staining (B), immunostaining for CD138 (C) and IgG4 (D) indicated in filtration of abundant IgG4-positive plasma cells in the tissue (original magnification  $\times 100$ ).



without any other organ involvement, such as lacrimal glands, submandibular glands, lymph nodes and pancreas. To the best of our knowledge, we have described for the first time a case of IgG4-related arthropathy without organ involvement.

#### Rheumatology key message

- We have described for the first time a case of IgG4-related arthropathy without organ involvement.

**Disclosure statement:** The authors have declared no conflicts of interest.

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