IgG4⁺ MOLPS associated with inflammatory abdominal aortic aneurysm, interstitial pneumonia and interstitial nephritis

Sir,

A 74-year-old man presented with anorexia, general fatigue, weight loss and purpura on the lower legs. Auscultation revealed trivial fine crackle. The white blood cell count was 5600/mm³, with 6.0% eosinophils. Haemoglobin was 8.5 g/dl. The C-reactive protein was 5.2 mg/dl. BUN, creatinine and uric acid were 11, 0.86 and 5.9 mg/dl, respectively. Liver enzymes were within normal limits. IgG, IgA and IgM were 6170 mg/dl, 129 mg/dl and 38 mg/dl, respectively. IgG1, IgG2, IgG3 and IgG4 were 3470, 1460, 552 and 807 mg/dl. IgE was 1070 IU/ml. Proteinuria was 100 mg/dl (0.7 g/day), and trivial microhaematuria was observed. NAG was 23.1 U/g-Crn. CH50, C3 and C4 were <6.3 CH50/ml, 19.2 mg/dl and <2.0 mg/dl, respectively. C1q was 36.0 µg/ml. The antinuclear antibody was 1280×. Rheumatoid factor and anti-cardiolipin β2 glycoprotein-I antibody were positive. Other serological tests, including ANCA, anti-ds-DNA antibody, anti-Sm antibody and anti-RNP antibody, were all negative. Enhanced computed tomography (enhanced CT) detected interstitial pneumonia and abdominal aortic aneurysm (AAA) with a wall thickness measuring 3.2 × 3.0 cm (Figure 1A). ¹⁸F-fluorodeoxyglucose positron emission tomography-CT (¹⁸F-FDG PET/CT) demonstrated increased

Fig. 1. Findings of enhanced CT. ¹⁸F-FDG PET/CT and renal biopsy. (A) Enhanced CT reveals wall thickness of abdominal aorta, compatible with IAAA (arrow). (B) PET-CT detects FDG uptake within thickened aortic wall, compatible with IAAA (arrow). (C) Light microscopic findings of a renal biopsy specimen. Patchy patterns of plasma cells infiltrations are observed in the interstitium. PAS stain. 200×. (D) Immunostaining of anti-IgG4 antibodies detected many IgG4⁺ plasma cells in the interstitium.
fluorodeoxyglucose activity in the thicken wall of AAA (Figure 1B). A renal biopsy specimen showed interstitial nephritis with patchy pattern infiltration of plasma cells (Figure 1C). Immunostaining of anti-IgG4 antibodies detected that a lot of IgG4-positive plasma cells infiltrated into the interstitium, compatible with IgG4-positive multi-organ lymphoproliferative syndrome (IgG4+MOLPS) (Figure 1D). He was treated with prednisolone (PSL) 40 mg daily. His clinical manifestations, laboratory data and imaging tests were all improved within 2 weeks.

IgG4+MOLPS is a new clinical entity, characterized by hyper-IgG4 gamma-globulinaemia, IgG4+ plasma cell infiltration in involved tissue with a favourable response to steroids, and includes Mikulicz’s disease, autoimmune pancreatitis (AIP), retroperitoneal and mediastinal fibrosis, interstitial nephritis and many other inflammatory conditions affecting multiple organs [1]. Though AAA is the most common type of aneurysm, IAAA is a rare variant of AAA, which is seen in 5–10% of all cases of AAA [2]. IAAA has some similarities to retroperitoneal fibrosis and had been previously considered to be one member of chronic periaortitis as well as idiopathic retroperitoneal fibrosis. Recently, IgG4+ IAAA has been proposed to be estimated as ‘IgG4-related periaortitis’ together with retroperitoneal fibrosis [3]. 18F-FDG uptake is caused by increased glucose utilization, observed not only in malignant cells but also in inflammatory tissue [4]. 18F-FDG PET/CT has been recently reported as being useful to diagnose and follow-up AIP and associated extrapancreatic lesions [4]. In the present case, steroid therapy could improve immediately the clinical manifestations of IgG4+MOLPS, such as interstitial nephritis, interstitial pneumonia and IAAA. 18F-FDG PET/CT is useful for monitoring both the disease activity of IgG4+MOLPS and the effect of steroid therapy.

Conflict of interest statement. None declared.

Supplementary data

Supplementary data are available online at http://ndtplus.oxfordjournals.org.

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Reversible proteinuria after adalimumab discontinuation in a patient with Crohn’s disease

Sir,

Renal complications are not infrequent in patients with inflammatory bowel diseases and seem to be more prevalent in patients with Crohn’s disease. The spectrum of renal complications in Crohn’s disease patients involves nephrolithiasis, amyloidosis, renal hypertension, glomerulonephritis (from minimal change nephropathy to rapidly progressive crescentic), tubulointerstitial abnormalities and iatrogenic complications related to medications such as aminosalicylates and cyclosporine.

Anti-tumour necrosis factor (anti-TNFα) agents, including adalimumab, constitute a new generation of biological agents used in the treatment of a variety of autoimmune diseases such as rheumatoid and psoriatic arthritis, ankylosing spondylitis and Crohn’s disease. We report herein a Crohn’s disease patient diagnosed with proteinuria that was totally reversed after discontinuation of adalimumab.

A 38-year-old male with terminal ileum Crohn’s disease diagnosed 6 months previously was admitted to our hospital due to a relapse. Before admission, the patient was administered methylprednisolone 32 mg/day with sub-optimal response. On admission, the patient underwent routine screening to exclude underlying infection prior to prescription of anti-TNF-α agents. Subsequently, the patient was started on adalimumab induction scheme (160 mg subcutaneously). Two weeks afterwards, the patient complained of lower limb oedema, and laboratory screening revealed proteinuria of 1600 mg/day without any evidence of other extraintestinal comorbidity. Adalimumab was discontinued and patient was followed up. Proteinuria resolved completely 4 weeks after adalimumab discontinuation, but we decided no adalimumab rechallenge and no renal biopsy. The patient was started on therapy with azathioprine 150 mg/day and is currently in excellent clinical status.

To the best of our knowledge, this is the first report of a patient with Crohn’s disease and adalimumab-associated proteinuria. Treatment with adalimumab may lead to antibody formation, but renal complications are rare and have so far been reported only in 11 patients with rheumatoid arthritis [1–5] but not in patients with inflammatory bowel disease. Of interest, in rheumatoid arthritis patients, proteinuria has also been reported during therapy with other than adalimumab biological agents such as infliximab and etanercept [3].

Renal histology, when performed in rheumatoid arthritis patients with adalimumab-related renal dysfunction, showed patterns of systemic lupus erythematosus-like...