weekly was added as a steroid-sparing agent. A repeat CT scan 6 months later (Fig. 1B) showed dramatic improvement and resolution of the periaortic tissue around the major abdominal arteries. Prednisolone was reduced to 15 mg, but methotrexate had to be discontinued due to abnormal liver function test.

After 7 months, her symptoms of abdominal discomfort, sweating and fatigue recurred. ESR was 80 mm/h and CRP 52 mg/l. A repeat CT scan this time showed left-sided hydropneumosis in addition to recurrence of periaortic inflammatory tissue (Fig. 1C). She was treated with intravenous pulse—Cyclophosphomide (1000 mg fortnightly, six pulses), and then commenced on MMF (2.5 g daily).

Four months after the start of MMF, she was asymptomatic. Her CRP normalized, prednisolone was reduced to 5 mg daily, and a repeat CT scan revealed complete resolution of the left hydropneumosis along with considerable reduction in the amount of soft tissue encasing the aorta and SMA (Fig. 1D). Fifteen months since the commencement of MMF she remains well, and her CRP is 15 mg/l.

Discussion

RPF is a rare disease with an estimated annual incidence of 0.1 per 100 000 person-years and a prevalence of 1.38 per 100 000 [6]. In view of the rarity of this disease, evidence for treatment is mainly in the form of either case reports or small series of patients. Hence it is important to report both positive and negative outcomes of treatment.

MMF is a potent inhibitor of inosine monophosphate dehydrogenase (IMPDH) which is a key enzyme in de novo synthesis of purines. Since T- and B-lymphocytes critically depend on purine synthesis for proliferation, inhibition of this key enzyme results in a potent cytostatic effect on the lymphocytes. MMF also inhibits various other lymphocyte functions like antibody formation, endothelial cell adhesion and recruitment of leucocytes to sites of inflammation. Although the pathogenesis of RPF is unclear, recent evidence suggests that it could be a B-cell dominant disease process. The evidence for this is the finding of lymphocytes (both B and T) and plasma cells in the aortic media and adventitia [7], increased expression of intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 in the aortic adventitial infiltrates [8] and finally several infiltrating B-cells showing clonal or oligoclonal immunoglobulin heavy chain rearrangement [9]. MMF may thus have a role in the treatment of RPF. The successful use of MMF to control disease activity in RPF has not been studied well. It is evident from literature review that there has been only one isolated report of successful use of MMF in disease control for as long as 14 months since initiation [10]. MMF was used as the initial immunosuppressive agent in this patient along with prednisolone (which was discontinued after one year). Our patient has done well since starting MMF, and her disease has been under control for almost 15 months since initiation. Although the initial response may have been due to cyclophosphamide, maintenance of immunosuppression with MMF has led to resolution of her symptoms, normalizing the inflammatory markers, reduction in steroid dosage along with a reduction in periaortic inflammatory tissue and hydropneumosis. Warnatz et al.’s [3] recent report of 20 patients with RPF included two patients who were treated with MMF as the initial immunosuppressive agent, and both did not respond. It is not clear from their report as to how long these patients received MMF. However, more evidence is necessary to confirm the exact role of MMF as an additional immunosuppressive agent in the armamentarium of drugs to treat RPF. We recommend that MMF should be tried as an alternative immunosuppressant in patients who fail to respond to the more routinely used drugs mainly for maintenance of remission.

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A case of Raynaud’s phenomenon in mixed connective tissue disease responding to rituximab therapy

Sir, We wish to report the first successful use of rituximab in Raynaud’s phenomenon associated with mixed connective tissue disease, with disappearance of associated anti-RNP antibodies.

A 40-year-old lady presented in 1997 with swelling of the small joints of her hands, Raynaud’s phenomenon and a restrictive lung defect on pulmonary function tests. She did not have features of other connective tissue diseases. She had a positive test for antibodies to ribonuclear protein (RNP) on two occasions and a diagnosis of mixed connective tissue disease was made. She remained stable on prednisolone 5–10 mg and hydroxychloroquine 200 mg bd until 2001.

Raynaud’s phenomenon then worsened, requiring intravenous infusion of iloprost (titrated from 0.5 to 2 mcg/kg/min on three successive days) every 3 months. Later, bosentan (125 mg bd) and tadalafil (10 mg bd) were tried. A digital sympathectomy helped briefly, but 3-monthly iloprost infusion continued, with infection of a femoral line on two occasions.

Falling DLCO and changes on high resolution CT was successfully treated with three fortnightly infusions of cyclophosphamide 500 mg. As skin healing also improved, further immunosuppressive therapy was considered, and the descriptions of rituximab in rheumatology [1–3] were therefore of particular interest. She had iloprost on two successive days (titrated as before), followed by 100 mg methylprednisolone i.v. and 1000 mg rituximab on day three. On the fourth day, she had a further 100 mg methylprednisolone and 500 mg cyclophosphamide. Two weeks later, the full schedule was repeated. There was a marked improvement in her hands with healing of skin ulceration and pain relief.

Symptoms began to re-occur 3 months later, and the schedule was repeated with omission of cyclophosphamide. Over the next 3 months, symptoms were minimal, and she described the treatment effect as ‘magical’. She has been since treated with the 3-day protocol (without cyclophosphamide) on two further occasions,
with no complications of treatment. Her RNP antibody test was negative when tested 3 months after the first, 2-week, schedule of treatment, and remained negative for over a year. However, her symptoms relapsed markedly in July 2006, with the RNP antibodies again detected (on two separate tests).

This is the first report of successful treatment of severe, refractory Raynaud’s phenomenon with rituximab (in combination with methylprednisolone, cyclophosphamide and ifoprost), with marked reduction in painful skin ulceration and disappearance of RNP antibodies. Recently, RNP antibodies were again detected associated with symptomatic relapse.

Significant reductions have been reported in antibody titre and/or in the proportion with a positive antibody test in a range of conditions [4–7], while clinical relapse correlated with rising antibody titre [8]. This was less striking with respect to dsDNA antibodies in SLE [6, 7].

RNP autoantibodies have not been implicated in the pathogenesis of Raynaud’s phenomenon. Senècal and colleagues [9] recently postulated a pathogenic role for autoantibodies in systemic sclerosis (though not for RNP). We suggest the improvement in Raynaud’s and the clearance of RNP antibodies are causally unrelated manifestations of the improved control of the underlying MCTD in response to rituximab.

We re-treated our patient without cyclophosphamide without any loss of efficacy. In SLE, a range of rituximab protocols have now been used [6, 7, 10]. Leandro et al. cautioned against the lower (<500 mg) doses of rituximab, while Weide [10] has retreated with 375 mg/m² every 3 months. Out of 24 patients from Leandro’s study [6], 13 remain in remission with a mean follow-up of 23 months (range 7–51 months). Seven patients from this cohort have been re-treated (interval to re-treatment unknown).

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Primary Sjögren’s syndrome associated with chronic periaortitis

Sir, Chronic periaortitis (CP) is a broad term that encompasses three disorders [idiopathic retroperitoneal fibrosis, inflammatory abdominal aortic aneurysm (IAAA) and periaurerealmsal fibroreti-7039 ] characterized by similar histopathological alterations, including adventitial and periadventitial inflammation, medial thinning, and advanced atherosclerosis [1].

CP has already been reported in association with various autoimmune disorders, such as Hashimoto’s thyroiditis, and systemic lupus erythematosus (SLE) [1–4].

We describe the first case of primary Sjögren’s syndrome in a patient with an IAAA.

Case report

A 79-yr-old male patient was admitted to our hospital because of dull, low-back pain that responded partially to non-steroidal anti-inflammatory drugs, fatigue and anorexia of a few months’ duration. The pain was aggravated by standing and walking.

Past medical history revealed xerophthalmia and xerostomia of 3–4 yrs’ duration.

The patient was taking regular ramipril 5 mg/day, acetylsalicylic acid 300 mg/day, lansoprazole 30 mg/day and medications for pain including diclofenac 75 mg/day, paracetamol 1 g/day and codeine prn.

On admission, physical examination was unremarkable, except for tenderness over the lumbar–sacral spine and the glutei.

Erythrocyte sedimentation rate (ESR) was 113 mm/1st h and C-reactive protein (CRP) was 13.8 mg/dl (normal values <0.5 mg/dl). A mild chronic disease type anaemia (Hb 11.4 g/dl; MCV 90) was noted. Serum creatinine, urine sediment and liver function tests were normal. Rheumatoid factor (111 IU/ml, normal, <20 IU/ml), antinuclear antibodies (titre 1/2560, speckled pattern) and anti-SSA and anti-LA (SSB) antibodies tested positive, whereas anti-neutrophil cytoplasmic-antibodies were negative. Serology for hepatitis C and Epstein–Barr viruses was negative.

X-rays of the lumbar–sacral spine and of the pelvis showed mild osteoarthritis of the spine and hips, which was felt not to be severe enough to account for the patient’s symptoms.

Both abdominal ultrasonography and computed tomography (CT) with enhancement demonstrated an abdominal aortic aneurysm with a diameter of maximum 7 cm.

Endoaneuroscopy and revascularization were performed to prevent aneurysm rupture. The aneurysm was partially excised and a vascular prosthesis was grafted into the aneurysm of the aortic wall. Histology of the excised aneurysm revealed an IAAA: the aortic wall showed a fibrotic tissue, scattered calcification, atherosclerotic degeneration of the intima and marked adventitial inflammation. The inflammatory infiltrate consisted of lymphocytes, plasma cells and some neutrophils prevalently surrounding the adventitial vasa vasorum (Fig. 1A).

A diagnosis of IAAA was made on the basis of the markedly increased inflammatory markers and of the histological findings.

To evaluate the extent of vasculitis a whole body 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) was performed. A vascular high-grade (grade 3) uptake in the abdominal aorta and iliac arteries was evident (Fig. 1B).

Twenty days after surgery, the patient was transferred to the Department of Internal Medicine for clinical re-evaluation and further investigations.

Schirmer’s test was positive (2 mm in the right eye and 4 mm in the left eye at 5 min, normal values ≥10 mm/5 min). Minor salivary gland biopsy showed a diffuse inflammatory interstitial