patients with contraindications to TNF blockers according to the recommendations established by an international expert committee [4]. However, in selected patients, combination of rituximab with MTX may not be warranted.

Pulmonary aspergillosis is a severe and potentially life-threatening infection complicating the clinical course of patients with immunodeficiency. It is infrequently encountered in patients with systemic autoimmune disorders treated with steroids and immunosuppressive drugs, but a recent survey demonstrated that mortality in these patients is even higher than in neutropenic patients [5]. In the randomized controlled clinical trials with rituximab in RA patients, only few cases of severe infections have been observed and noteworthy, no cases of tuberculosis or aspergillosis were recorded [6]. Thus, in individual patients with underlying chronic infections that are controlled by appropriate anti-microbial treatment, rituximab may represent a therapeutic option. However, two case reports have been published that describe the occurrence of aspergillosis in a patient with autoimmune thrombocytopenic purpura and in two patients with post-transplant lymphoproliferative disorders that were treated with rituximab [7–9]. As all these patients received extensive additional immunosuppressive treatment, the exact role of rituximab is difficult to define. However, experiments in B-cell deficient mice are in line with a slightly deteriorated anti-fungal immunity [10].

Our case report suggests that rituximab may present a therapeutic option in patients with severe RA and underlying chronic infections given that appropriate anti-microbial treatment is continued. However, in the individual patient, a careful consideration of the potential benefits of controlling RA and the risk of aggravating the underlying chronic infection has to be undertaken.

**Rheumatology key message**

• Rituximab is a therapeutic option for RA and chronic infections.

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


Department of Internal Medicine I, Division of Immunology and Rheumatology, University of Cologne, Cologne, Germany.

Accepted 14 March 2008

*N. Jung and K. Owczarczyk equally contributed to this work. Correspondence to: N. Jung, Department of Internal Medicine I, Division of Immunology and Rheumatology, University of Cologne, Kerpener Str. 62, 50935 Cologne, Germany. E-mail: norma.jung@uni-koeln.de

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ANCA, Anti-glomerular basement membrane Antibodies, cryoglobulins and normal immunoglobulins and protein electrophoresis. Serum glucose was 5.9. A renal ultrasound showed 11 cm unobstructed kidneys. Renal biopsy confirmed tubulointerstitial nephritis with severe generalized acute tubular damage and a mixed inflammatory cell infiltrate throughout the interstitium. She was treated with a short course of high-dose prednisolone (60 mg). She required temporary renal replacement therapy, but on discharge was off prednisolone and diuresing well.

One month later, she developed a painful and erythematous left eye. She was diagnosed with a left anterior uveitis and 2 weeks later developed a right anterior uveitis. She was treated with steroid eye drops and started on prednisolone, 30 mg. Review of the renal biopsy showed no granulomata and serum angiotensin-converting enzyme (ACE) was normal.

Five months after her initial presentation she was well with a creatinine of 180 and ESR of 26. On reducing the prednisolone she developed sicca symptoms with unilateral parotid swelling and was investigated for SS. RF, Ro and La were negative. Parotid ultrasound was normal. Schirmer’s test was negative and although a salivary gland biopsy showed mild chronic sialadenitis, she failed to fulfil the diagnostic criteria for SS. She was noted to be hyperthyroid with an elevated T4 of 33.5 pmol/l and low TSH of 0.1 mU/l that corrected spontaneously.

She remained on prednisolone, 2.5 mg for a number of years during which time her ESR ranged between 5 and 23, and creatinine remained stable at ~130. On attempting to reduce her prednisolone to <2.5 mg, she developed a flare of uveitis and what appeared to be an inflammatory arthropathy with pain, stiffness and swelling of the small joints of both hands. The dose of prednisolone was increased with good response.

Eight years following her initial presentation she began to complain of a nagging pain in the left buttock and thigh. Plain radiographs showed an erosive inflammatory arthropathy at the left hip. These findings were confirmed on MRI with no evidence of avascular necrosis (Fig. 1a). Hand and SI joint radiographs were normal Fig. 1b and c. Haematological investigations included an ESR of 26, CRP of 5, negative RF, Anti-CCP, ANA, serum ACE and HLA-B27 serotyping.

This patient presented with a severe tubulointerstitial nephritis and subsequent bilateral anterior uveitis consistent with TINU syndrome. Eight years later, she developed evidence of an erosive arthropathy.
inflammatory arthropathy of the left hip joint. An erosive arthropathy, in association with TINU syndrome, has not been previously described.

Between 2 and 8% of patients presenting to tertiary referral hospitals with uveitis have TINU syndrome [6]. The median age of onset is 13 yrs but there are reports of TINU amongst adults and even the elderly [7]. There is a tendency for TINU to occur earlier in males than females (mean age 16.8 vs 28 yrs) [8]. There are no specific racial affinities. The majority of cases occur in adolescent women with most recent series showing a 2:1 female to male predominance [9].

The pathogenesis is not well understood. Delayed-type hypersensitivity and suppressed cell-mediated immunity with a predominance of lymphocytes is likely to play a large role [2, 3]. Proliferation and activation of T lymphocytes is thought to be IL-2 mediated [10]. Polyclonal hypergammaglobulinaemia, circulating immune complexes and serological evidence of autoantibodies suggest that a disturbance in humoral immunity also plays a role [10, 11]. There is believed to be a genetic association, supported by the sequential development of TINU syndrome in monozygotic twins [11, 12] and a strong association with HLA-DQA1*01, HLA-DQB1*05, HLA-DQB1*01 in a series of 15 patients [13]. TINU syndrome has been reported in association with certain autoimmune diseases including primary hyperparathyroidism [14], RA [14, 15] and SS [16]. Although 50% of the cases are idiopathic [10, 16], antibiotics (24%), NSAIDS (18%) [16] and infections such as Chlamydia and EBV [17–19] play an aetiological role.

In addition to uveitis and renal disease, patients have often associated systemic features such as fever, weight loss, fatigue, malaise, anorexia, asthenia, abdominal or flank pain, headache, polyuria and nocturia. Uveitis is typically anterior (80%) [20], non-granulomatous [17] and bilateral (77%) [21]. The uveitis can occur up to 2 months before (21%) [17, 21] concurrently or up to 13 months after the onset of interstitial nephritis [10]. Renal disease may present with flank pain, sterile pyuria, haematuria, subnephrotic proteinuria and renal insufficiency. Proximal and distal tubular defects lead to glycosuria, amino-aciduria, phosphaturia and acidification defects [21]. Transient hyperthyroidism [22], as seen in our case and granulomatous hepatitis [23] have also been described. Our patient had salivary gland swelling and chronic sialadenitis; these features whilst suggestive of SS have also been described in TINU [1, 24]. There is an association between SS and the B27 SpAs [25]. Our patient was HLA-B27 negative and has evidence of an inflammatory arthritis that has not been previously reported in association with TINU.

Anergy has been reported in some patients with TINU [14, 25, 26] and may suggest a reduction in peripheral T helper function. This suppression of the systemic immune response with locally increased immune reactivity in the uveal tract and kidney is analogous to sarcoidosis. Granulomatous hepatitis, a recognized feature of sarcoidosis, has also been reported in TINU [23] and two cases of TINU have been described whose mothers had sarcoidosis suggesting a possible genetic link between these two conditions [17].

Laboratory findings in TINU include eosinophilia, anaemia, an elevated ESR, deranged liver function tests, polyclonal hypergammaglobulinaemia and elevated urinary β2 microglobulin. Associations with certain serological markers such as ANCA [28], ANA and RF have also been described.

Renal biopsy reveals tubulointerstitial oedema and a predominantly mononuclear cell inflammatory infiltrate. Eosinophils and non-caseating granulomas are frequently seen together with intratubular neutrophils. Glomerular and vascular structures are preserved and immunofluorescence and electron microscopy show non-specific changes.

The differential diagnosis is wide and includes sarcoidosis, SS, SLE, Wegener’s, Behçet’s and infectious diseases such as tuberculosis, brucellosis, toxoplasmosis and histoplasmosis. Renal dysfunction in TINU is usually self-limiting; this contrasts with SS or sarcoidosis, where renal function will continue to progress without treatment. A few cases of TINU do show progressive renal failure which may require temporary renal replacement therapy [29]. These patients respond favourably to systemic corticosteroids as observed in our case. Eleven percent of patients may show some persistent renal impairment [21] seen again in our case. Persistent renal dysfunction is more common amongst adults, the outcome in children even if untreated being more favourable [14, 17]. Uveitis tends to recur and relapses are common. Immunosuppression with cyclosporin may be required to achieve control of the intraocular inflammation and prevent relapses [30].

Historically, patients with TINU have presented predominantly to the renal and ophthalmology specialities. With the similarities of TINU syndrome to sarcoidosis and SS, and now its description in association with an inflammatory arthropathy, rheumatologists should also be increasingly aware of this syndrome.

Rheumatology key message

- Historically, patients with TINU have presented predominantly to renal physicians and ophthalmologists. With similarities to sarcoidosis and SS, and now its description with inflammatory arthropitis, rheumatologists should also be increasingly aware of this syndrome.

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

P. MANGAT, A. S. M. JAWAD, W. BROWNLEE

The Royal London Hospital, London, UK.

Accepted 19 March 2008

Correspondence to: A. S. M. Jawad, The Royal London Hospital, Bancroft Road, London, E1 4DG, UK.
E-mail: alismjawad1@hotmail.com

Letters to the Editor


20 Mandeville JT, Levinson RD, Holland GN. The tubulointerstitial nephritis and uveitis syndrome. Ocular Inflammatory Disease Center, Jules Stein Eye Institute, Los Angeles, CA 90095-7003, USA.


