33% [3, 7]. In our case, the plain radiograph showed a clear fracture line. The therapy for the navicular insufficiency fracture was performed non-operatively. Previously, we had experienced that conservative therapy for insufficiency fractures in patients with RA was an efficient treatment. A non-displaced fracture should be treated with conservative therapy if the patient is unable to be very active.

The ethical committee of Hamamatsu University School of Medicine authorized this work.

The authors have declared no conflicts of interest.

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Necrotizing scleritis associated with rheumatoid arthritis: long-term remission with high-dose infliximab therapy

Sir, Scleritis is a well-recognized and severe manifestation of rheumatoid eye disease [1, 2]. Treatment is systemic, usually with steroids and other immunomodulating drugs [1–3]. We report a resistant case of necrotizing scleritis associated with rheumatoid disease, which has been successfully treated for over 2 yr with infliximab. A 51-yr-old woman presented in 2002 with bilateral painful red eyes associated with photophobia but no visual disturbance, orbital discharge or evidence of infection. She had a 30-yr history of seropositive erosive rheumatoid arthritis (RA) which had not responded over the years to numerous disease-modifying drugs, including penicillamine, methotrexate, sulphasalazine and hydroxychloroquine. Ten years earlier she had had two MCP joint replacements. The past history included hypothyroidism, alopecia areata and hypertension. At presentation with eye disease, she was taking prednisolone 15 mg daily, penicillamine 750 mg daily, hydroxychloroquine 200 mg daily, thyrroxine, amlodipine, frusemid and fenbren.

Ophthalmological examination (Fig. 1) revealed perilimbal injection in the right eye (ciliary flush) and generalized redness of the bulbar conjunctiva of the left eye. There were keratic precipitates in both eyes with vision in right eye 6/6 and left 6/9. She had mild flare, resulting from extra protein in the aqueous. The findings were compatible with bilateral diffuse scleritis with anterior chamber activity.

Systemic examination revealed evidence of active synovitis with five swollen and six tender joints (out of 28), a DAS28 score of 5.84, long-standing rheumatoid nodules, but no signs of cutaneous small vessel vasculitis either around the nails or in association with rheumatoid nodules.

The scleritis was initially treated with continued oral prednisolone and topical prednisolone acetate 1%, one drop every 2 h. This had no effect over several months, so systemic treatment was changed, with an increase in oral prednisolone to 60 mg daily and substitution of sulphasalazine for penicillamine with no change in hydroxychloroquine. After 8 weeks a lack of effect led to the addition of oral cyclosporin 150 mg twice daily (2.6 mg/kg) and prednisolone was tapered to 25 mg daily. A further 6 weeks later no response had occurred. Signs of bilateral scleritis persisted and new areas of necrotizing scleritis and peripheral ulcerative keratitis with blurring of vision developed. Cyclosporin could not be increased because of hypertension, and high-dose methotrexate was avoided because of previous intolerance of this agent at a dose of 2.5 mg per week, in combination with sulphasalazine and t-penicillamine. In view of this, infliximab was commenced at a dose of 3 mg/kg at 0, 2 and 6 weeks followed by an infusion every 6 weeks, with methotrexate 5 mg/week.

The symptoms and signs of scleritis responded dramatically after three infusions of infliximab, and visual acuity improved to 6/6 in both eyes. Methotrexate was tolerated and so the dose was increased to 7.5 mg/week, and prednisolone was reduced to 12.5 mg daily. This led to a relapse in orbital pain and redness 2 weeks before the fourth infusion was due. Methotrexate was increased to 10 mg/week, but despite this the same pattern of relapse in scleritis recurred between the fourth and fifth infusions. Therefore the dose of infliximab was increased to 5 mg/kg at the fifth infusion. Subsequently, this dose every 8 weeks has been completely effective in controlling scleritis. At present she has received a total of 16 infliximab infusions over a period of 2 yr and the scleritis has become totally quiescent, with residual areas of scleral discolouration from previous disease and some inferior corneal scarring from previous keratitis. Prednisolone has been reduced to 6 mg, methotrexate continued at 12.5 mg, and both sulphasalazine and hydroxychloroquine discontinued. The peripheral joint disease has also improved, with resolution of morning stiffness and a fall in the DAS28 score from 5.92 before infliximab to between 3.45 and 3.96 over the follow-up period.
The eye is commonly involved in rheumatoid disease. After the sicca syndrome, the usual manifestation is in the form of episcleritis, a benign and often self-limiting condition characterized by redness and irritation. Scleritis is rare, occurring in 0.6% of rheumatoid patients. It is differentiated from episcleritis by the presence of pain and dilatation of scleral vessels. Slit-lamp examination reveals scleral thickening either focally (nodular scleritis) or diffusely. More severe cases may show areas of necrotic avascular sclera (necrotizing scleritis), as seen in this case. Anterior scleritis in rheumatoid disease is more likely to be focal rather than diffuse, and is histologically indistinguishable from scleritis associated with other systemic autoimmune diseases [3]. All types of anterior scleritis may involve the cornea, causing infiltration and melting peripheral ulcerative keratitis (PUK), as seen in this case. PUK may also occur in the absence of scleritis. Posterior scleritis is difficult to diagnose, and results in proptosis, serious retinal detachment and a swollen optic disc. Irrespective of the threat to vision, the occurrence of scleritis in rheumatoid disease is indicative of worsening of overall disease severity and an increased incidence of severe systemic disease, and cardiovascular mortality.

Topical steroids are ineffective but may be used to control associated anterior uveitis. Systemic therapy with high-dose corticosteroids and immunosuppressant agents is required for treatment of scleritis. Cyclosporin, methotrexate or methylprednisolone with cyclophosphamide are generally used [4–7]. Treatment-resistant scleritis represents a serious problem as both loss of vision and toxicity from corticosteroids and cytotoxic immunosuppression are undesirable. Our patient failed to respond to systemic corticosteroids or cyclosporin and so anti-TNF therapy was commenced. The rapid and dramatic response in both eyes, maintained for 2yr without relapse, is impressive, though it should be noted that the standard infliximab dose of 3 mg/kg given at intervals of 8 weeks was not adequate, and a dose of 5 mg/kg has been required. Infliximab and etanercept have been reported to be effective in a few other cases of scleritis in association with a variety of systemic autoimmune diseases [8–10]. However, there is some uncertainty about the use of etanercept, given a report of scleritis not responding in one RA patient treated with this agent [10]. Furthermore, there are reports of scleritis developing in four RA patients for the first time after the commencement of etanercept, in three cases between 1 and 6 months later [10] and in the remaining case 3yr later [11].

We report a patient with resistant severe bilateral rheumatoid-associated anterior necrotizing scleritis which has responded to high-dose infliximab and remained in remission for 2yr. Infliximab should be considered for resistant rheumatoid-associated scleritis.

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FATAL PROGRESSIVE SYSTEMIC SCLEROSIS FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANTATION AND HIGH-DOSE CHEMOTHERAPY

Sir, The prognosis of diffuse systemic sclerosis (SSc) and the lack of effective therapies together with well-defined prognostic factors for early mortality have allowed trials of high-dose chemotherapy (HDT) followed by autologous stem cell transplantation (ASCT) in severe SSc [1–3]. These trials have suggested that such regimens could improve SSc, especially skin involvement.

We report the first case of fatal diffuse SSc occurring after HDT including total body irradiation (TBI) and ASCT for treatment of a multiple myeloma (MM).

In 1999, a 48-yr-old woman was diagnosed as having a stage III IgG kappa-type MM with hypercalcemia and diffuse bone lesions. Primary Sjögren’s syndrome (SS) had been diagnosed in 1985 on sicca syndrome, arthritis, positive speckled anti-nuclear antibodies (ANA) (1:640), anti-SSA/ Ro and anti-SSB/La antibodies and Chisholm’s grade IV on salivary gland biopsy. Clinical and biological features remained unchanged for 14 years. Low-dose steroids were given during the 4yr preceding diagnosis of MM to control arthritis. During this period, the patient had no Raynaud’s phenomenon and anti-Scl70 antibodies were negative.

Following diagnosis of MM, it was decided to perform HDT and ASCT. Induction chemotherapy consisted of vincristine, adriamycin and dexamethasone infusions. The mobilization regimen used methylprednisolone and cyclophosphamide before stem cell apheresis. The conditioning regimen consisted of total body irradiation (TBI) (abdomen 12 Gy, chest 9 Gy and brain 11 Gy) followed by polychemotherapy including lomustine, etoposide, cyclophosphamide and melphalan. Rescue with ASCT was done 2 days after completion of chemotherapy. The patient was discharged 1 month later after ASCT. During the next 2yr, myeloma was in remission and the course uneventful.

In 2001, 24 months after ASCT, finger swelling occurred with severe Raynaud’s phenomenon involving all fingers and toes, with pulpal ulcerations. Nailfold capillary microscopy was