

Rituximab was well tolerated, and within 6 weeks, the patient's DAS28 score had fallen to 4.22, with a corresponding reduction in ESR to 5 mm/h (Fig. 1), enabling corticosteroid dose reduction. A marked functional improvement was reflected in her renewed ability to walk and drive. Review at 3 months showed maintenance of disease remission with a DAS28 of 3.97 paralleling the depletion of circulating B-cells.

Originally approved for the treatment of B-cell lymphomas, rituximab has been investigated in a variety of immune-mediated conditions in which B-lymphocytes are thought to play a role including open-label studies of systemic lupus erythematosus, idiopathic thrombocytopenic purpura, Wegener's granulomatosis and dermatomyositis [8]. The most convincing evidence of efficacy, however, comes from studies in RA with significant clinical improvements when used either as a single agent or in combination with methotrexate or cyclophosphamide [7].

That rituximab was successful in our case of polyarticular JIA strongly supports the hypothesis that B-cells play a role in the pathogenesis of the disorder. This would seem intuitive since this subset of JIA shares many features consistent with RA. Although studies suggest that response to rituximab in RA is related to RF positivity, treatment was beneficial in our patient despite the absence of autoantibodies. This would indicate that loss of B-cell tolerance is not the only B-cell process operating in JIA. It is now known that B-lymphocytes have much broader functions within the immune system, including T-cell activation and cytokine synthesis [9]. Disruption of these tightly regulated processes may lead to autoimmune disease.

To our knowledge, this is the first reported case of the successful treatment of JIA with rituximab. Specific B-cell depletion may represent a true alternative to conventional immunosuppressive therapy in the treatment of refractory polyarticular JIA, and we encourage further investigation in this area.

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1. Gare BA. Epidemiology. *Baillieres Clin Rheumatol* 1998;12:192–208.
2. Minden K, Niewerth M, Listing J *et al.* Long-term outcome in patients with juvenile idiopathic arthritis. *Arthritis Rheum* 2002;46:2392–401.
3. Lovell DJ, Giannini EH, Reiff A *et al.* Etanercept in children with polyarticular juvenile rheumatoid arthritis. Pediatric Rheumatology Collaborative Study Group. *N Engl J Med* 2000;342:763–9.
4. Lahdenne P, Vahasalo P, Honkanen V. Infliximab or etanercept in the treatment of children with refractory juvenile idiopathic arthritis: an open label study. *Ann Rheum Dis* 2003;62:245–7.
5. Reiff A. The use of anakinra in juvenile arthritis. *Curr Rheumatol Rep* 2005;7:434–40.

6. Woo P, Wilkinson N, Prieur AM *et al.* Open label phase II trial of single, ascending doses of MRA in Caucasian children with severe systemic juvenile idiopathic arthritis: proof of the efficacy of IL-6 receptor blockade in this type of arthritis and demonstration of prolonged clinical improvement. *Arthritis Res Ther* 2005;7:R1281–8.
7. Edwards JC, Szczepanski L, Szechinski J *et al.* Efficacy of B-cell-targeted therapy with rituximab in patients with rheumatoid arthritis. *N Engl J Med* 2004;350:2572–81.
8. Looney RJ. B cell-targeted therapy in diseases other than rheumatoid arthritis. *J Rheumatol Suppl* 2005;73:25–8.
9. Youinou P, Hillion S, Jamin C, Pers JO, Saraux A, Renaudineau Y. B lymphocytes on the front line of autoimmunity. *Autoimmune Rev* 2006;5:215–21.

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Chikungunya outbreak—remember the arthropathy

SIR, Chikungunya (CHIK) virus, a member of the Alphavirus genus in the family Togaviridae, was first isolated from the serum of a febrile human in the Newala district, Tanzania, in 1953 [1].

CHIK is an important human pathogen that causes a syndrome characterized by fever, chills, headache and severe joint pain with or without swelling (usually the smaller joints). The name is derived from the Makonde word meaning 'that which bends up' in reference to the stooped posture developed as a result of the arthritic symptoms of the disease [2, 3].

CHIK is geographically distributed from Africa through Southeast Asia and South America, and its transmission to humans is mainly through *Aedes* species mosquitoes [4].

Since 1953, CHIK has caused numerous well-documented outbreaks and epidemics in both Africa and Southeast Asia, involving hundreds of thousands of people [2].

CHIK virus outbreak of unprecedented magnitude is currently ongoing in Indian Ocean territories principally involving Réunion Island, Comoro, Mauritius, Seychelles and southwestern India [3, 5].

On Réunion Island, between March 2005 and March 2006, 3115 cases of CHIK were notified. Estimates from a mathematical model indicate that 204 000 people may have been infected by CHIK virus since March 2005 on Réunion Island. The peak of the outbreak was during the week of 30 January to 5 February 2006 [6]. Currently, although a decreasing trend is reported since mid February, the epidemic is still very active.

Case report

A 46-yr-old woman was admitted to our department of Tropical Medicine with a 1 month history of polyarthralgia affecting the wrists, hands and ankles. She became ill 5 days before her return to Italy after 2 weeks holiday on Réunion Island (from 15th to 30th of January 2006). She had acute symptoms of fever, shivering, headache and joint pain. Fever lasted only 2 days while joint symptoms persisted and she had to take non-steroidal anti-inflammatory drugs (NSAIDs) continuously. Her past history included hypothyroidism for which she has been currently taking levotiroxin 75 mcg daily.

The physical examination was non-contributory except wrists, hand and ankles tenderness, while there was no synovitis. Laboratory tests were normal except slightly increased C-reactive protein (1.35 mg/dl, normal value 0–1.0). Standard tests for rheumatological disorders including rheumatoid factor, anti-cyclic citrullinated peptide antibodies and antinuclear antibodies were negative. Tests for dengue and malaria were also negative.

On the grounds of the clinical and epidemiological features, CHIK arthropathy was suspected. The diagnosis was confirmed

with specific haemagglutination inhibition test. The patient was treated with NSAID (ibuprofen 1200 daily); joint pain was relieved in 2 months, but a residual joint stiffness persists.

Discussion

Arthritogenic alphaviruses are globally distributed mosquito-borne RNA viruses causing epidemics of polyarthritis/polyarthralgia, with disease emerging or re-emerging and increasingly being reported in travellers. Only six of the many alphavirus known to affect humans can cause articular manifestations. They are the CHIK, O'Nyong Nyong and Sindbis viruses from tropical Africa, the Ross River and Barmah Forest viruses from the South Pacific and the Mayaro virus from South America [7]. The current outbreak induced us to pay attention to CHIK arthropathy.

Most cases of CHIK arthropathy recover from the severe joint pains within several weeks but up to 12% retain some residual joint symptoms for a long time (up to 18 months) [8]. Usually, CHIK arthropathy does not cause permanent joint damage, but one case of destructive arthropathy was described [9].

Treatment of CHIK arthropathy with NSAID is usually sufficient; in refractory cases, Brighton SW [10] found significant improvement with chloroquine phosphate.

After the recent CHIK outbreak, several European countries including Germany, Italy, Belgium, Switzerland and Norway have been reporting cases imported in people returning from Indian Ocean islands [11].

CHIK arthropathy should be considered in the differential diagnosis of joint pain in people returning from areas where transmission occurs (sub-Saharan Africa, South East Asia, Indian subcontinent).

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1. Ross RW. The Newala epidemic. III. The virus: isolation, pathogenic properties and relationship to the epidemic. *Journal of Hygiene* 1956;54:177–91.
2. Rao TR. Recent epidemics caused by Chikungunya virus in India, 1963–1965. *Scientific Culture* 1966;32:215.
3. Ravi V. Re-emergence of Chikungunya virus in India. *Indian J Med Microbiol* 2006;24:83–4.
4. Diallo M, Thonnon J, Traore-Lamizana M, Fontenille D. Vectors of Chikungunya virus in Senegal: current data and transmission cycles. *Am J Trop Med Hyg* 1999;60:281–6.
5. Chastel C. Chikungunya virus: its recent spread to the southern Indian Ocean and Reunion Island (2005–2006). *Bull Acad Natl Med* 2005;189:1827–35.
6. Outbreak news. Chikungunya and dengue, south-west Indian Ocean. *Wkly Epidemiol Rec* 2006;81:106–8.
7. McGill PE. Viral infections: alpha-viral arthropathy. *Baillieres Clin Rheumatol* 1995;9:145–50.
8. Kennedy AC, Fleming J, Solomon L. Chikungunya viral arthropathy: a clinical description. *J Rheumatol* 1980;7:231–6.

9. Brighton SW, Prozesky OW, de la Harpe AL. Chikungunya virus infection. A retrospective study of 107 cases. *S Afr Med J* 1983; 63:313–5.
10. Brighton SW. Chloroquine phosphate treatment of chronic Chikungunya arthritis. An open pilot study. *S Afr Med J* 1984; 66:217–8.
11. Editorial Team, Pfeffer M, Löscher T. Cases of Chikungunya imported into Europe. *Eurosurveillance Weekly* 2006;11. Available from: <http://www.eurosurveillance.org/ew/2006/060316.asp#2>

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Successful treatment of rheumatoid vasculitis-associated foot drop with rituximab

SIR, B-lymphocyte depletion with rituximab, either alone or in combination with cyclophosphamide or methotrexate, has been shown to have efficacy in rheumatoid arthritis [1]. Rituximab has also been used as an alternative agent for anti-neutrophil cytoplasmic antibody (ANCA)-positive vasculitis [2, 3] and for giant cell arteritis [4]. We report our experience in using repeated courses of rituximab in a patient with severe refractory rheumatoid arthritis, complicated by vasculitis, who was unable to tolerate conventional disease modifying antirheumatic drug (DMARD) therapy and did not respond to other biological therapy.

A 68-year-old white male presented with symmetric synovitis of both wrists, of the metacarpophalangeal and proximal interphalangeal joints of both hands, and synovitis of the right knee, associated with a rheumatoid factor of 495 IU/ml. Because of his history of a past liver biopsy showing non-specific inflammation and focal fibrosis, he was unable to take methotrexate or leflunomide. Multiple DMARD agents including sulfasalazine, plaquenil, etanercept and anakinra were tried, but the patient failed to respond. During this time, he lost approximately 35 pounds and 7 months after diagnosis, developed a left foot drop. Biopsy of the sural nerve showed necrotizing vasculitis; ANCA and cryoglobulins were negative. Cyclophosphamide at 75 mg daily and high dose prednisone were started, but he developed febrile neutropenia requiring discontinuation of cyclophosphamide. Azathioprine at 75 mg daily was tried, but caused severe leucopenia and was discontinued. Rituximab at 700 mg weekly for 4 weeks for a total dose of 2800 mg was given to the patient along with a daily dose of 40 mg prednisone; he tolerated this well without leucopenia and with resolution of synovitis, and his erythrocyte sedimentation rate (ESR) declined from 100 to 35 mm/h. Despite continuation of prednisone at 30–35 mg daily, 5 months later, he developed recurrence of his synovitis, peripheral-oedema and hypoalbuminaemia, with an increase in his ESR to 62 mm/h and an increase in the rheumatoid factor (RF) to 6810 IU/ml. He was treated with a second 4-week course of rituximab, and responded well with resolution of his synovitis and oedema and normalization of his serum albumin. Prednisone was slowly tapered, and the ESR normalized to 12 mm/h and RF declined to 2970 IU/ml over the course of 6 weeks. After another 3 months, however, he again developed synovitis, elevation in his ESR to 75 mm/h and the appearance of new nodules on his forearms. His RF, however, was lower at 1690 IU/ml. Rituximab was reinstituted with the same weekly regimen and he again responded well, though he was noted to have a rash after the third infusion, which resolved without treatment. Three months after the third course, the ESR was 30 mm/h, RF was 484 IU/ml, and he was without synovitis and had regained the strength in his left foot affected initially by the vasculitis-associated foot drop.