without evidence of trauma while he was going downstairs. Physical examination showed a palpable defect in the quadriceps tendons, inferior displacement of the patella (patella baja), proximal ecchymosis, and swelling. Evaluation of range of motion revealed complete loss of active knee extension. The diagnosis of bilateral simultaneous rupture of the quadriceps tendons was suspected and further confirmed by knee radiographs, showing inferior patellar displacements without fracture. Additionally, marked radiological signs of osteitis fibrosa as well as dystrophic calcifications of the tendons were noted (Fig. 1). The patient never took glucocorticoids, aluminium compounds or fluoroquinolone. His past medical history was, however, significant for chronic renal failure (calculated creatinine clearance 12 ml/min) due to Berger’s disease diagnosed 8.5 yr before. He was also known to have severe secondary hyperparathyroidism [parathyroid hormone (PTH) 1099 pg/ml; normal range 10–46 pg/ml] with high calcium phosphate product (5.88 mmol²/l²; normal range: 1.8–3.7 mmol²/l²) and increased plasma alkaline phosphatase activity (368 UI/l; normal range: 40–130 UI/l) because he was non-compliant with the vitamin–calcium therapy.

The tendons were repaired using a non-absorbable suture passed through the patella using three tunnels. After surgery, his knees were immobilized in extension for 6 weeks, followed by gradual weight-bearing and gait training with braces. He was weaned off the braces as he increased the range of motion and strength in his knees. The course was satisfactory, both knees recovering a full range of motion within a 4-month period.

Simultaneous bilateral rupture of the quadriceps tendon is a very rare condition, which generally occurs in association with underlying chronic metabolic disorders such as gout, obesity, diabetes mellitus or end-stage renal failure [1]. In this last situation, the frequency of this complication, although difficult to determine, is thought to be lower than 3.5% [2]. Previous reports have pointed out a relation between the duration of haemodialysis and the occurrence of spontaneous tendon ruptures, suggesting that tendinous weakness resulted in these patients, from malnutrition, \( \beta_2 \)-amyloidosis [3] or accumulation of uraemic toxins [4], all classical complications of long-term chronic haemodialysis. Our observation, however, does not support such hypotheses. The spontaneous tendon rupture in our patient seems thus to have resulted rather from secondary hyperparathyroidism, as previously proposed by De Franco et al. [5]. Secondary hyperparathyroidism is indeed a classical complication of chronic kidney disease [6]. The pathophysiology of the disorder starts with retention of phosphorus resulting from the decrease in glomerular filtration rate, which leads to hypocalcaemia that stimulates PTH. The latter causes phosphaturia, with restoration of serum phosphorus and calcium towards normal. However, this occurs only at the expense of elevated serum PTH levels. High PTH levels result in high bone turnover, which in turn is responsible for subtenidous bone resorption at the sites of insertion. The occurrence of repeated minor avulsion fractures of the weakened bone cortex at the tendon insertion site precedes the final total tendon rupture, which then occurs after a minor trauma (spontaneous rupture) [2].

In addition to the previous mechanism, high calcium phosphate product in such patients leads to dystrophic calcifications of soft tissue, which further weaken the tendon and participate in the rupture [7, 8].

In conclusion, this case supports the role of secondary hyperparathyroidism in spontaneous rupture of the quadriceps tendon in chronic renal disease. Clinicians should be aware that careful management of vitamin–calcium therapy in such patients should efficiently prevent this severe complication, which is responsible for long hospitalization and prolonged morbidity.

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Successful treatment of severe Kikuchi’s disease with intravenous immunoglobulin

SIR, A 35-yr-old woman presented with a 2-week febrile illness associated with drenching night sweats and progressive swelling in the neck. An excision lymph node biopsy was undertaken (Fig. 1a). This showed reactive hyperplasia with expansion of the paracortex, rich in apoptotic plasmacytoid monocytes (CD123⁺, CD68⁺, BCL2⁻) and phagocytic histiocytes, typical of Kikuchi’s lymphadenitis. In view of her protracted symptoms and marked constitutional features, comprising a persistent fever with debilitating malaise, we elected to treat her with prednisolone 40 mg/day. She initially improved, but within 2 weeks had recurrent symptoms. These improved briefly on increasing the prednisolone to 80 mg/day and adding non-steroidal anti-inflammatory drugs,
but recurred. Over the subsequent 2–4 weeks she developed progressive cushingoid changes and the steroid dose was gradually reduced. Her lymph nodes continued to enlarge (Fig. 1b), culminating in an emergency admission when she presented with signs of impending airway obstruction, dysphagia to solids and periorbital oedema. Because of the unusual clinical progression, a further lymph node biopsy was performed and confirmed the diagnosis. There was no sustained therapeutic response to either 1 g intravenous methylprednisolone daily for 3 days or a trial of thalidomide 200 mg/day for 7 days.

The severity of her head and neck swelling made us consider other empirical anti-inflammatory therapies. Intravenous immunoglobulin (IVIG) was chosen because, compared with cyclophosphamide, anti-tumour necrosis factor (TNF) antibodies (e.g. infliximab) or soluble TNF receptor (etanercept), it incurred least risk of adverse effects. We administered IVIG at 0.4 g/kg per day for 3 days. A definite improvement in her facial swelling occurred within 4 days, followed by gradual but complete resolution of lymphadenopathy over the subsequent 8 weeks, despite stopping steroid medication altogether. Her lymphadenopathy resolved completely by 8 weeks and she remained well during 8 months of follow-up.

Kikuchi’s disease is an idiopathic illness characterized by a self-limiting lymphadenitis that normally resolves over subsequent weeks or months without specific treatment [1]. A handful of fatal cases have been described in addition to sparse reports of empirical treatment with a diverse selection of agents, which include antimicrobial and anti-inflammatory drugs [1–4]. Although associations with infective agents have been reported, a causal link has not been established. Instead, several lines of evidence support an association with systemic lupus erythematosus (SLE). This may preclude, coincide with or develop after the presentation of Kikuchi’s disease [5, 6]. Lymph node expansion in Kikuchi’s disease is principally due to apoptotic CD123+ plasmacytoid monocytes [1, 7], which are also recruited to cutaneous lesions in SLE and may be the source of high IFN-α levels in active disease [7]. Furthermore, accumulation of apoptotic plasmacytoid monocytes in Kikuchi’s disease shows parallels with defective clearance of apoptotic cells in SLE [8] and supports a pathogenetic association. Tender lymphadenitis and fever in Kikuchi’s disease may cause significant morbidity and has led to a range of empirical treatments. Apparent therapeutic responses to minocycline [2] and ciprofloxacin [3] have been used as supportive evidence for an infective aetiology in Kikuchi’s disease, but in each case the time course of recovery was consistent with the natural history in most patients. A similar observation has been made for hydroxychloroquine [4] and used to support the association with SLE. The most frequent reports are of treatment with corticosteroids, to which most patients seem to respond, even with relatively short courses or low doses [1]. Despite transient remission of symptoms when we treated our patient with prednisolone, her prompt relapse was subsequently resistant to further corticosteroids, even at very high doses. By the time she presented with thoracic outlet obstruction due to lymphadenopathy, her illness had lasted longer than expected, with no signs of resolution. Her subsequent recovery within days of starting the course of IVIG was therefore striking.

The specific therapeutic effect of IVIG in a patient presenting solely with Kikuchi’s disease has not been described before. Interestingly, however, two case reports describe a therapeutic response to combined treatment with IVIG and corticosteroids in children with haemophagocytic syndrome and concurrent Kikuchi’s lymphadenitis [9, 10], providing additional support for our observation. IVIG has become established in the treatment immunological and inflammatory diseases, including SLE, by virtue of diverse immunomodulatory mechanisms [11]. Anti-idiotypic antibodies against autoantibodies and competition with endogenous autoantibodies for binding of Fcγ receptors or complement components may be important in autoimmune diseases. Its interaction with complement, which normally provides potent amplification of inflammatory responses, may underlie the observation that IVIG has more non-specific anti-inflammatory effects, and may be effective in conditions where no autoantibody has been demonstrated. Modulation of T-cell-dependent inflammation is also described, although the mechanism is not clear. In view of its pluripotent effects, IVIG therefore represents a suitable candidate for empirical treatment of idiopathic inflammatory conditions such as Kikuchi’s disease, which may ultimately represent common downstream effects of dysregulated immunological responses with heterogeneous aetiologies.

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Letters to the Editor


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Two cases of serious food-borne infection in patients treated with anti-TNF-α.
Are we doing enough to reduce the risk?

Sirs. We would like to report two cases of serious food-borne infection in patients receiving anti-TNF-α drugs, review previous case reports and suggest that the delivery of appropriate food hygiene advice to patients prescribed these drugs could be important.

Case 1 was a 65-yr-old man with ankylosing spondylitis and chronic renal failure (serum creatinine stable at 190 μmol/l) due to NSAID-induced interstitial nephritis. He had been receiving infliximab infusions at 5 mg/kg once every 8 weeks for the previous 11 months. Treatment had been successful in reducing symptoms, improving function and reducing his dependence on indomethacin. He presented with a 7-day history of fever and watery diarrhoea, which started a week after an infliximab infusion. On examination, temperature was 38.6°C, respiratory rate 24/min and blood pressure 110/70 mmHg. Blood tests showed a white cell count of 11.2 × 10^9/l, CRP 307 mg/l (normal 0–10), urea 6.7 mmol/l and creatinine 250 μmol/l. Stool cultures were negative for enteric pathogens but blood cultures grew Listeria monocytogenes. He was treated with amoxicillin 2 g intravenously 6-hourly for 10 days and supportive measures. On further questioning, the patient admitted to eating unpasteurized cheese purchased from a local farm prior to the onset of the symptoms. He was fond of soft cheeses and obtained them from this source regularly. Unfortunately, no sample of cheese was available for culture. He made a good clinical recovery and his renal function and electrolytes returned to baseline levels within a week. Treatment with etanercept was restarted 6 weeks after the end of the antibiotic course.

Case 2 was a 67-yr-old lady with rheumatoid arthritis (RA). She had received infliximab infusions 3 mg/kg once every 6 weeks for 6 months with prednisolone 7 mg daily and methotrexate 15 mg weekly. Her RA had been well controlled on this drug combination. She then presented with a very painful swollen left knee joint 2 weeks after an infliximab infusion. There was no history of fever, diarrhoea or pain and swelling in other joints. On examination her temperature was 37°C, pulse was 90 beats/min and blood pressure 154/90 mmHg. Her left knee was swollen, warm and markedly tender with gross limitation of movement. No synovitis was obvious in other joints. Blood tests showed a white cell count of 12.4 × 10^9/l with neutrophilia; ESR was 52 mm/h and CRP 153 mg/l. Initial analysis of joint fluid showed no evidence of organisms on Gram staining and culture. A second synovial fluid aspirate 1 week later grew Salmonella; however, blood and stool cultures were negative for salmonella. Further questioning revealed that the patient regularly obtained hens eggs directly from a nearby farm and had recently eaten partly cooked eggs. Management consisted of initial bed rest, analgesia, arthroscopic joint lavage and oral ciprofloxacin for 4 weeks. The patient recovered completely from the infection and infliximab was recommenced 8 weeks after the end of the course of the antibiotics. She remains well, with no evidence of recrudescence of the joint sepsis 4 months later.

These two serious infections are likely to have been transferred from food sources. L. monocytogenes can be found in uncooked meat and vegetables, unpasteurized milk or foods prepared from raw milk [1]. Contamination of some food, such as hot dogs and delicatessen meats, can occur during packaging after the food has been processed [1]. The organisms are killed by cooking but can grow in refrigerated foods. The incidence of L. monocytogenes infection reported through the National Enhanced Listeria Surveillance System has increased since 2001 (146 and 139 cases reported in 2001 and 2002, respectively [2]). The incidence is higher in Yorkshire and Humberside, East Midlands and Wales compared with other regions [2]. L. monocytogenes infection has been reported in 15 patients receiving anti-TNF-α drugs [3]. Notably, 14/15 patients were receiving infliximab. Six deaths were reported in this group, suggesting the potentially serious nature of this infection. Additionally, cases of Listeria meningitis have been reported in RA patients treated with anti-TNF-α drugs [4, 5].

Salmonella can be spread through contaminated raw eggs, in unpasteurized milk and in under cooked meat. Two cases of Salmonella septicaemia were reported to the BSR Biologic Register [6]. Both of these patients were receiving etanercept. Katsarolis et al. [7] have reported a case of septic arthritis caused by Salmonella enteritidis in a patient receiving infliximab for RA. Netea et al. [8] have also reported two cases of Salmonella septicaemia in RA patients during anti-TNF-α therapy.

Food-borne infection from typical identifiable sources might be avoided with appropriate knowledge and advice. There are two main risk issues. The first is consumption of food that is typically known to have a high risk of specifically carrying and spreading potentially infectious organisms. This includes soft cheese contaminated with Listeria and eggs carrying Salmonella. The second issue—and a more general phenomenon—is transfer or spread of potentially infective organisms from poorly prepared foods. Listeria infection (1.5 cases per million/yr), though relatively rare in the general population, has clearly made an impact in patients treated with anti-TNF-α drugs. Salmonella infection is more common than Listeria infection in the general population (11 cases/1000 people/yr in UK, European and North American populations [9]) and therefore potentially poses a greater risk burden.