rheumatic disease over a 6-week period on 253 consecutive patients who had been attending the rheumatology outpatient clinic for >12 months. A record was made of their diagnosis, current disease-modifying-drugs (DMARDs) and all interventions that had been undertaken in the clinic in the preceding 12 months. Anti-rheumatic ethical approval and informed patient consent was not required for this case-review-based study as confirmed by the trust research office.

The majority of patients had a chronic inflammatory arthritis; the largest subgroup being rheumatoid arthritis (47%) with psoriatic arthritis the next biggest group (14%), followed by osteoarthritis (13%), systemic lupus erythematosus (6%), ankylosing spondylitis (4.5%), seronegative arthritis (3%), amyloidosis (1%), juvenile idiopathic arthritis (1%) and others (8%).

In the previous 12 months, 90% of patients had required at least one specialist intervention including the following:

- Thirty percent of the patients had received an intra-articular or soft-tissue steroid injection.
- Thirty percent of the patients had required a dose adjustment or change of DMARD.
- Twenty-six percent had a change or new prescription of an analgesic or anti-inflammatory drug.
- Thirty-two percent of patients had a radiological investigation, five percent had diagnostic musculoskeletal ultrasound performed at the clinic.
- Twenty percent were referred to another member of the multidisciplinary team or medical specialty.
- Other interventions included adjustment of oral steroids (11%), adjustment of other rheumatological treatments (10%), blood testing other than for routine monitoring (11%), pulse of methylprednisolone (10%), admission to day ward or inpatient ward (10%).

Only 25 patients (10%) had no interventions in the preceding 12 months. Ninety percent of patients had one intervention, 31% had two, 23% had three, 10% had four, 4% had five, 2% had six and one patient (<1%) had seven interventions. The median number of investigations per patient was 2, with a mean of 2.07 interventions per patient. Of the 25 patients who had no intervention, 22 had a chronic inflammatory arthritis, and 15 were maintained on DMARD therapy.

This study was conducted in a general rheumatology outpatient clinic in a teaching hospital. The staff involved were Consultant, Specialist Registrar (SpR), Senior House Officer (SHO) and Nurse Specialist. The review patients are largely seen every 6–8 months during a 15 minute appointment. There were no complex connective tissue disease/vasculitis patients and few patients on biological therapies as they are seen in separate clinics. The patients at this clinic could therefore be considered to be a ‘stable’, less ill population and yet 90% of them required a specialist intervention in a 12 month period, 64% requiring between two and four interventions. Even the majority of those who had no intervention had chronic inflammatory disease and most were on DMARDs.

These results suggest that very few of our review patients could be discharged without the need for further ongoing care. In this practice, the consultant already receives on average 2–3 referrals per week as well as 3–4 letters or phone calls per week from GPs seeking advice.

It appears that those involved in these management decisions consider the surgical ‘one stop shop’ model of care to be appropriate, suggesting a fundamental lack of understanding of the management of chronic disease.

In the era of biological therapies, early aggressive treatment, ‘tight control’ of inflammatory disease [1], cardiovascular risk assessment, etc., we are now able to influence the natural history of rheumatic disease more than ever. It is likely, therefore, that patients will require more frequent review by trained specialists rather than less.

In our view, the care of review patients cannot be sacrificed to free up clinic time for new patients who may in turn become review patients. This study has highlighted the need for long-term specialist care for all patients with chronic rheumatological disease.

Rheumatology key message

- Patients with chronic rheumatological disease require long-term specialist review.

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Mevalonate kinase deficiency syndrome with structural damage responsive to anakinra

Sir, mevalonate kinase deficiency (MKD) syndrome is an autosomal recessive autoinflammatory disorder caused by mutations in the MVK gene. We describe the first case of MKD syndrome with structural damage successfully treated with anakinra.

A 32-year-old French Caucasian woman experienced relapsing flares of progressively destructive bilateral and symmetrical polyarthritis involving small and large joints with morning stiffness (lasting 2–4 h). Synovial fluid, drained several times, was inflammatory and contained an average of 30,000 leucocytes/mm3 (98% neutrophils), without crystals or bacteria. X-rays detected joint-space narrowing and erosions in several joints (Fig. 1). She had three or four polyarthritis attacks/year, each lasting 2–3 weeks, associated with fever (38–39°C), chills, fatigue, headaches, maculopapular rash, diarrhoea, vomiting with severe abdominal pain (macroscopically inflammatory peritonitis without bacteria), splenomegaly, bronchopneumopathy, elevated ESR (40–100 mm/1st h) and high CRP (50–200 mg/l). Since childhood, no autoantibodies (rheumatoid factor, antinuclear antibodies, anti-citrullinated antibodies) have ever been detected.

The extra-articular symptoms started at 3 months (1974) with flares occurring at irregular intervals; atypical systemic juvenile idiopathic arthritis (sJIA) was diagnosed, but was considered in 2004 when laboratory investigations showed high serum immunoglobulin D (IgD) [166.4 mg/l (28.2 < normal range <141 mg/l)], elevated mevalonaciduria [19.2 mmol/mol of creatinine (normal range <1.3 mmol/mol)] and low mevalonate kinase activity in lymphocytes [0.7 μkat/kg of protein (2.5 < normal range < 7.8 μkat/kg)]. Sequencing of the 10 MVK-gene exons detected a four-base deletion (c.475–478 delACTG) and an
undescribed Q390P mutation, but no mutations were found in the genes encoding cold-induced autoinflammatory syndrome 1 (CIAS1) or tumour necrosis factor-receptor–1A (TNFR1A). MKD or hyper-IgD syndrome (HIDS) was diagnosed. Because of earlier successive failures of sulfasalazine, leflunomide and etanercept before MKD diagnosis, and corticoid dependency since childhood (5–10 mg/day), subcutaneous IL-1Ra (100 mg/day; anakinra) was started and has been continued since July 2005. Most disease manifestations regressed dramatically (joint pain with morning stiffness resolved completely; ESR and CRP normalized) and no new flares have occurred. In November 2005, erysipela led to anakinra interruption and a typical MKD flare ensued (CRP, 200 mg/l; ESR, 100 mm/1st h; serum IgD, 478 mg/l; mevalonaciduria, 9 mmol/mol of creatinine). Anakinra reintroduction obtained complete resolution of all clinical manifestations and normalization of biological parameters. This response has persisted for ≥14 months. IL-1Ra is well tolerated. In January 2006, the patient was able to stop corticosteroids.

Until 2004, this patient’s polyarthritis and joint destructions were thought to be aSJIA. During childhood, her IgD level was slightly above normal only once, which was insufficient to diagnose HIDS. Extensive clinical investigations failed to discover any definitive microbiological or immunological abnormalities. Recent genetic identification of autoinflammatory disorders and biological investigations established MKD and HIDS during flares. The severe structural damage of her atypical MKD broadens the spectrum of this disease and contributed to its late diagnosis. Indeed, 80% of HIDS patients have arthralgias and joint flares but destructive arthritis is extremely uncommon. Joint involvement usually consists of symmetrical non-destructive oligoarthritis of enlarged joints in 68% of the patients [1–4]. A continuously high serum IgD (>100 IU/ml or 141 mg/l) constitutes a unique hallmark of HIDS, but is not HIDS-specific and can be observed in TNF-receptor-associated periodic syndrome or Mediterranean fever. The precise role of IgD in HIDS pathogenesis has not yet been elucidated and the serum IgD level in HIDS is not correlated with disease severity or frequency of attacks. The abnormal immunoglobulin pattern in HIDS is not specific to IgD, since >80% of patients also have high IgA levels, meaning elevated IgG levels could be an epiphenomenon. Thus, MKD diagnosis is based on the detection of elevated mevalonate excretion in urine alone or in combination with increased IgD. In accordance with the literature, our patient suffered successive therapy failures [5]. Anakinra effectively achieved 42.1% fewer fever peaks/month with CRP and ESR normalization in two patients [6, 7]. To the best of our knowledge, this is the first report of successful and sustained anakinra efficacy against clinical and biological symptoms of MKD syndrome with structural damage that was confirmed by the spectacular regression of an MKD relapse suffered after its temporary withdrawal.

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Relapse of skin thickening after discontinuation or decrease of azathioprine therapy in a patient with diffuse cutaneous systemic sclerosis

Sir, Skin thickening in diffuse cutaneous systemic sclerosis (dcSSc) is reported to reach its maximum early in the course of disease, usually within 1–3 yrs from the onset of skin involvement, during which period internal organ involvement mainly arises [1]. Here we report on a male patient with dcSSc who had two periods of relapsing skin involvement occurring after discontinuation or decrease of azathioprine therapy. The relapses were registered by palpation and by ultrasound (US) assessment.

A man born in 1931 with a history of hypertension, macroscopic haematuria and a diagnosis of benign prostate hyperplasia was admitted in October 1995 with a 1-yr history of Raynaud’s phenomenon. In addition, he had developed swelling and stiffness of hands and feet for half a year and complained of fatigue. Skin palpation revealed thickening over fingers, arms and feet but not proximal to elbows and knees. A diagnosis of limited cutaneous systemic sclerosis (lcSSc) was established, with involvement of skin (skin score 15 points with a modified Rodnan skin score [2]), gastrointestinal tract and lungs [vital capacity (VC) 76% of predicted value (%p) and carbon monoxide diffusing capacity (DLCO) 64%p]. High-resolution computed tomography (HRCT) was not available at the time at our department but chest radiography was normal. Because of the pulmonary involvement, evidenced by decreased pulmonary function despite short disease duration, oral cyclophosphamide therapy was started in November 1995. Clinical assessment in December 1995 showed progression of skin involvement (Fig. 1A), which by then was also present proximal of the knees, and the diagnosis was revised to dcSSc. The cyclophosphamide therapy was stopped after only a few weeks due to haematuria. The patient was admitted to the urology service where the haematuria was assessed and associated to the benign prostate hyperplasia. Transurethral prostatectomy was performed and the cyclophosphamide therapy was restarted with three i.v. pulses (500, 700 and 700 mg) during March and April 1996 followed by oral therapy. Assessment in October 1996 showed stabilized VC 79%p, with DLCO 52%p and normal X-ray of the chest. The cyclophosphamide therapy was discontinued and azathioprine was started in February 1997 at which time the patient had been treated for 1 yr with cyclophosphamide. At repeated assessments, the skin involvement decreased and the pulmonary function remained stable. The gradual decrease in skin thickness was verified by high-frequency (20 MHz) US (Fig. 1B), which also showed an increase in echogenicity compared with that in 1995. In September 2000, the skin score was only 1 point and in June 2001, the azathioprine therapy was discontinued. Five months later, in November 2001, stiffness of hands and arms had recurred and the skin score was now assessed as 20 points (Fig. 1A). The increase in skin thickness was verified by US (Fig. 1B) that also showed lower echogenicity. No decrease in pulmonary function was noted and HRCT was normal. Azathioprine was reintroduced at a dosage of 150 mg/day. Subsequently, the skin involvement again regressed. In December 2003, after 2 yrs of azathioprine treatment, the dose was tapered to 100 mg/day and in September 2005, after another 18 months, further to 50 mg/day. However, at the yearly check-up in September 2006, a new skin worsening was noted by the patient. The examination showed increased skin score and US indicated increased skin involvement. The azathioprine dose was again increased to 150 mg/day. At the most recent visit to the outpatient clinic in April 2007, the patient reported that the skin stiffness had disappeared. The skin score and the US assessment showed a modest improvement. The pulmonary function tests remained stable.

Several open reports [5, 6] and two controlled studies [7, 8] have shown a beneficial effect of cyclophosphamide in patients with interstitial lung disease in SSC. One of the controlled studies in addition reported an improved skin score compared with the placebo group [8]. Due to the risk for serious dose-related side-effects, most centres try to restrict cyclophosphamide therapy to between 6 and 12 months. This is then followed by maintenance therapy with e.g. azathioprine or more recently with mycophenolate mofetil [9]. There are no agreed recommendations for how long the maintenance therapy should be continued. We show in the present case report that relapses of skin involvement can occur...