Raynaud’s phenomenon associated with Kimura’s disease

Sir, Kimura’s disease (KD) is a rare chronic inflammatory condition classically presenting as a subcutaneous mass in the head and neck region, peripheral eosinophilia and elevated serum immunoglobulin E (IgE) which has rarely been recorded in the rheumatological literature [1]. We describe a man presenting with Raynaud’s phenomenon as a manifestation of KD which to our knowledge has not been previously reported. We briefly discuss the pathology of KD and its treatment, and suggest that rheumatologists should be aware of the existence of this unusual condition.

A 54-yr-old man presented in November 1998 complaining of a left groin mass of 6–7 months’ duration, generalized pruritus and symptoms of recent onset Raynaud’s phenomenon in an asymmetrical distribution, complicated by ulcer formation on the left little fingertip. He was taking allopurinol in the absence of a confirmed classical clinical history of gout.

Initial investigations showed a white cell count of 11.4 × 10^9/l (differential not available), erythrocyte sedimentation rate (ESR) 6 mm/h, haemoglobin 16.3 g/dl, alkaline phosphatase 324 IU/L (normal range 0–300 IU/L), alanine aminotransferase 37 IU/L (5–35 IU/L) and gamma-glutamyl transpeptidase 122 IU/L (0–50 IU/L). Chest radiograph, liver biopsy and computed tomography (CT) of his abdomen and pelvis were normal other than bilaterally enlarged groin nodes. Lymph node biopsy showed retained architecture with prominent reactive follicular hyperplasia and geographic mantle regions. The paracortex was markedly expanded with prominent vasoproliferation of high endothelial venules and contained mixed chronic inflammatory cells including conspicuous eosinophils forming eosinophil microabscesses. There was no morphological immunophenotypic or genotypic evidence of malignant lymphoma or other malignancy. The pathological findings were indicative of KD [2]. Initial treatment was conservative.

Persistent eosinophilia was noted over the subsequent 6 months (eosinophil count up to 5.1 × 10^9/l). Further investigation revealed serum IgE 349 kU/L (0–81 kU/L), complement C3c component 1.84 g/L (0.75–1.65 g/L) and serum immune complex enzyme-linked immunosorbent assay (ELISA) 23 units (0–10 units). ESR, rheumatoid factor (RF), antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), protein electrophoresis and cryoglobulins were normal or negative.

On haematological review for persistent eosinophilia, he was noted to have splinter haemorrhages, digital infarcts and axillary lymphadenopathy. Urinalysis was negative. A bone marrow aspirate and trephine showed eosinophilic infiltration of the marrow in keeping with the clinical diagnosis of KD. He was commenced on oral prednisolone 40 mg/day.

Fig. 1. Thermographic images of our patient’s hands before (A) and 10 min after (B) a cold challenge showing significant negative gradient and asymmetry. Some of the fingers are not easily seen on the second image because of similar temperature to the (cold) background (shown better on a colour scale—colour figures available at Rheumatology Online). The grey scale on the right of each image shows temperature in °C.
At an initial rheumatological assessment 2 months later, continuing clinical response was noted on a reducing dose of prednisolone (20 mg/day) with normalization of his eosinophilia. Allopurinol was stopped at this stage due to the potential rare association reported between this drug and hypersensitivity reactions. Subsequent reduction in prednisolone dosage to 7.5 mg/day led to a flare of his Raynaud’s symptoms and the development of ulcerated pre-gangrenous changes on multiple digits. He had an excellent clinical response following intravenous prostacyclin (Iloprost) over a 72-h period. His prednisolone dose was further reduced to 5 mg/day and this has been continued as maintenance therapy. Nifedipine, amlodipine and losartan were discontinued due to intolerance but no further iloprost therapy has been required. Thermography was performed on his hands using an Aga Thermovision 782 I-R thermal imaging camera. Most of the fingers were uniformly cold on the baseline image. Ten minutes following the cold challenge (1 min immersion of gloved hands in water at 20°C) asymmetrical thermal indices were recorded of −8.36 for the left hand and wrist and −7.09 on the right (−4 to −14 = Raynaud’s phenomenon) (see Fig. 1).

KD classically presents in young and middle-aged males with a triad of features: painless masses (with a predilection for the head and neck region), eosinophilia and raised serum IgE [3]. There is a high incidence of renal involvement, most notably proteinuria and nephrotic syndrome [6], and arthropathy and asthma have been noted [1].

The aetiology of KD is unknown but viral infection or toxins have been speculated as the precipitating event [4]. Elevated levels of interleukin (IL)-5, IL-4 and IL-13 have been found in peripheral blood mononuclear cells and IL-5 in lymph nodes of affected patients. IL-5 accelerates the differentiation, proliferation, chemotaxis and activation of eosinophils. IL-4 and IL-13 initiate and enhance IgE synthesis. After successful treatment the number of eosinophils plus the levels of IgE and cytokines normalize [5]. There is tissue evidence to suggest elevated CD4 T helper 2 (Th2) cells and only Th2-type renal diseases have been observed in KD [6]. The mainstays of treatment in KD are glucocorticoids and/or surgery for masses (with or without radiotherapy) [4], though ciclosporin has been used effectively in resistant cases [7].

We confirmed the presence of Raynaud’s phenomenon using thermography, a non-invasive technique that detects infrared radiation from the skin surface giving an indirect measure of skin blood flow [8]. Normal response to cooling is rapid rewarming of the fingers from finger tips down to the dorsum of the hand. The prolonged reduced temperature and the opposite direction of rewarming of the fingers occurs in Raynaud’s phenomenon [9]. The use of thermography in several areas of rheumatology has been discussed recently in this journal [10].

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The authors have declared no conflicts of interest.

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**Humanized anti-CD20 monoclonal antibody in the treatment of severe resistant systemic lupus erythematosus in a patient with antibodies against rituximab**

Sir, We present, to the best of our knowledge, the first case antibodies against rituximab lupus erythematosus in a patient with the treatment of severe resistant systemic

In mid-February 2004, our patient developed a flare with features of polyarthralgia, polyserositis, mild glomerulonephritis (WHO grade 2) and a haemolytic anaemia (Coomb’s test positive). She developed severe pneumococcal septicaemia and adult respiratory distress syndrome requiring intensive care (ICU) admission.

Her SLE was initially managed with i.v. methylprednisolone (MP) (3 g in total), oral prednisolone (PDN) (100 mg/day) and then mycophenolate mofetil (MMF) (2 g/day) followed by i.v. CYC (6 monthly pulses) 10.4 g/kg. Within a week a dramatic response in her clinical symptoms with a single dose of hA20 (375 mg/m²) in combination with i.v. MP. Within a week a dramatic response in her clinical symptoms was noted (Table 1) and her haemoglobin count had increased to 12.4 g/dl and her platelet count 177 x 10⁹/l. Remarkably 2 weeks later her haemoglobin dropped to 2.9 g/dl and platelets to 2 x 10⁹/l. She refused a blood transfusion as she is a Jehovah’s Witness.

Rituximab could not be used as she had developed an HACA response. However, on a compassionate use basis, we were able to obtain humanized anti-CD20 monoclonal antibody (hA20), which was being used in a phase 1 trial as a humanized anti-CD20 monoclonal antibody for patients with non-Hodgkin’s lymphoma [3]. Having obtained full consent, our patient was treated initially with a single dose of hA20 (375 mg/m²) in combination with i.v. MP. Within a week a dramatic response in her clinical symptoms was noted (Table 1) and her haemoglobin count had increased to 8.8 g/dl; however, her platelet count remained low at 8 x 10⁹/l.

Our patient’s course was complicated with thoracic shingles, which was being used in a phase 1 trial as a humanized anti-CD20 monoclonal antibody for patients with non-Hodgkin’s lymphoma [3]. Having obtained full consent, our patient was treated initially with a single dose of hA20 (375 mg/m²) in combination with i.v. MP. Within a week a dramatic response in her clinical symptoms was noted (Table 1) and her haemoglobin count had increased to 8.8 g/dl; however, her platelet count remained low at 8 x 10⁹/l.

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