Figure 1 Biopsy specimen from colon

before, the findings were consistent with Crohn's colitis with relative preservation of mucosal architecture, but unexpectedly there was evidence of cytomegalovirus infection in the form of multiple large cells with eccentric nuclei surrounded by a clear halo and viral inclusion bodies in the cytoplasm (Figure 1). Rectal biopsies a year later revealed Crohn's colitis but no cytomegalovirus infection.

COMMENT

Cytomegalovirus infection can complicate both ulcerative colitis and Crohn's disease. The virus belongs to the herpes virus family and 40–100%¹ of the adult population have been infected. Most infections are subclinical and lead to lifelong latency. However, in immunocompromised individuals such as transplant recipients and AIDS patients, the virus can cause severe disease. A connection has been suspected between cytomegalovirus inclusion disease and ulcerative colitis since 1961.² The prevalence of cytomegalovirus complicated colitis in patients with inflammatory bowel disease has been estimated at 0.53–4%,^{3–4} but in patients presenting with severe steroid refractive Crohn's disease it is thought to be much higher at 11–36%.⁵ Clinical pointers to viral complications include persistent severe hypokalaemia, high spiking pyrexia, lymphadenopathy and bone marrow suppression³ but such features are seen also in patients with uncomplicated severe steroid-resistant Crohn's colitis. The recommended means of diagnosis is histological examination of biopsies from the affected mucosa and ulcer beds.^{3,5–6} Serological tests and virus isolation from blood or faeces do not prove colonic infection.

With earlier diagnosis the present patient might have been spared surgery. When cytomegalovirus infection is found to be complicating Crohn's colitis, steroid treatment should be reduced, other immunomodulatory treatments stopped, and ganciclovir 10–15 mg/kg daily in divided doses given for 2–3 weeks.^{3,6} Such treatment has reduced

emergency colectomy rates from 80% to 33% and case fatality from 33% to 5% in patients with severe steroid-refractory inflammatory bowel disease complicated by cytomegalovirus infection. However, about one-fifth of patients so treated need colectomy within three months because the underlying bowel disease has become reactivated or the viral infection has persisted.⁶

REFERENCES

- 1 Nankervis GA. Diseases produced by cytomegalovirus. *Med Clin N Am* 1978;**62**:1021–35
- 2 Powell RD. Cytomegalic inclusion disease and ulcerative colitis: report of a case in a young adult. *Am J Med* 1961;**30**:334–40
- 3 Konstantinos A. Outcome of cytomegalovirus infections in patients with inflammatory bowel disease. *Am J Gastroenterol* 2001;**97**:2137–42
- 4 Vega R. Cytomegalovirus infection in patients with inflammatory bowel disease. *Am J Gastroenterol* 1999;**94**:1053–6
- 5 Cottone M, Pietrosi G, Martorana G, *et al.* Prevalence of cytomegalovirus infection in severe refractory ulcerative and Crohn's colitis. *Am J Gastroenterol* 2001;**96**:773–5
- 6 Pfau P, Kochman ML, Furth EE, Lichtenstein GR. Cytomegalovirus colitis complicating ulcerative colitis in the steroid-naïve patient. *Am J Gastroenterol* 2001;**96**:895–9

Pyrexia and lymphadenopathy in a south Asian woman

Teng Teng Chung MRCP¹

Nada Chowdhury MBBS¹ Kim Piper PhD MRCPATH²

Tahseen A Chowdhury MD FRCP¹

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In a person coming from the Indian subcontinent to the UK the combination of fever, night sweats and lymphadenopathy is most likely to be due to tuberculosis; but a less common diagnosis must be borne in mind.

CASE HISTORY

A Bangladeshi woman age 24, who had arrived in the UK three months previously, described episodes of fever and night sweats without rigors for the past three weeks; she had also developed non-tender cervical lymphadenopathy

¹Department of Diabetes and Metabolism, Royal London Hospital, London;

²Department of Histopathology, St Bartholomew's Hospital, London, UK

Correspondence to: Dr T A Chowdhury, Consultant Physician, Department of Diabetes and Metabolism, 5th Floor Alexandra Wing, Royal London Hospital, Whitechapel, London E1 1BB, UK

E-mail: Tahseen.Chowdhury@bartsandthelondon.nhs.uk

Figure 1 Histological slide showing zones of necrosis containing apoptotic cellular debris surrounded by pale staining histiocytes and scattered lymphocytes, characteristic of Kikuchi's disease [for colour reproduction see www.jrsm.org]

and an itchy rash over the trunk and arms. There was no story of cough, dyspnoea, haemoptysis, dysuria or gastrointestinal symptoms and she had not lost weight. A year earlier she had been investigated in Bangladesh for similar symptoms, when a fine-needle aspirate of a cervical node had shown chronic non-specific lymphadenitis; at that time a Heaf test had been negative and the chest X-ray normal, though the erythrocyte sedimentation rate (ESR) had been raised at 20 mm/h. She had been started on antituberculosis chemotherapy, but this had been changed after a few weeks to doxycycline for a presumed diagnosis of rickettsial fever.

On the present admission her temperature was 38°C. Firm lymphadenopathy was apparent in the anterior cervical chain of the neck and a single pea-sized submental lymph node could be felt on the right. There were no cardiac murmurs or stigmata of infective endocarditis, the lungs were clear and nothing abnormal was found on abdominal examination. The rash on her trunk and arms was pale pink, itchy and scaly. Haemoglobin was 12.3 g/L; mean cell volume 87.5 fL; white cell count low at $2.7 \times 10^9/L$ (normal range 4–11); neutrophil count low at $1.2 \times 10^9/L$ (2.5–7.58). Urea and electrolytes, liver function tests and calcium were all normal. ESR was 41 mm/h and C-reactive protein 10 mg/L (normal <5). Chest radiograph was normal, urinalysis clear and pregnancy test negative. Blood and urine cultures were negative, as was a full autoantibody screen, including antinuclear antibody and anti-dsDNA antibody.

Over the next 72 hours her low-grade pyrexia settled without antibiotic therapy. An excision biopsy specimen from the submental node showed zones of necrosis containing apoptotic cellular debris surrounded by pale staining histiocytes and scattered lymphocytes (Figure 1). There was no evidence of granuloma formation. The

features were consistent with histiocytic necrotizing lymphadenitis, or Kikuchi's disease. At review, her pyrexia was less troublesome but the lymphadenopathy and rash had persisted. She was reassured that the condition was likely to settle spontaneously.

COMMENT

Kikuchi's disease was first described in Japan in 1972.¹ Typically it presents with painless unilateral cervical lymphadenopathy, although adenopathy elsewhere, including mediastinal and retroperitoneal sites,² is reported. 20% of cases show generalized lymphadenopathy, and splenomegaly is an occasional feature.³ Fever and neutropenia are common. Cutaneous manifestations of Kikuchi's disease are well recognized, and in a review of ten patients these included indurated erythematous macules, papules, plaques and nodules on the face, arms and trunk.⁴ Seemingly the patients with cutaneous lesions are those most likely to have high fever and liver dysfunction with raised transaminases. Less common clinical features include arthralgia, epididymitis, pancytopenia and bone marrow involvement. Most patients recover in time, although many have recurrences. No specific treatment is suggested apart from symptomatic therapy; severe cutaneous manifestations have been treated with oral prednisolone.⁴ A single fatal outcome, from myocardial infarction, has been reported.⁵

In the affected lymph nodes, involvement is almost confined to T-cell regions, with patchy paracortical necrosis consisting of eosinophilic fibrinoid material and nuclear debris.⁶ Foamy histiocytes and reactive T cells infiltrate the tissue but polymorphonuclear leucocytes are absent and plasma cells infrequent. The proliferation of reactive foamy histiocytes and abnormal nodal architecture make for possible confusion with malignant lymphoma or Hodgkin's disease; infective causes of lymph node hyperplasia such as tuberculosis can be readily distinguished.

The pathogenesis of Kikuchi's disease is not clear. This uncommon condition seems to affect women more than men, with a male to female ratio of around 4:1, and a mean age of 30 years at onset.⁶ Most of the reported cases are in persons of south Asian or oriental descent, though some of these were born in Europe or the US, suggesting a racial or genetic predisposition. An infective agent has been suggested, with toxoplasma, *Yersinia enterocolitica* and herpesvirus 6 all proposed.⁷ Apoptosis may be important: cytotoxic T lymphocytes are considered to be apoptotic effectors, as well as target cells, while histiocytes could enhance apoptosis.⁸ One suggestion is that Kikuchi's disease is a variant of systemic lupus erythematosus—based on cases in which histologically diagnosed cases have progressed to SLE.⁹ An association with autoimmune Hashimoto's thyroiditis has also been reported.⁹

Nevertheless, in the largest case series SLE developed in only 2 of 108 patients, so the association may be a chance finding.⁶

REFERENCES

- 1 Kikuchi M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytes: a clinicopathological study [In Japanese]. *Nippon Ketsueki Gakkai Zasshi* 1972;**35**:379–80
- 2 Pearl D, Strauchen JA. Kikuchi's disease as a cause of fever of unknown origin. *N Engl J Med* 1989;**320**:1147–8
- 3 Turner RR, Martin J, Dorfman RF. Necrotising lymphadenitis: a study of 30 cases. *Am J Surg Pathol* 1983;**7**:115–23
- 4 Yasukawa K, Matsumura T, Sato-Matsumura KC, *et al*. Kikuchi's disease and the skin: case report and review of the literature. *Br J Dermatol* 2001;**144**:885–9
- 5 Chan JKC, Wong K-C, Ng C-S. A fatal case of multicentric Kikuchi's histiocytic necrotising lymphadenitis. *Cancer* 1989;**63**:1856–62
- 6 Dorfman RF, Berry GJ. Kikuchi's histiocytic necrotizing lymphadenitis: an analysis of 108 cases with emphasis on differential diagnosis. *Semin Diagn Pathol* 1988;**5**:329–45
- 7 Feller AC, Lennert K, Stein H, Bruhn H-D, Wuthe H-H. Immunohistology and etiology of histiocytic necrotising lymphadenitis: report of three instructive cases. *Histopathology* 1983;**7**:825–39
- 8 Fergar RE, Furth EE, Wasik MA. Histiocytic necrotising lymphadenitis (Kikuchi's disease): *in situ* end labelling, immunohistochemical and serological evidence supporting cytotoxic lymphocyte-mediated apoptotic cell death. *Mod Pathol* 1997;**10**:231–41
- 9 Biasi D, Caramaschi P, Carletto A. Three clinical reports of Kikuchi's lymphadenitis combined with systemic lupus erythematosus. *Clin Rheumatol* 1996;**15**:81–3

Chronic inflammatory demyelinating polyradiculoneuropathy with ataxia

R C Stockdale MB MRCP C K Biswas MB FRCP

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Occasionally, chronic inflammatory demyelinating polyradiculopathy presents with ataxic features. This should be borne in mind to prevent misdiagnosis and delay in treatment.

CASE HISTORY

A woman aged 80 had for six months been experiencing unsteadiness, right shoulder pain, paraesthesia in her

forearms and fatigue. Previously she had been fit and well, and her only medication was quinine sulphate for muscle cramps. She was a non-smoker, drinking alcohol occasionally. On examination, muscle power was sub-normal (4/5) in the distal arms and legs but 5/5 elsewhere; tone was normal. Reflexes were reduced, with flexor plantar responses. There was mild ataxia in the upper limbs but more severe ataxia of the lower limbs prevented her from standing. The cranial nerves were normal. Initially there were no sensory changes but after three weeks sensory impairment was noted in the distal upper limbs, with pseudoathetosis. Laboratory indices, including full blood count, blood sugar, vitamin B12, red cell folate, protein electrophoresis, autoantibody screen and tests of liver and thyroid function were unrevealing. MRI of the head showed no focal lesions and normal ventricular size. On neurophysiological testing all sensory action potentials were absent; in motor conduction there was no definite block but distant latencies were delayed, proximal conduction was slow (Table 1) and there was temporal dispersion of compound action potentials. The suggested diagnosis was chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Cerebrospinal fluid had a raised protein at 1.87 g/L with no organisms or cells seen.

The patient was then further investigated to exclude paraneoplastic inflammatory neuropathy, all tests being negative. Because paraprotein was absent, antibody to myelin-associated glycoprotein was not sought. CIDP was diagnosed and she received a five-day course of intravenous immunoglobulins followed by prednisolone, 60 mg daily with reducing dose, and additionally bisphosphonate for bone protection and gabapentin for neuropathic pain. She recovered well and six months later she was mobile and independent.

COMMENT

CIDP can be difficult to diagnose because of its wide variation in symptoms and signs and its slowly progressive nature. Without treatment, mortality is about 10%. It occurs at all ages (prevalence 1–2 per 100 000) and affects men more frequently than women. The disease is seen as the chronic form of Guillain-Barré syndrome. Because of the inflammatory cells and macrophage-mediated demyelination seen on electron microscopy of sural nerve biopsy specimens and its responsiveness to immune-modulating treatments, an autoimmune basis is suspected. No target has definitely been identified, although myelin protein P0 has been suggested.¹ Demyelination is multifocal and can involve the distal nerve terminals, intermediate nerve segments, and nerve roots. Cranial nerves are mildly affected in some patients. On occasion, as here, CIDP presents with a mainly ataxic clinical picture,² caused by demyelination of proprioceptive

Department of Medicine for the Elderly, Dewsbury and District Hospital, Dewsbury WF13 4HS, UK

Correspondence to: Dr R C Stockdale

E-mail: rcs1002@hotmail.com