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CASE REPORTS

Churg-Strauss vasculitis and ascaris infection

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Abstract

A patient with Churg-Strauss vasculitis presenting with mononeuritis multiplex, who developed obstructive jaundice, is described. On investigation the jaundice proved to be due to ascaris infestation. As the immune abnormalities associated with ascaris infection are also typical of those seen in the Churg-Strauss syndrome it is speculated that the vasculitis occurred because of a failure to regulate the anti-ascaris immune response.

Churg-Strauss vasculitis or allergic granulomatous angiitis is a rare disease of unknown cause. The disorder is characterised by eosinophilia of both blood and tissues and a severe systemic necrotising vasculitis; it is associated with late onset allergic disorders such as asthma or rhinitis.[1] Although eosinophilia accompanies allergic disorders in developed countries, the commonest cause world wide is parasitic infestation, especially by helminths. The infestation in turn may be associated with asthma when the larvae of—for instance, ascaris, migrate through the pulmonary vasculature.[2] There are no reports of worm infestation progressing to a systemic vasculitis, however. We wish to report a case of typical Churg-Strauss vasculitis associated with infection of the biliary tree by ascaris. The coexistence of these two disorders in a white patient in the United Kingdom suggests that in patients with the appropriate genetic background it may be possible for an infection which is associated with an eosinophilic immune response to progress to a systemic vasculitis of the Churg-Strauss type.

Case report

A 55 year old white man presented in February 1987 eight days after developing acute bilateral foot drop, dysaesthesia in both hands, and impaired sensation in both hands and feet. He also felt generally unwell, had intermittent upper abdominal pain, and had lost more than 6 kg in weight during the preceding two months. He had mild asthma; this began in childhood and resolved, but reoccurred at age 36, requiring continuing treatment with bronchodilators. There was no other significant past medical history, or history of foreign travel. In addition to working for a children's charity, he farmed a smallholding in the Welsh borders.

On examination he had a fever (39°C) and had features of a bilateral sensorimotor neuropathy with a marked proprioceptive component. In addition there was a mild purpuric rash over his legs. Initial investigations were as follows: haemoglobin 139 g/l; white blood cell count $26{\cdot}5\times10^9$/l (eosinophils $22{\cdot}5\times10^9$/l); erythrocyte sedimentation rate 24 mm/h; urea and electrolytes normal; alkaline phosphatase 167 U/l (normal 35–120), aspartate transaminase 68 U/l (normal 5–50), albumin 34 g/l. Cultures of blood, urine, and cerebrospinal fluid were negative (cerebrospinal fluid protein 0·2 g/l, <1 cell/mm^3). Biopsy of a cervical lymph node showed moderate numbers of eosinophils and reactive changes only. Coeliac axis angiography suggested the presence of arterial microaneuryms. The patient was transferred to the Queen Elizabeth Hospital, Birmingham, for further investigation and treatment.

On examination he continued to show a fever and was now clearly affected with jaundice. In the previous three weeks he had also noted several episodes of transient visual loss or disturbance. Investigations were as follows: haemoglobin 113 g/l; white blood cell count $17{\cdot}6\times10^9$/l (eosinophils $7{\cdot}4\times10^9$/l); erythrocyte sedimentation rate 71 mm/h; C reactive protein 105 mg/l; alkaline phosphatase 4900 U/l, aspartate transaminase 360 U/l, bilirubin 131 μmol/l, albumin 23 g/l; globulin 39 g/l; prothrombin time 24 s (control 14 s); midstream urine values up to $0{\cdot}24\times10^9$ red blood cells/l; renal function otherwise normal. Chest and abdominal radiographs were normal; echocardiography showed a small pericardial effusion. Neurophysiological studies showed unrecordable sensory potentials in both sural and the left median nerves, and severe denervation of the muscles of both legs. A diagnosis of vasculitis was suggested by sural nerve biopsy, which showed marked axonal damage and increased endomysial and perimysial fibrosis consistent with ischaemia; small arterioles in the biopsy specimen showed intimal proliferation and disruption of the internal elastic lamina. A skin biopsy specimen also showed a leucocytoclastic vasculitis. A repeat coeliac axis angiogram did not confirm the presence of microaneurysms, however.

Because the severity of the obstructive jaundice was not considered to be a typical feature of systemic vasculitis, further investigations were undertaken: antibodies to hepatitis B, toxoplasma, leptospira, cytomegalovirus, hydatid, rickettsia, and fasciola were negative; the patient was immune to hepatitis A. Liver biopsy showed cholestasis with mild portal oedema; the possibility of diclofenac induced liver damage was suggested, but there was no response in the liver function tests when the drug was withdrawn. Upper gastrointestinal endoscopy was normal and no dilated biliary ducts were detected

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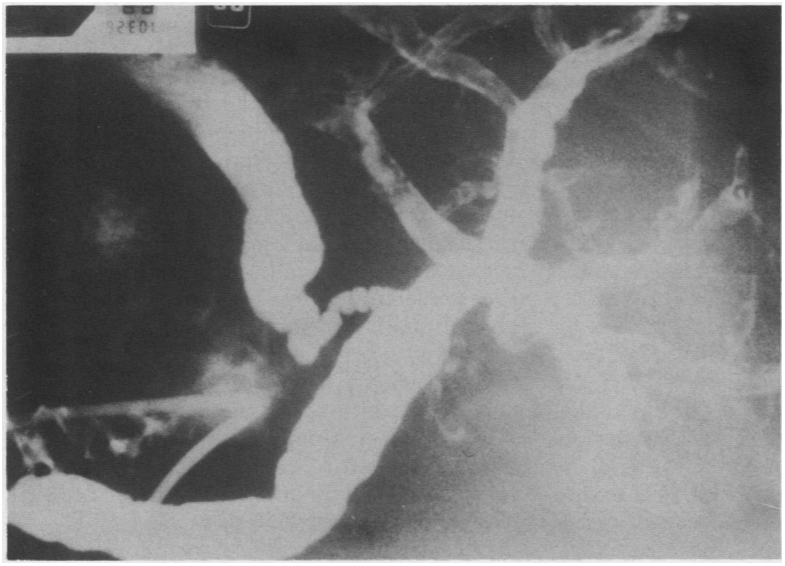

Figure 1: Radiograph of the biliary and pancreatic ducts after the injection of contrast medium at endoscopic retrograde cholangiopancreatography. Filling defects are clearly visible in the common bile duct and intrahepatic ducts.

by ultrasound examination. Endoscopic retrograde cholangiopancreatography, however, showed multiple filling defects in the common bile duct and distal biliary tree (fig 1). These were thought to be consistent with either fluke or worm infestation, but repeated attempts to detect ova, cysts, or parasites by stool culture and microscopy were negative.

Results of immunological investigations were as follows: serum IgA 5·4 g/l (normal <4·5); IgM and IgG normal; IgE 995 U/l (normal <200); rheumatoid factor negative; antinuclear, mitochondrial, and smooth muscle antibodies not detected; antineutrophil cytoplasmic antibodies weakly positive; cryoglobulins strongly positive; protein electrophoresis, no monoclonal band. Immune complexes were detected by platelet aggregation (titre 1/2560).

Course

A diagnosis of Churg-Strauss vasculitis was made on the basis of characteristic clinical and histological features of systemic vasculitis together with an allergic history and pronounced eosinophilia. Treatment was started with intermittent boluses of oral cyclophosphamide and prednisolone, with a moderate (up to 20 mg) daily dose of prednisolone.[3] On this regimen there was clinical improvement; no further neurological lesions developed and there was weight gain and resolution of persistent fever. The obstructive jaundice persisted, however, and despite repeated examination by endoscopic retrograde cholangiopancreatography, stool microscopy and culture, and biliary drainage no evidence to confirm the endoscopic impression of infestation of the biliary tree was obtained. Because of continuing abnormal liver function tests, and intermittent fevers in which enteric organisms were cultured from both blood and bile, treatment proceeded to exploration of the bile ducts and cholecystectomy three months after starting treatment with cyclophosphamide. Debris removed from the common bile duct and gall bladder was identified as dead ascaris worms (fig 2). He was therefore treated with mebendazole. Immediately after this treatment he developed a recurrence of the purpuric rash seen at presentation. Rebiopsy of the rash again showed leucocytoclastic vasculitis; the rash subsided spontaneously.

During the next year he remained well with no recurrence of vasculitis. He has, however, continued to have intermittent fevers, thought to indicate biliary sepsis, and has mild chronic biliary obstruction.

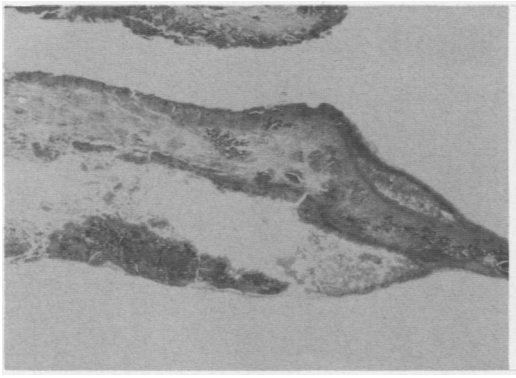

Figure 2: Sagittal section of a fragment of ascaris worm identified in debris obtained from the common bile duct and gall bladder. (Haematoxylin and eosin.)

Discussion

This patient had the typical features of Churg-Strauss vasculitis, including late onset asthma, eosinophilia, mononeuritis multiplex, and raised concentrations of serum IgE. The vasculitis was confirmed by sural nerve biopsy. Granulomata were not seen on histological examination, but Lanham *et al* have suggested that a clinical pattern of disease consisting of asthma, eosinophil counts greater than $1{\cdot}5\times10^9$/l, and systemic vasculitis involving two or more extrapulmonary organs is sufficiently distinctive to allow a diagnosis of Churg-Strauss vasculitis to be made.[4] Granulomata were indeed part of the diagnostic criteria formulated by Churg and Strauss,[1] but their original series was based on the histological findings at necropsy, and consequently they had increased opportunities for demonstrating granulomata. The patient also developed an obstructive jaundice during the illness. Although mild abnormalities of liver function are common in systemic vasculitis, marked obstructive jaundice is rare[5] and led to further investigation of this patient. Despite the clear demonstration at endoscopic retrograde cholangiopancreatography of filling defects consistent with worm infestation, conclusive evidence for this diagnosis was only obtained at cholecystectomy.

The cause of Churg-Strauss vasculitis is unknown, but the immunological abnormalities (eosinophilia and raised IgE) are seen elsewhere in response to parasites or allergens. There are generally no clues to the antigens eliciting this response in Churg-Strauss vasculitis, but in our case ascaris infestation was clearly recorded. As this organism usually elicits an immune response characterised by eosinophilia and high concentrations of serum IgE it is possible that a failure to control this immune response to ascaris resulted in vasculitis. Immune complexes are

often implicated in vasculitis and were detected at diagnosis in this patient as cryoglobulins and at high titre (1/2560) by platelet aggregation; further measurements during a year's treatment with intermittent cyclophosphamide were usually negative and never greater than 1/160. Furthermore, when the serum was subjected to high performance liquid chromatography and an IgE specific enzyme linked immunosorbent assay (ELISA) applied to the fractions obtained, the presence of high molecular weight material containing IgE was shown, strongly suggesting the presence of complexed IgE. These complexes also disappeared after treatment, though the concentration of IgE was still greatly increased (maximum 3140 U/l) and only began to decline after cholecystectomy (and removal of the 'depot' of ascaris antigen). Skin testing with ascaris antigen showed no evidence of either immediate or delayed-type hypersensitivity responses, but it was only carried out after the start of treatment with steroids. Peripheral blood lymphocytes, both before and after treatment, showed no proliferative responses to the ascaris antigen, tested at concentrations from 3·5 to 28 μg/ml. Thus, in summary, the patient's immune response seemed to be biased towards excessive antibody production with a relative absence of T cell mediated responses. In addition to the pathogenic effect of IgE containing immune complexes, the vascular damage might also have been releated to the very high concentrations of eosinophils as these cells may be toxic to vascular endothelium through their release of cationic proteins.[6]

It is possible to speculate on the nature of the aberrant immune response to the ascaris. Although the situation in man is not yet clear, work in mice has shown that subsets exist within helper T cells—namely, those which augment specific antibody secretion and those which mediate delayed-type hypersensitivity responses.[7] The former produce the lymphokines interleukin 4 (essential for the production of IgE) and interleukin 5 (an eosinophil growth factor). In an appropriate immune response both T cell subsets would be activated; interferon gamma from the delayed-type hypersensitivity subset acts as a negative feedback on the activities of interleukin 4 and interleukin 5. Inbred strains of mice have been described in which the immune response to leishmania is biased towards one T cell subset, and this results in increased mortality.[8] Although the response of the vasculitis to cyclophosphamide was satisfactory in this case, interferon gamma may be another therapeutic option.

In this case the ascaris infestation was discovered owing to an obstructive jaundice; in the absence of this the diagnosis might not have been made as examination of the stool was repeatedly negative. Thus hyperresponsiveness to an antigenic stimulus such as a parasite or allergen may underlie other cases of Churg-Strauss vasculitis, and this possibility should be borne in mind during the investigation of such cases.

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