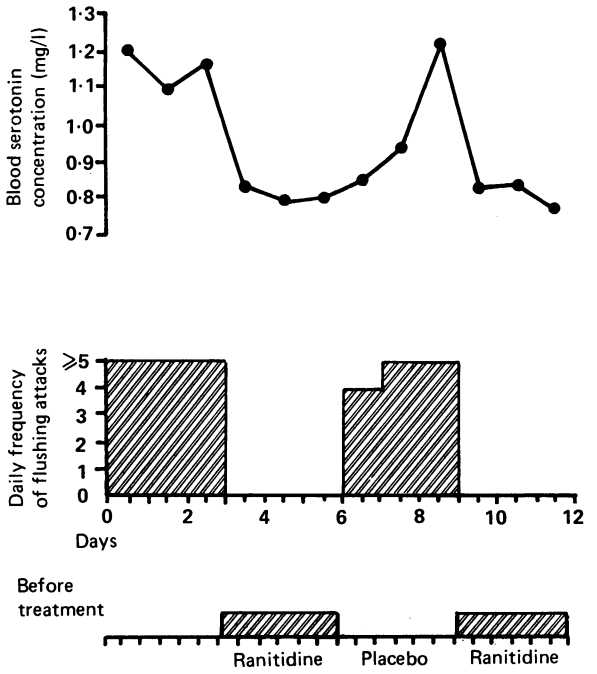

Frequency of flushing and blood serotonin concentrations during administration of ranitidine and placebo.

Comment

The cause of flushing attacks in patients with carcinoid syndrome is unknown. In a subgroup of patients (many of whom have metastatic gastric carcinoid tumours) histamine excretion is frequently and consistently raised.[4,5] Two reports have shown significant reductions in both frequency and duration of flushing attacks during combined treatment with H_1 and H_2 receptor antagonists in two patients with metastatic gastric and ileal carcinoid tumours.[1,2] In one of these patients,[1] the duration (but not the frequency) of flushing attacks was reduced by cimetidine alone. The authors concluded that in some patients with carcinoid tumours histamine may be the cause of the flushing attacks. In one patient,[2] however, histamine excretion in the urine was normal during the flushing attacks, whereas the serum serotonin concentration was raised. We know of no data on serum serotonin concentrations during treatment with antihistamines.

In our patient administration of ranitidine alone caused prompt cessation of flushing attacks and a significant reduction in serum serotonin concentrations. This suggests that the beneficial effects of H_2 receptor antagonists seen in some patients with the carcinoid syndrome, may not necessarily be caused by inhibition of the action of histamine but may be partially mediated by a reduction in serum serotonin concentrations.

We thank Dr E Moerman (J F & C Heymans Institute, Ghent, Belgium) for carrying out the measurements of serum serotonin concentrations and Mrs S Goossens for secretarial help.

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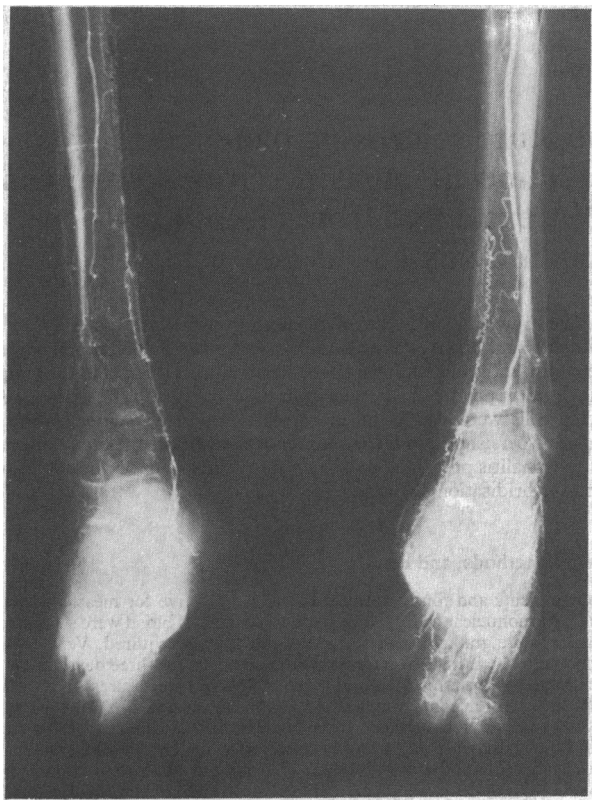
Buerger's disease associated with IgA nephropathy: report of two cases

Buerger's disease is a non-atherosclerotic, segmental, inflammatory, occlusive vascular disease of unknown aetiology that affects male smokers under the age of 50. It is characterised by multiple occlusions of small and medium sized arteries and veins in both hands and feet. We describe for the first time two cases of Buerger's disease associated with IgA nephritis. Buerger's disease was diagnosed according to the clinical and angiographic criteria described by Adar,[1] and IgA nephritis by examination of a percutaneous renal biopsy specimen with an immunofluorescence technique.

Case reports

Case 1—A 21 year old Algerian had had severe Buerger's disease for five years and had had several toes amputated (figure). Over six months he developed renal failure with a serum creatinine concentration of 200 μmol/l, nephrotic syndrome, macroscopic haematuria, and high blood pressure. His Buerger's disease worsened. Histological examination of a renal biopsy specimen showed necrotic glomerulonephritis with mesangial deposition of IgA, and endocapillary proliferation with segmental crescents. His serum IgA concentration was 3·2 g/l (normal range 0·8-5·0 g/l). The serum creatinine concentration reached a peak of 500 μmol/l before spontaneous improvement occurred. Six months later his serum creatinine concentration had fallen to 200 μmol/l and his vascular disease had improved with healing of the previous amputation scars.



Case 1: Angiogram showing amputation of toes and multiple distal arterial occlusions.

Case 2—Buerger's disease and IgA glomerulonephritis were diagnosed at the same time in a 21 year old man with a five year history of thrombophlebitis migrans, Raynaud's phenomenon, high blood pressure (180/110 mm Hg), proteinuria (0·50 g/24 hours), and microscopic haematuria but no renal failure. The serum IgA concentration was 1·9 g/l. Seventeen years later his condition was unchanged; he did not have renal failure or the nephrotic syndrome and had not required any amputations. His blood pressure was well controlled with treatment.

Comment

Circulating antibodies to collagen are present in the blood of 45% of patients with Buerger's disease, and limited data have recently been published that suggest that these are accompanied by increased cellular sensitivity to human type I or type III collagen, or both.[2] An immune

disorder may therefore play a part in the pathogenesis of both IgA nephropathy and Buerger's disease.[3] The lymphocytes of our first patient carried HLA B5 antigen, which has been associated with both Buerger's disease[4] and, in some cases, familial IgA nephritis.[5] The association of the two diseases in our patients may not have been coincidental.

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Subacute sclerosing panencephalitis: detection of measles virus sequences in RNA extracted from circulating lymphocytes

We have shown by an in situ hybridisation technique that measles virus ribonucleic acid (RNA) was present in the peripheral blood lymphocytes of a patient with subacute sclerosing panencephalitis,[1] as well as in the lymphoid tissue of the appendix of a patient before she developed the disease.[2] A few infected cells were also found in normal seropositive subjects. The large number of persistently infected mononuclear cells in the blood of patients with encephalitis prompted us to look for the presence of viral RNA with a dot blot hybridisation technique.

Patients, methods, and results

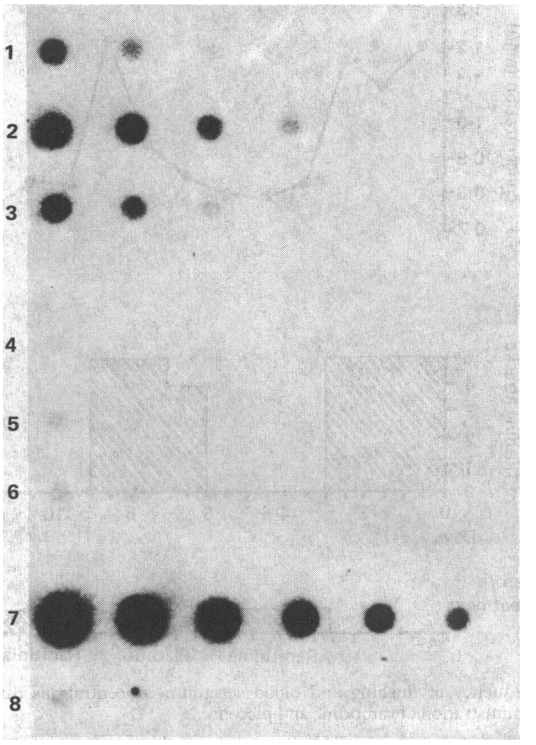
Four patients and four healthy subjects seropositive for measles virus were studied. Mononuclear cells from 5-10 ml of peripheral blood were separated on a Ficoll-Hypaque gradient[1] and stored at −80°C until required. Vero cells were infected with the Edmonston strain of measles virus for three days. Total RNA was extracted by the lithium chloride urea and phenol procedures[3] and hybridised at 42°C in a solution containing a deoxyribonucleic acid (DNA) labelled with ^{32}P that was specific for measles virus nucleocapsid protein[1] (specific activity 5×10^9 Bq/μg) in 50% formamide; 5×standard saline citrate (SSC) (1×standard saline citrate contains 0·15 mol/l sodium chloride and 0·015 mol/l sodium citrate); 0·1% sodium dodecyl sulphate (SDS); and 10% dextran sulphate. After hybridisation the nitrocellulose filter blots were washed four times for five minutes each in 2×SSC and 0·1% SDS at room temperature; twice for five minutes each in 2×SSC and 0·1% SDS at 42°C, once for eight minutes each in 0·1×SSC and 0·1% SDS at 42°C; three times for five minutes each in 0·1×SSC and 0·1% SDS at 50°C, and dried. Autoradiography was then carried out.

The figure shows 5 μg of total RNA then successive twofold dilutions spotted on to the filters. Only background was seen in non-infected Vero cells and in those from seropositive control subjects, whereas measles virus RNA sequences could be seen in the RNA that had been extracted from infected Vero cells and in three of the four preparations of lymphocytes from patients with encephalitis.

In cases 1 and 2 parallel in situ hybridisations indicated detection of viral RNA in over 50% of the positive cells in case 2; less than 0·1% were detected in two out of four of the control subjects.

Comment

The dot hybridisation assays that we undertook showed that RNA containing measles virus sequences could be extracted from the circulating lymphocytes of patients with subacute sclerosing panencephalitis. The different autoradiographic signals that we saw among samples from the seropositive patients suggested that a variable amount of viral RNA was conserved in lymphocytes. Loss of the RNA during cell storage and sample handling, however, could also explain the variability in the intensity of the signal. This is suggested by the fact that in a subsequent RNA dot hybridisation analysis performed for case 2 we failed to detect any signal specific for the virus.



Autoradiograph of dot hybridisation for measles virus RNA in mononuclear cells. Rows 1-3: cells from patients with subacute sclerosing panencephalitis; rows 4-6: cells from seropositive control subjects; row 7: Vero cells infected with measles virus; row 8: non-infected Vero cells.

These findings indicate that in subacute sclerosing panencephalitis the presence of measles virus RNA in lymphocytes can be analysed by a biochemical method that confirms our previous studies of in situ hybridisation. Such a method has also permitted the detection of measles virus RNA in blood mononuclear cells during the acute and convalescent phases of measles,[4] and in autoimmune disease associated with high antibody titres to measles virus.[5] These data confirm our observations that viral genetic information persists in the immune system long after an attack of measles is over.[1] We are currently carrying out experiments to find out which species of molecule contain measles virus sequences.

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