had developed a duodenal ulcer, one a gastric ulcer, one a combined duodenal and gastric ulcer, and one was found to have radiological evidence of achalasia of the cardia. These patients were referred for surgical treatment, with excellent results in all except the patient with achalasia. Of the four remaining patients, further radiological investigation had shown renal disease in two, but with no evidence of gastrointestinal disease, and two were again found to have no abnormality.

When the radiological diagnosis for the 1964 barium-meal study was compared with the follow-up diagnosis six years later it changed in eight cases. Six, as indicated above, developed upper gastrointestinal lesions, and two were found to have renal disease. None of these patients experienced gastrointestinal haemorrhage or perforation during the period of follow-up. Six had died, but in none was the recorded cause of death attributable to a lesion in the upper gastrointestinal tract.

Discussion

An increasing number of patients with dyspepsia are referred for radiological investigations by their general practitioners because a peptic ulcer is suspected. In this series few (3-5%) of those patients with a normal finding on barium-meal examination in 1964 were later found to have a peptic ulcer. Most showed appreciable symptomatic improvement, 65 (76%) claiming to have little or no dyspepsia when questioned in 1970. Fifteen patients claimed there had been no change in their symptoms. The five patients shown by the questionnaire to have deteriorated symptomatically were reinvestigated, and in two a positive diagnosis was obtained.

Similar groups of patients studied over an extended period have shown a much higher incidence of peptic ulceration in follow-up. In a group of 174 hospital patients who were followed for 27 years, 40% were shown to have a peptic ulcer at subsequent investigations (Krag, 1965). Brummer and Hakkinen (1959) followed 102 patients over a six-year period and found that 12 had developed a peptic ulcer. Barfred (1959) followed 235 patients over a 10-year period, and 30% developed a peptic ulcer during this time.

The lower incidence of peptic ulcer in our study may be related to two factors. Firstly, all of the present patients were referred directly from general practitioners, whereas the reports referred to above all dealt with a hospital population. Secondly, a longer follow-up period would possibly have given a higher incidence of the subsequent development of peptic ulceration. We believe that this would be unlikely as 76% of the present patients were virtually symptomless six years later.

If we assume that "x-ray-negative dyspepsia" represents a separate disease entity then its prognosis is more favourable than for peptic ulcer, most patients showing appreciable improvement with time. If further investigations are reserved only for those patients who show a deterioration symptomatically then the burden of repeated reinvestigations both for the radiological services and the patients will be eased, so reducing unnecessary investigations.

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References


Viral Infection and Renal Transplant Rejection

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Introduction

Rejection remains the most common and important complication of renal transplantation. In some cases factors which precipitate the rejection can be defined, such as a reduction in dosage of immunosuppressive drugs. In most patients, however, rejection episodes occur without warning and in the absence of obvious precipitating factors. Rarely, an association has been noted between viral infection and rejection (Simmons et al., 1970; David et al. 1972). This paper describes the occurrence of a localized outbreak of influenza associated with acute rejection.

Outbreak

In the winter of 1971-2 there was an epidemic of influenza due to A1/Hong Kong/68 virus in the West of Scotland. In January and February 1972 a localized outbreak of influenza occurred in the renal transplant unit of the Western Infirmary, Glasgow, which affected five patients with renal transplants and one patient on regular haemodialysis. The main features of the outbreak in the patients with transplants are summarized in the Table. Details of the clinical history of each patient are given below.

Case 1.—A 20-year-old man with membranous glomerulonephritis received a cadaver kidney on 30 October 1971. Tissue typing showed HL-A antigens 2, 10, and 12 in both the donor and recipient, with one unidentified antigen at the second sublocus.
The kidney began to function after two weeks, and during the next four weeks the serum creatinine stabilized at a mean value of 1.2 mg/100 ml. On 28 January 1972 he developed corvza with a sore throat and cough. On 3 February he became pyrexial with shivering and headache, and these symptoms settled over the next five days. A deterioration in renal function was first noted on 31 January with a rise in serum creatinine to 2.2 mg/100 ml. By 6 February the level had reached a peak of 3.5 mg/100 ml, and fell steadily thereafter. Other features suggestive of acute rejection were an increase in bodyweight of 2.9 kg and a rise of blood urea from 60 to 130 mg/100 ml between 31 January and 6 February. Four 1-2 mg doses of intravenous prednisolone were given during this seven-day period. The oral immunosuppressive regimen, consisting of prednisolone 25 mg/day and azathioprine 25 to 50 mg/day, was not altered. His renal function did not return to pre-rejection levels, and in the months following the mean serum creatinine was 2.2 mg/100 ml although renal function was stable and his general condition excellent. On 14 February, 17 days after the initial onset of the influenza-like symptoms, complement fixation tests showed antibody to influenza virus A at a titre of 512. This contrasted with a titre of less than 8 in a blood sample obtained two months earlier.

Case 2.—A 21-year-old girl with chronic glomerulonephritis received a cadaver kidney on 4 January 1972. Both HL-A antigens at the second sublocus were identical while there were two mismatches at the first sublocus. The diuretic phase began 10 days later, and the serum creatinine had fallen to 2.2 mg/100 ml by 27 January. On 29 January she developed corvza with a productive cough, shivering, and pyrexia. By 3 February her temperature had risen to 103°F (39.4°C) and signs of pneumonia had developed. This was slow to resolve but had begun to improve by 9 February. On 30 January renal function began to deteriorate and the serum creatinine rose from 3.0 mg/100 ml on 4 January to 4.0 mg/100 ml on 9 February, thereafter falling to 2.1 mg eight days later. Other features suggestive of acute rejection between 30 January and 9 February were a rise in serum urea from 106 to 146 mg/100 ml and a fall in creatinine clearance from 28 to 17 ml/min. Three months later the mean serum creatinine was 1.4 mg/100 ml. The rejection episode was treated with a total of three doses of intravenous prednisolone, each of one gramme. The oral prednisolone dose was reduced from 35 to 20 mg/day on 3 February because of the pneumonia. Leucopenia developed on 30 January despite previously small daily doses of azathioprine, on average 25 mg. No azathioprine was therefore given between 31 January and 8 February. Eighteen days after the onset of the influenza-like symptoms complement fixation tests showed antibody to influenza virus A at a titre of 512. The titre in a blood sample taken two months earlier was less than 8.

Case 3.—A 19-year-old girl with chronic pyelonephritis received a cadaver kidney on 18 September 1971. There was identity of HL-A antigens between the donor and recipient at the first sublocus with two mismatches at the second sublocus. The diuretic phase started two weeks later with a steady improvement in renal function. On 24 January 1972 she developed an acute rejection with a rise in serum creatinine to 1.17 mg/100 ml five days later. Thereafter it began to fall, but on 31 January a pyrexial illness developed with a productive cough and dyspnoea, and two days later the serum creatinine began to rise again to a peak of 4.2 mg/100 ml on 1 February. Clinical and radiological signs of pneumonia were present at this stage. By 6 February the pyrexial illness had begun to resolve, the body weight had fallen by 3 kg from its peak on 4 February, and the serum creatinine had begun to fall, reaching a value of 2.6 mg/100 ml by 15 February. These features suggested acute rejection occurring in association with the pyrexial illness. The patient tolerated only small doses of azathioprine, and from the end of February 1972 this led to a progressive deterioration in renal function. The kidney was removed at the end of March and regular haemodialysis was instituted. A total of seven 1-g intravenous doses of prednisolone were used to treat the rejection episodes between 24 January and 4 February. Sixteen days after the onset of the pyrexial illness the titre of complement fixing antibody to influenza virus A was 128, compared to a titre of less than 8 in a blood sample obtained two months earlier.

Case 4.—A 42-year-old woman developed influenzal symptoms on 25 January 1972, four months after a cadaver transplant. Her serum creatinine at this time was in the range 1.5 to 2.0 mg/100 ml, and the daily prednisolone dosage was 30 mg. No evidence of rejection developed. Twenty-one days after the onset of the influenza-like symptoms the titre of antibody to influenza virus A by complement fixation test was 64, compared to a titre of less than 8 in a blood sample obtained two months earlier.

Case 5.—A 41-year-old man received a cadaver kidney on 27 August 1971. On 14 January 1972 he developed shivering, pyrexia, cough, and dyspnoea. Influenza-like symptoms began on 25 January and were not return tipped. Twenty-one days after the onset of the influenza-like symptoms the titre of antibody to influenza virus A by complement fixation test was 64, compared to a titre of less than 8 in a blood sample obtained two months earlier.

Discussion

During a two-week period an outbreak of influenza occurred which involved five transplanted patients. The clinical features were typical, consisting of corvza, shivering, cough, and pyrexia. In two of the patients (Cases 2 and 3) the illness was complicated by pneumonia. In all five patients the diagnosis of influenza was confirmed serologically by the finding of a significant rise in the complement fixation titres to influenza virus A when compared to the titres in blood samples obtained before the illness. Tests for antibody to other respiratory viruses were negative. In three of the five patients there was an associated temporary decline in renal function, as indicated by the serum creatinine and creatinine clearance values with, in addition, fluid retention. Also, in one of these three patients (Case 1) there was inhibition of leucocyte migration, using donor liver tissue as the antigen, at the onset of the deterioration in renal function. Serial tests in this patient up to this time had shown absence of inhibition. The leucocyte migration test has been shown to be of value in the prediction of rejection (Smith et al., 1969; Galamaud et al., 1972) and studies in our unit have confirmed this (R. F. M. Wood and A. R. Raftery, unpublished observations, 1972). Leucocyte migration tests were not carried out in Cases 2 and 3.

There are several possible explanations for the temporary deterioration in renal function which occurred in the three patients. Infection with influenza virus A might have caused renal damage by direct infection of the kidney (Kaji et al., 1959) or by the deposition within the kidney of immune complexes of virus and antiviral antibody (Oldstone and Dixon, 1967). The clinical and biochemical features, however, rapid response in each case to intravenous prednisolone (Bell et al., 1971), and the inhibition of leucocyte migration in the patient in whom this test was performed provide good evidence for the diagnosis of rejection.

The interval between the onset of the influenza-like symptoms and the first signs of rejection in these three patients was 1, 2, and 3 days respectively. There were no clear-cut differences between the three who rejected and the two who did not, other
Specific IgM Antibody in Serum of Patients with Herpes Zoster Infections

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Summary

Specific IgM varicella-zoster antibody was detected in "convalescent" sera from 20 out of 40 patients (50%) with herpes zoster infections. Since these were not primary infections with varicella-zoster virus, it seems that detection of IgM antibody specific for a particular virus may not differentiate a primary infection from secondary infections with that virus.

Introduction

Several studies have shown that after primary immunization with many protein antigens an initial transitory IgM serum antibody response is obtained, whereas after secondary immunization an IgM response is usually difficult to detect (Pike, 1967). In several human viral infections it has also been shown that specific IgM antibody may be detected during the first few weeks of a primary infection (Schluenderberg, 1965; Vesikari and Vaheri, 1968; Haire and Hadden, 1972). There have, however, been few opportunities to determine if IgM specific antibody can be detected during subsequent infections with a particular virus.

Epidemiological and clinical evidence indicate that herpes zoster is a secondary infection with varicella-zoster probably due to reactivation of virus which has remained latent for many years in the sensory ganglia after the primary infecton chickenpox (Hope-Simpson, 1965). The purpose of the present study was to determine if specific IgM antibodies could be detected by indirect immunofluorescence in sera of patients with herpes zoster infections.

Materials and Methods

Paired sera for the indirect immunofluorescence test were collected by general practitioners from 40 patients aged from 33 to 80 years with clinical herpes zoster, the first specimen being taken generally during the first few days of the illness...