cancer bearing patients show this change is unknown. Repeated observations on patients at risk of developing metastases or recurrence, however, indicate that transient rises of serum muramidase are not an uncommon feature in this group of patients. Only time will tell if such rises have any real prognostic significance.

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MEDICAL MEMORANDA

Case of Glomerulonephritis associated with Acute Toxoplasmosis

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Experimental studies on mice and rabbits have shown that toxoplasmosis can be accompanied by immune-complex nephritis (Huldt, 1970, 1971). A case has also appeared in which the nephrotic syndrome was diagnosed in an infant with congenital toxoplasmosis (Wickbom and Winberg, 1972). In view of these reports an investigation was begun for the detection of toxoplasma antigen in renal biopsy specimens. During 1971-2, 150 such specimens taken consecutively were tested by immunofluorescence for reactivity with an anti-toxoplasma conjugate.

We report here a case found during that study. The patient, a child, had immune-complex disease including glomerulonephritis. Material stainable with anti-toxoplasma conjugate was found in the glomeruli and a rise in circulating anti-toxoplasma antibodies was shown.

Case Report

An 8-year-old boy was admitted to hospital acutely ill with abdominal pain, pain in the joints, and fever (38.2°C). He had a maculopapular rash on the neck and arthralgia. Palpation of the lymph nodes showed no striking enlargement. Urine contained a trace of protein. Blood pressure was 140/100 mm Hg.

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During the first weeks he was somnolent and had increasing muscular tenderness. There was a granulocytosis (16,200/mm³), a slight monocytosis (900/mm³), and a marked increase in platelets (712,000/mm³). Muscle enzymes (serum creatin kinase and aldolase) were raised, but total lactate dehydrogenase was normal. Electromyography showed a myositis pattern. Renal biopsy findings were compatible with an immune-complex nephritis.

The presence of toxoplasma antigen in the glomeruli led to a serological examination for antibodies to toxoplasma (see table). The mother gave a negative dye test result. The dye tests were performed according to the method of Sabin and Feldman (1948) as modified by Huldt (1958). Whole serum was tested by immunofluorescence using class-specific conjugates as described previously (Huldt et al., 1973).

Reciprocal Antibody Titres

Date	Dye Test	IgM	IgA	IgG
7/2/72	50	20	Neg.	80
11/2/72	250	5	10	80
14/2/72	1,250	5	10	80
16/2/72	1,250	5	10	160
11/4/72	50	Neg.	Neg.	40
24/4/72	50	Neg.	Neg.	20
17/5/73	50	Neg.	Neg.	20

Titres were obtained by simultaneous testing of all sera.

The following conjugates were used: sheep antihuman IgM, Wellcome batch K 2142; sheep antihuman IgA, Wellcome batch K 5777; and sheep antihuman IgG, Wellcome batch 100¹¹A. Specificity tests for the conjugates were performed according to Bergquist and Kreisler's (1974) method. Toxoplasma was not isolated from samples of heparinized blood and urine taken on days 15 and 22.

Over the next few months the patient's condition deteriorated. He developed oedema, gross haematuria, an increase in proteinuria to 7.2 g/l., and glucosuria. Haemoglobin was 7.7 g/100 ml, blood urea nitrogen 44.6 mg/100 ml, and serum cholesterol 642 mg/100 ml. Antistreptolysin titre was 400 IU/ml. Antinuclear antibodies were not detected.

Prednisolone 0.5 mg/kg was given daily for five months. Pyrimethamine and sulphafurazole were given for six weeks starting on day 16. After five months a gradual improvement was seen and after 10 months there were no clinical symptoms.

Two further renal biopsies were performed 5 and 17 months after the onset of the disease.

LIGHT MICROSCOPY

First Biopsy (fig. 1)—The glomeruli were large with increased cellularity and swelling of endothelial and mesangial cells. The narrow,

FIG. 1—First biopsy. Acute glomerulonephritis with swelling of endothelial and mesangial cells. Polymorphonuclear leucocytes are trapped in capillary lumina. (Haematoxylin, $\times 433$.)

FIG. 2—Immunofluorescence microscopy. Focal granular deposits of γ -globulin along glomerular basement membranes and in mesangial regions.

slit-like capillary lumina contained numerous granulocytes. The capillary tufts showed increased lobulation. Deposits of fibrin or fibrinoid material were observed in a few capillary walls. Tubular or vascular changes were not observed in any of the specimens.

Second Biopsy.—The glomeruli showed segmental sclerosis of the capillary tufts with adhesion to the capsule or an increase in cellularity and in the amount of hyaline substance in the mesangial areas. There was also a slight interstitial fibrosis around some of the glomeruli with a few lymphocytes.

Third Biopsy.—The lesions remained principally unchanged but there was very little segmental sclerosing. The glomerular mesangial lesions and periglomerular fibrosis were also less conspicuous.

IMMUNOFLUORESCENT EXAMINATION

Evaluable material was obtained from the first and third biopsies. Strongly positive staining (3+) with heterospecific antihuman- γ -globulin (National Bacteriological Laboratory, Stockholm), anti IgG, anti-IgA, anti-C₃, and anti-fibrinogen and somewhat weaker staining (2+) with anti-IgM (these latter conjugates were purchased from Hyland Laboratories, Costa Mesa, California, U.S.A.) was seen along the glomerular capillary walls and in the mesangial regions in renal tissue from both biopsies. The distribution of the precipitates was focal and the pattern of staining granular. Both the intensity and the pattern of staining was the same in both biopsies (fig. 2). Material stainable with the antitoxoplasma conjugate (Wellcome Reagents, England) was present only in the first biopsy specimen. Its distribution and pattern were similar to those of the immunoglobulins but there were fewer foci and the staining was less intense (1+).

Comment

The early clinical picture in this case closely resembled a purpuric nephritis. There was little to suggest toxoplasmosis, so that this diagnosis was initially not considered. The finding, however, of material stainable with anti-toxoplasma conjugate in the glomeruli led to an examination for anti-toxoplasma antibodies. A significant rise in dye test titres from day 12 was shown together with a shift in the antibody population from IgM to IgG. Furthermore, specific IgA was present for a short period from day 16. It has been shown that in parasitic infections circulating antibodies of IgA class are often associated with activity of the infection or presence of antigen or both (Kane *et al.*, 1971; Hultdt *et al.*, 1973).

Reactivity of the glomerular deposits with anti-toxoplasma conjugate was shown only in the first biopsy and not later. It is well known that in immune-complex nephritis the antigen responsible can often be shown only early in the disease. Later the antigenic determinants in the complexes might be covered by specific antibodies. It has also been assumed that immune-complex deposition might trigger a subsequent local autoimmune reaction (Allison *et al.*, 1969).

The present case indicates that *Toxoplasma gondii* should be included in the group of agents which can give rise to immune-complex disease. In obscure cases of such disease, therefore, the possibility of active toxoplasmosis should be considered.

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