Acquired toxoplasmosis in children

BRIAN McNICHOLL AND JOHN FLYNN

From the Departments of Paediatrics and Bacteriology, Regional Hospital and University College, Galway

SUMMARY Nine cases of acquired toxoplasmosis, 8 from rural backgrounds, are described, illustrating the wide variety of clinical pictures. Evidence of familial infection was found whenever sought, and was also found in cattle in one case. The availability of an easily performed screening test should make diagnosis of this common disease more frequent.

Toxoplasmosis is an ubiquitous disease affecting all warm blooded vertebrates, its highest incidence in man being in rural communities and warmer climates. Frequencies of 7% in Navaho Indians, rising to 100% in Guatemala have been described by Feldman and Miller (1956). Beattie (1957) found 30% of an adult population in the UK to have evidence of infection, and a small study carried out in our region in 1973 showed an incidence of 40% (D. Ashford and J. Flynn, 1973, unpublished).

We have diagnosed toxoplasmosis in children about five times as frequently as brucellosis, an incidence of toxoplasmosis of about 1 in 2000 new patients seen over the last 10 years. The high incidence of significant titres in adults, particularly in rural areas, together with the low incidence of diagnosis, suggests that most infections are symptomless or very mild. Infection may cause a mild influenza-like picture, but lymphadenopathy, particularly cervical, is probably the most common overt presentation. Pneumonia, hepatitis, myocarditis, encephalitis, chorioretinitis, myositis, and arthritis may occur singly or in various combinations, and severe multiple organ involvement is occasionally seen.

We here describe a group of children whose illnesses illustrate the variations in the presentation of the disease in the West of Ireland. 8 of the 9 families were rural dwellers. Diagnosis on clinical grounds alone is rarely possible, and as isolation of the parasite is difficult serological tests are the mainstay of diagnosis. The toxoplasma dye test (TDT), while difficult to perform, is the best established test; titres of 1/512 or over are regarded as indicative of active or recent infection, lower titres indicating previous infection (Fleck and Ludlam, 1965). The indirect haemagglutination test (IHA) as described by Jacobs and Lunde (1957) is easier to perform

than the dye test. We have used a modification of this test as described by Karim and Ludlam (1975) and find it a reliable screening test.

Case reports

Case 1: persistent malaise. A girl of 12 years who had had contact with many farm and domestic animals and who regularly drank raw milk experienced malaise, sweating, and syncopal attacks since a febrile sore throat with cervical adenitis 3 months previously. She had been hospitalised elsewhere a month previously and brucellosis had been suspected. Physical examination was normal, but the TDT was 1/2048. Some malaise persisted for 11 months, when the TDT was 1/128.

Case 2: malaise and growth retardation. A boy of 5 years had increasing fatigue for a year after the discovery of some enlargement of his groin lymph glands by his parents. He lived in a country town, where for some years before his illness the next door neighbours had kept 16 cats which ranged freely over both gardens and outhouses. He was thought not to have grown during the year and had been sweating in bed in recent weeks. Height and weight were on the 15th and 10th centiles respectively, and the bone age was 4½ years, the midparental height being above average. Minimal enlargement of lymph glands in axillae and groins was noted. TDT was 1/16 000. His symptoms slowly disappeared during the next year after which the TDT was 1/8192.

Case 3: acute tonsillitis. A boy of 6½ years had vomiting, pyrexia, and rigors for 2 days with no response to ampicillin. He had drunk raw milk from a cow later found to have brucellosis. Moderate tonsillar inflammation with slight enlargement of the 'tonsillar' lymph glands and spleen was present. Eosinophils were $0.133 \times 10^9/l$ ($133/mm^3$). TDT was 1/512,

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rising to 1/1024 four months later. He made a good recovery while having intramuscular penicillin.

Case 4: multiple organ involvement. A girl of 3½ years had a sore throat and urticarial rash for 4 days with marked cervical adenitis. Pyrexia persisted for a week with worsening of the rash, appearance of a severe stomatitis, and gradual progression to deep coma with signs of myocarditis and an ESR of 80 mm/h. TDT was 1/2048, rising to 1/16 000 five months later. Considerable improvement had occurred by 15 days, when specific treatment was started; by then the sensorium was normal, but some ataxia persisted and the palms and soles desquamated.

Case 5: acute polymyositis. A boy of 9 years waddled into the clinic and was found to have generalised muscular weakness and tenderness with slight swelling of the calf muscles and absent deep tendon reflexes. He had to 'climb' up with hands on legs from floor sitting. 5 weeks previously he had become ill with a productive cough and an itchy rash on the trunk; a week earlier he had been too weak to lift his arms over his head. Lymph glands in neck, axillae, and groins were slightly enlarged and eosinophils were $0.67 \times 10^9/l$ ($670/mm^3$). TDT was 1/16 000 and was 1/1024 eight months later. Biopsy of the left gastrocnemius 2 weeks after admission showed no organisms. 4 weeks after admission he was walking almost normally and subsequently he made a full recovery. This case has been reported in detail (McNicholl and Underhill, 1970).

Case 6: polyarthritis. A boy of 8 years complained 6 months previously of pains in wrists, elbows, knees, and ankles the day after a febrile tonsillitis associated with cervical adenitis; his ESR was then 80 mm/h. Febrile sore throats and joint pains recurred on several occasions, and general malaise and night sweating persisted. He drank raw milk regularly. When seen there was moderate enlargement of both tonsillar glands and of one gland in the left axilla. The streptozyme titre was 200 units (titres > 200 suggest recent streptococcal infection or rheumatic fever) and TDT was 1/1024. Treatment was not advised at the time of diagnosis but was begun 3 months later because of persistent joint pains and malaise.

Case 7: disseminated intravascular coagulation. A boy of 9½ years suffered gradual blackening of the skin on the ears, nose, and tips of digits of hands and feet. The affected areas, including some on limbs and trunk, were cold, cyanosed, and tender. Disseminated intravascular coagulation was suspected because of a platelet count of $15.0 \times 10^9/l$ ($15\ 000/mm^3$), serum

fibrinogen 1.32 g/l (132 mg/100 ml), and evidence of fibrinolysis. Intravenous heparin was given for 7 days with gradual resolution of the lesions, some superficial skin loss occurring on the pinnae. Eosinophils were $0.302 \times 10^9/l$ ($302/mm^3$). No cause for the illness could be found at the time, but TDT was 1/1024 ten weeks after the onset.

Case 8: focal encephalitis; hemiparesis. A girl of 5½ years was limping for a week before admission in association with a tremor in the ipsilateral hand and cough. She had a mild right hemiparesis and persistent eosinophilia, between 0.603 and $1.410 \times 10^9/l$ (603 and $1410/mm^3$). CSF was normal. TDT was 1/4096 four weeks later and had fallen to 1/1024 three months after the onset, but eosinophilia persisted, and TDT had risen to 1/8192 three months later. When last seen, aged 12 years, her IQ was 77 and she had little physical disability, but had become left handed.

Case 9: focal encephalitis; basal ganglia lesion. A girl of 8 years who was right handed had begun to use her left hand preferentially for the previous 6 months and had recently developed a tremor in the right hand. She had a coarse tremor and some choreiform movements of the right hand, which gradually spread to the left hand and head. Serum caeruloplasmin and copper were normal, and electroencephalogram showed changes suggestive of a degenerative lesion in the left hemisphere. TDT was 1/2048. 2½ years after the onset the process seemed to have arrested and the EEG was almost normal; she was again writing with her right hand, although still using the left for most household and other activities.

Family and animal infections

Coincidental with the illness of Case 3, three of his siblings had febrile sore throats; TDT in these 3 siblings, and in a fourth sibling some months after Case 3 was seen, ranged from 1/256 to 1/1024; his parents had titres of 1/32 and 1/64. A year previous to the illness, 8 calves on the farm had been treated for pneumonia; serum obtained from 4 of these cattle at the same time as from the family gave TDTs 1/512, 1/1024, 1/2048, and 1/4096. Some difficulties arose in attempting to obtain serum from the farm cats. An 11-year-old sister of Case 1 suffered a similar but milder illness and her TDT was 1/512 a year after onset. Both she and her sister had levels of IgG and IgM below our laboratory range. The mother of Case 4 had a TDT 1/64, and the parents of Case 9 had TDTs 1/64 and 1/32, her 3 siblings having TDTs 1/32.

Management

Treatment with a 3-week course of sulphadimidine and pyrimethamine was given to Cases 4, 6, 8, and 9, the only obvious benefit being in Case 6, whose joint pains ceased after treatment. In the other treated children, it is difficult to know whether treatment was of benefit, since each appeared to be recovering at the time of treatment. We believe that treatment should be given when there is cerebral involvement, in the hope of killing any parasites that may be still active, and also when there is severe generalised infection. Treatment was suggested for Cases 1 and 2 in the event of symptoms persisting or worsening, but it was not thought necessary by the family doctor, and treatment was not advised for the remaining children as recovery was well advanced when the results of the TDT became available.

Discussion

We believe toxoplasmosis to have been the probable cause of illness in these children, although *Toxoplasma gondii* was neither seen nor cultured. None had serological evidence of brucellosis or infectious mononucleosis, nor did we find evidence of other infectious or degenerative disease. Recovery appears to be complete in all except the 2 girls with focal encephalitis. While the dye test is still perhaps the most acceptable serological test, in a routine clinical laboratory the indirect haemagglutination test (IHA) is easier to perform and in our experience is reliable. This test was positive in the 5 cases in which it was done (Cases 1, 2, 3, 6, 9) at a standard dilution of 1/128. It can be done in parallel with the complement fixation test and the IgM indirect fluorescent test and should help to identify most cases of infection. The latter test is thought to give a better indication of activity than others previously described, titres of 1/64 or higher suggesting active infection (Karim and Ludlam, 1975). It seems probable that the routine use of the toxoplasma IHA test as a screening test in many acute and subacute illnesses of uncertain aetiology, particularly in rural areas, would discover more examples of this disease.

As a result of seeing the child with the poly-arthritis, some recent findings may be of interest. A girl of 12 years had been diagnosed as having rheumatic fever in another hospital 6 years ago and was still on penicillin prophylaxis; on noting that the antistreptolysin O titre had been negative during the initial acute illness, serological testing showed a positive IHA test and TDT 1/256. We thought the evidence sufficient to suggest that the original illness might have been due to toxoplasmosis and advised stopping the penicillin. Another girl of 11 years

had been thought by us to have mild juvenile rheumatoid arthritis at age 2 years, but had had no further signs of joint involvement or illness 9 years later, when the IHA test was positive (1/128), TDT being 1/8. Again we believe it possible that the original illness may have been due to toxoplasma infection. We suggest that this infection might be considered in the diagnosis of arthritis in children.

Since cat faeces are regarded as the most likely vector in human infection (Hutchison *et al.*, 1970), care in their handling and disposal is indicated, particularly by pregnant women. Eating raw or uncooked meats should be avoided, since the parasite frequently encysts in mammalian muscle. The French Ministry of Health now advocates screening of all pregnant women for toxoplasmosis and regular surveillance of those found negative, and is considering toxoplasma vaccination for the future, as part of its programme to prevent mental and physical handicap (Wynn and Wynn, 1976). We have begun screening all pregnant women attending this hospital.

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Correspondence to Professor B. McNicholl, Department of Paediatrics, Regional Hospital, Galway, Ireland.