TOXOPLASMOSIS

A REPORT OF FOUR CASES

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To date only 5 cases of toxoplasmosis have been reported from this country, and of these 3 were diagnosed postmortem. Klenerman[1] recorded the first case in 1951—an African child presenting with an encephalitic picture at the age of 6 weeks and dying after 2 days, in whom the diagnosis was made on autopsy material. The mother's serology provided confirmatory evidence. The second case, that of a 4-year-old European child with mental retardation, choroido-retinitis and cerebral calcification, was reported by Rabkin and Javett in 1952.[2] Becker, in 1954,[3] recorded 2 cases diagnosed postmortem—an infant of 5 months with hydrocephalus, and a child of 4½ years who presented a picture of acute encephalitis and died after a 6 weeks' illness. Fasser, in 1955,[4] reported the case of a 2-year-old Indian child with mental retardation, hydrocephalus, and cerebral atrophy, but with no retinal changes or cerebral calcification.

The purpose of this paper is to report a further 4 cases, all diagnosed during life, and all in European children in Durban. It is not our intention to review the subject, for this has recently been done in this *Journal* by Spencer;[5] and other excellent reviews, such as that by Feldman,[6] are available to the interested reader.

It is not out of place, however, to recall that the parasite, a protozoon, first described in 1909 by Nicolle and Manceaux[7] in the North African rodent, *Ctenodactylus gondii*, is widely distributed geographically and has an unusual lack of host specificity, infection having been reported in a great variety of vertebrates. Human infection, apart from the congenital form, is presumably acquired accidentally from contact with animals. Since 1939, when the first human cases were described,[8,9] it has become evident from serological surveys that toxoplasmosis is a common infection in man. The vast majority of acquired infections, however, are subclinical, giving rise to no recognizable disease. Conventional classification groups the manifestations of acquired disease into glandular, ocular, encephalitic, and exanthematous forms.

Of the 4 cases presented here, the first 2 illustrate the

congenital type of toxoplasmosis, case 3 the ocular type, and case 4, reported in some detail, shows widespread systemic involvement with the production of a most confusing clinical picture.

CASE REPORTS

Case 1

L.G. was the fourth child of normal, healthy parents. Pregnancy had been perfectly normal and labour was uncomplicated. The birth weight was 7 lb. 11 oz. The 3 elder siblings were well.

She presented first on 18 March 1954, at the age of 4½ months, with a history of feeding difficulty since birth, and generalized convulsions with loss of consciousness. The mother had observed 16 convulsions during the previous 3 weeks.

Examination revealed a well-nourished child with a head circumference of only 14½ inches, who was obviously grossly retarded. Apart from some questionable pallor of the discs, the fundi were normal. X-ray of the skull revealed paraventricular and tentorial calcification. Subsequent pneumo-encephalography showed 'dilatation of the falcine and tentorial spaces and of the cisternae, and ? ventricular dilatation. The hemispheres appear retracted'. The cerebrospinal fluid (CSF) showed no abnormality. Serum calcium was 12·0 mg. per 100 ml., alkaline phosphatase 17 K-A units, and WR negative.

Serological tests for toxoplasmosis were carried out in Hanover, Germany, and were reported as follows: Sabin-Feldman test, positive 1 : 64; complement-fixation test, uncertain negative; and cadmium-sulphate test, +++. The maternal serum unfortunately became contaminated.

The child was seen repeatedly until the age of 1 year, when admission to a mental institution was arranged. She made virtually no progress and the fits were not controlled by a variety of anticonvulsants.

Case 2

M.W. presented on 30 January 1956, at the age of 4 months, with a history of diarrhoea for 2 months, vomiting for 3 weeks, and fever and irritability for 12 hours. He was the only child of healthy parents and the product of a normal pregnancy and delivery. Birth weight was 8 lb. 12 oz.

Examination revealed an extremely irritable baby with a temperature of 102° F.; the eyes were constantly deviated to the left. There was no neck stiffness, but the fontanelle was slightly tense. Lumbar puncture produced clear CSF containing 3 lymphocytes per c.mm. and protein 70 mg. per 100 ml., with a moderate increase of globulin.

The following day he developed a left sixth-nerve palsy, and the fever continued for 9 days, during which time he was drowsy and irritable when disturbed. Examination of the fundi on 2 February showed pigmented areas of choroido-retinitis in both eyes, typical of toxoplasmosis. The blood count was normal. Head X-ray revealed no intracranial calcification or other pathology. He was treated with sulphadiazine, and when he was discharged on 22 February the strabismus had disappeared and he seemed well. The CSF at this time contained 1 lymphocyte per c.mm. and protein 35 mg. per 100 ml., with only a slight increase of globulin. A month later he was apparently well and thereafter could not be traced. Both the patient's and his mother's sera were sent for dye and complement-fixation tests, but the records of these results were lost. The clinical picture in itself, however, leaves little doubt that this child was suffering from toxoplasmosis.

Case 3

L.B., a girl of 12 years, was admitted in August 1959 for investigation of deteriorating vision. This had first been complained of in 1957 when a choroido-retinitis of the right macular region was discovered. Since then the lesion had progressed until she had no central vision in the right eye. Recently similar changes had been observed in the left eye though vision was, as yet, unimpaired.

Her past history was complex, including 3 episodes of 'glandular fever' in 1951, 1953 and 1954, each time, it was said, with a positive Paul-Bunnell test. In 1952 she had a febrile illness and was investigated for, *inter alia*, tuberculosis and leukaemia. In 1956 she was treated for alleged amoebic hepatitis. In January 1958 she was said to have had tick-bite fever, and up to the time of admission was getting recurrent episodes of fever with glandular swellings.

Examination was essentially negative apart from the eyes. The right macular region was destroyed by a patch of choroido-retinitis which appeared inactive. Similar, but much less marked, changes were present in the left eye. A blood count showed no abnormality, and the ESR was 6 mm. per hour (Wintrobe). The Paul-Bunnell test was negative. Head and chest X-rays revealed no abnormality. The CSF was normal.

The whole history was so suggestive of toxoplasmosis that we were surprised and disappointed when the tests proved negative. However, the child was subsequently seen and re-investigated in Johannesburg when the Sabin-Feldman dye test was positive (1 : 64) and the toxoplasma complement-fixation test positive at 1 : 4 and dubious at 1 : 8. Opinion differed among the 8 ophthalmologists who saw her regarding the activity of the lesion, but she was treated with methylprednisolone, sulphadimidine and pyrimethamine, and to our knowledge there has been no further progression of the disease.

Case 4

F.M., a boy of 11 years, was admitted in July 1958, with a 4-day history of fever, headache, pain in the neck, lethargy, vomiting, constipation, photophobia and a dry cough. Previous illnesses included pertussis, measles and rubella. Later a history of haematuria 4 years before admission was obtained, and he admitted to frequent exposure to bilharzia in the Umhlatuzana River, a notorious local source of both *S. haematobium* and *S. mansoni*.

Examination revealed a small, ill boy, febrile (Fig. 1), with slight non-tender cervical lymphadenopathy, a liver enlarged 2 inches below the costal margin, and a very large, firm, tender spleen extending to below the level of the umbilicus. There were no signs of meningitis, and the fundi were normal on admission. He presented, therefore, as a patient with pyrexia of unknown origin associated with hepatosplenomegaly.

Special investigations were performed as follows:

1. *Blood count.* Haemoglobin 10·0 G. per 100 ml., PCV 29%, MCHC 34%, ESR 28 mm. per hr. (Wintrobe), WBC 4,000 per c.mm., neutrophils 40%, lymphocytes 54%, eosinophils 5%, basophils 1%. Repeated counts failed to demonstrate an absolute eosinophilia of more than 440 per c.mm. Red-cell fragility was normal. LE cells were not found.

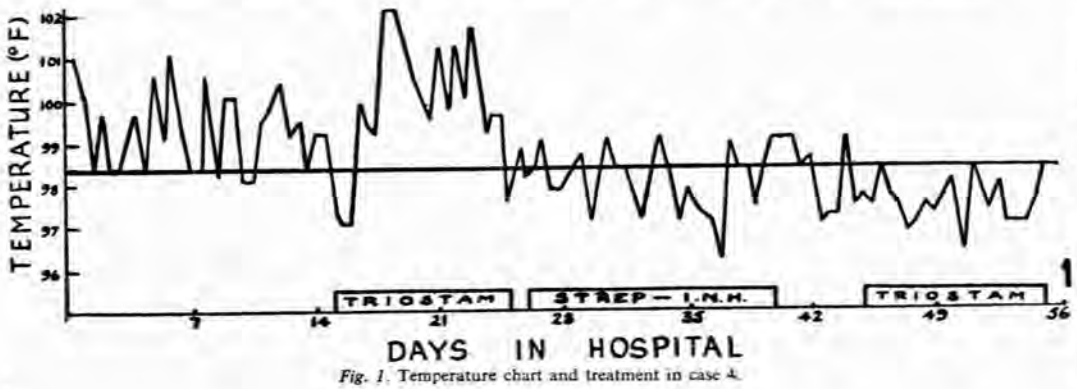

Fig. 1. Temperature chart and treatment in case 4.

2. *Urine examination.* Repeated examinations, including 24-hour specimens, failed to reveal any ova.

3. *Stool examination.* Repeated examinations showed trichuris ova only. No schistosomal ova were demonstrated.

4. *X-ray studies.* Chest: 31 July—'No evidence of any pathology noted'. 6 August—'right upper and mid-zone inter-

stitial consolidation. Remainder of the lung fields show generalized plethora with appearances suggestive of alveolar involvement. There is hilar calcification'. 21 August—'Perihilar adenopathy. There is bilateral, diffuse, increasingly confluent lung mottling with pulmonary hyperaemia—? reticulosis, sarcoidosis or lymphoma'. No pathology was demonstrated in the skeleton.

5. *Agglutination tests.* All tests for typhoid, paratyphoid, typhus, and brucellosis were negative. The Paul-Bunnell test was also negative.

6. *Tuberculin tests.* Patch and intradermal tests were negative. Gastric washings were negative for acid-fast bacilli.

7. *Liver-function tests:*

	5 August	14 August	24 October
Van den Bergh reaction ..	neg.	neg.	neg.
Bilirubin (mg. per 100 ml.) ..	0·7	0·5	1·0
Alkaline phosphatase (K-A units)	4·0	40·0	18
Zinc turbidity (units)	18	16	10
Cephalin cholesterol	4	4	1
Thymol turbidity (units) ..	9	10	7
Total protein (G. per 100 ml.) ..	9·2	8·8	8·8
albumin (G. per 100 ml.) ..	3·7	3·7	4·7
globulin (G. per 100 ml.) ..	5·5	5·1	4·1

8. *Bone-marrow examination.* This showed a slight leucocytosis with a mild eosinophilia only.

9. *Rectal biopsy* done on 11 August demonstrated old degenerate ova of *S. haematobium*, but *S. mansoni* ova were not found.

10. *Liver biopsy* on 27 August. Serial sections showed focal granulomata with an eosinophilic cellular reaction suggestive of bilharzia, but no ova were seen on differential staining. A mild periportal fibrosis was also present.

11. *Splenic biopsy* also performed on 27 August merely showed increased fibrosis and pigment deposits. No ova were found.

(Subsequent re-examination revealed no toxoplasma in either liver or spleen biopsy specimens.)

After 2 weeks in hospital the boy's general condition had deteriorated considerably. He was still pyrexial and cough was a troublesome symptom. The only positive findings were the pulmonary radiological changes and the schistosomal ova on rectal biopsy. In spite of the low eosinophilia it was decided to treat him for bilharzia, and he was accordingly given a course of antimonyl gluconate ('triostam'), 75 mg. daily for 10 days. In spite of the unusual febrile response (Fig. 1) he improved remarkably towards the end of the treatment.

Three weeks after admission fundoscopy was repeated, and lesions were seen consisting of small yellow patches, one in each eye, located about 2 disc-diameters above the optic discs. These were so suggestive of tubercles that the patient was started on a course of streptomycin and INH, but this was stopped when it was felt that his clinical condition was incompatible with a diagnosis of miliary tuberculosis. The ocular lesions progressed, gradually hardening in appearance, until at the time of discharge from hospital they appeared as white areas of choroido-retinitis with a thin rim of pigment, indistinguishable from healed tubercles. They have remained unchanged.

Although the ocular lesions should have suggested a diagnosis of toxoplasmosis, they were regarded as possibly bilharzial granulomata, and a second course of triostam was administered. The patient was then well, but the enlargement of the liver and spleen persisted, receding slowly over the following year. Only in May 1959 was the patient investigated for toxoplasmosis. The dye test proved positive to a titre of 1 : 1024, and the complement-fixation test was positive 1 : 4. Since there was then no evidence of activity of the disease he was given no further treatment.

DISCUSSION

Cases 1 and 2 illustrate the congenital form of toxoplasmosis in which the infection is acquired by the foetus in utero as a result of (usually clinically inapparent) maternal infection with parasitaemia. This type may present various manifestations, among which choroido-retinitis and cerebral calcification are common. Other features include hepatomegaly, splenomegaly, jaundice, skin rashes, hydrocephalus, microcephalus, myocarditis, and still-birth. Later, convulsions and mental retardation are found in the vast majority of survivors.

Case 3 illustrates the common glandular manifestations of acquired disease. Glandular fever may be simulated, not only clinically, but also in regard to the blood picture. The Paul-Bunnell test is, however, alleged to be always negative in toxoplasmosis. In this child it was said to have been positive on several occasions before we saw her, but was completely negative when done in hospital. In addition to the febrile lymphadenopathy this case demonstrated typical toxoplasmic uveitis, which may occur as a very late manifestation of acquired infection.

Case 4 presented with extensive visceral involvement, manifested by marked hepatosplenomegaly, pulmonary infiltration and fever. The subsequent choroido-retinitis should, perhaps, have led to an earlier diagnosis. Of considerable interest in this case was the apparent favourable response to treatment with antimony. This has not, to our knowledge, been previously recorded, and it would appear to be a line of therapy worthy of further investigation. The results of standard treatment—sulphadiazine and pyrimethamine—are generally satisfactory in the acquired case, in that the disease is halted and further damage prevented. In the congenital form, however, there is usually extensive and irreversible destruction of cerebral tissue and treatment is, therefore, of little avail.

SUMMARY

Four cases of toxoplasmosis in European children—2 congenital and 2 acquired—are reported, all of which were diagnosed during life.

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