TOXOPLASMOSIS IN CHILDHOOD

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TOXOPLASMOSIS—infection with the intra-cellular parasite Toxoplasma gondii, has been shown by the specific serological Dye Test to be much more widespread than at first thought. About 33 per cent. of normal adults give a positive test at titres of between 1/8 and 1/128 (Feldman, 1962). A positive test indicates past or present infection and a titre higher than 1/256 or a rising titre very strongly suggests active infection.

Recognition of the clinical entity and Dye Testing of suspect cases will lead to more frequent diagnosis of the active disease. The ophthalmologist will encounter the retino-choroiditis of toxoplasmosis in childhood or adolescence; the obstetrician may see the more widespread neonatal infection, frequently fatal; and the pædiatrician is likely to manage most of the acute cases of childhood with their pleomorphic manifestations. In some instances toxoplasmosis causes upper respiratory symptoms and enlargement of cervical lymph glands, when the laryngologist is consulted (Remington *et al*, 1960). The clinical picture in its earlier stages is similar to that encountered in the anginose type of glandular fever, without the characteristic blood film findings. Three such childhood cases are now presented.

Case Reports

Case I. E.P. Male. Date of birth September, 1958.

November, 1963 (aged 5 years). Admitted with acute tonsillitis and enlarged neck glands. One month before admission he developed "mumps"—malaise, and swellings in both upper cervical regions. These subsided after a fortnight but malaise and intermittent abdominal pain continued. For 5 days before admission he had had headaches, a painful stiff neck and the neck swellings had recurred. Examination showed an acutely ill child with a temperature of 102° F (rising to 105° F after 48 hours). There were large tender nodes palpable in both anterior triangles of the neck and in the left axilla. The tonsils were acutely inflamed and grossly enlarged. The liver and spleen were impalpable. Investigations showed a white count of 24,500/c.mm. with 76 per cent. polymorphs, 18 per cent. lymphocytes and 6 per cent. monocytes. Treatment with intramuscular penicillin was started; the pyrexia gradually settled and the nodes became smaller. The white count fell to 10,900/c.mm. after a week and he was discharged 20 days after admission.

He was next seen in Out-Patients 5 months later, in April, 1964. Since discharge he had suffered from intermittent anorexia, malaise, cervical lympha-

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denopathy and sore throats. He was afebrile, the cervical nodes were grossly enlarged and there were more small nodes palpable in the axillae and groins. The spleen was just palpable. The white count was 13,900/c.mm., sedimentation rate 11 mm. in the first hour, the Paul Bunnell Test was negative and the Toxoplasma dye test positive at 1/64.

In May, 1964, he was ill at home with another episode of fever and lymphadenopathy. When seen again in Out-Patients shortly after, the clinical picture was unchanged and the fundi noted to be normal. Further investigations showed a negative Mantoux at 1/1000, negative Heaf test, normal white count and sedimentation rate, and a Toxoplasma dye test positive at 1/16. Dye tests on his family were negative in the case of father, mother and brother but positive at 1/64 in the grandmother. It was decided to treat him as a case of Toxoplasmosis and a fortnight's course of Daraprim 6·25 mg. q.d.s. and Sulphadimidine 1 g. t.d.s. were given.

He was followed up in Out-Patients and remained well. When last seen, in August, 1965, he was thriving, the fundi were normal and spleen impalpable, though there were still small nodes palpable in the neck and axillae.

Case II. D.T. Male. Date of birth October, 1958.

November, 1960 (aged 2 years). Seen in Out-Patients with a 6 month history of progressive obstruction due to gross enlargement of tonsils and adenoids, and some cervical lymphadenopathy. In December, 1960, he underwent tonsillectomy and adenoidectomy and was seen in Out-Patients 1 month after and discharged.

In March, 1964 (aged 6 years) he was admitted with lingual tonsillitis and cervical lymphadenopathy. Two months previously he had developed a "mumps-like illness" with a stiff neck and swellings in both upper cervical regions. Since then the nodes had fluctuated in size and he had been intermittently off-colour. Three days prior to admission stiffness of the neck was noted and left earache and dysphagia developed. Examination showed an acutely ill child with a temperature of 104° F, neck stiffness, left acute otitis media and acute lingual tonsillitis with gross œdema of the fauces. There were numerous firm, tender nodes palpable in both anterior triangles of the neck. The fundi were normal, and the spleen and liver impalpable. Investigations showed hæmoglobin 80 per cent., white count 23,100/c.mm. with 72 per cent. polymorphs, 26 per cent. lymphocytes and 2 per cent. monocytes, sedimentation rate 48 mm. in the first hour. The cerebro-spinal fluid was normal in all respects and a chest X-ray was clear. A swab from the left ear grew Staph. Aureus and nose and throat swabs were overgrown with Proteus. Brucella Agglutination tests were negative but the Toxoplasma dye test was positive in the high titre of 1/2048. Dye tests on his family showed his sister positive at 1/4, his father positive at 1/32 and his mother and the family dog both negative at 1/4.

He was treated initially with a 7 day course of Tetracycline 250 mg. q.d.s. and then 6 days of Erythromycin 250 mg. q.d.s. before the diagnosis was made. During this time the temperature fluctuated between 102° F and 106° F, he remained very ill and the lingual tonsillitis did not settle. The nodes on the right side of the neck decreased in size but those on the left got larger and looked as if about to suppurate and point. Treatment with Daraprim 6·25 mg. t.d.s.

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and Sulphadimidine 1 g., t.d.s. was commenced on April 14th, 1964 and given for a week. On April 23rd, 1964, the temperature, having returned to normal, rose again to 103° F and he developed an erythematous papular rash and started to vomit. A white count showed a total count of 3,900/c.mm. with 22 per cent. polymorphs and 78 per cent. lymphocytes, the platelet count was 142,000/c.mm. and the sedimentation rate 35 mm. in the first hour. Blood culture was sterile. He was treated with phenergan and intramuscular penicillin. On April 29th, 1965, an agranulocytic ulcer developed on the buccal aspect of the right cheek and the white count was 5,400/c.mm. with only 9 per cent. polymorphs, i.e. a total polymorph count of 486/c.mm. This ulcer had healed by May 7th, 1964 at which time the total polymorph count had risen to 3,120/c.mm. and the total white count to 7,800/c.mm. The temperature had by now settled, the neck nodes were smaller and the throat had returned to normal. A repeat Dye test was now positive at 1/256. He was discharged a few days later and when seen in Out-Patients 1 month later was still having intermittent swelling of the neck nodes but no associated malaise. Following this the nodes slowly settled and he was very well when last seen in February, 1965.

Case III. P.K. Male. Date of birth September, 1960.

June, 1964 (aged 4 years). Admitted with a cervical abscess. Three weeks previously he had had an attack of tonsillitis, slight cervical adenitis and otorrhœa treated with penicillin and ear-drops. Three days before admission he developed a rapidly enlarging swelling on the left side of the neck with torticollis. On examination he was found to be apyrexial but looked toxic. The throat was slightly inflamed and the left ear-drum injected. There was a large inflamed fluctuant swelling in the left anterior triangle and a few slightly enlarged nodes on the right side of the neck. No other nodes were palpable nor were the liver or spleen enlarged. Investigations were as follows: hæmoglobin 70 per cent., white count 8,500/c.mm. with 57 per cent. polymorphs, 36 per cent. lymphocytes and 6 per cent. monocytes; sedimentation rate 90 mm. in the first hour, chest X-ray normal, Mantoux negative and the dye test positive at 1/1024. The abscess was incised and drained of greenish pus which grew hæmolytic streptococci but no tubercle bacilli. The drainage incision healed quickly without sinus formation. Treatment was commenced with Daraprim 12·5 mg. daily, Folic acid 5 mg. daily and Sulphadiazine 250 mg. q.d.s. This was continued as an Out-Patient for 17 days in all and then the Daraprim was reduced to 12·5 mg. weekly for 4 weeks more and the Sulphadiazine to 250 mg. daily for 1 week more. After this the neck swelling was smaller and he was better in himself though at this time—6 weeks after admission—the Dye test was positive in the very high titre of 1/4096. The Mantoux test remained negative. His mother's Dye test was negative at 1/4 and his father's positive at 1/16.

In November, 1964, although he was well in himself, the node had become fluctuant again, though not acutely inflamed and he was re-admitted and the abscess incised. This produced thick pus again, with no growth on culture, and biopsy of the abscess wall showed caseating tuberculosis whilst the Mantoux test became positive at 1/1000. At the same time the Dye test was still positive at 1/4096 so that a double pathology had to be assumed. Treatment was com-

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menced with PAS and INAH and continued until July, 1965, when all neck glands had disappeared. Since December, 1964, he has remained well and a cervical sinus healed 2 weeks after commencing anti-tuberculous drugs.

Discussion

These three cases, whilst differing in details, show a similar sequence in that in all the first thing noticed was malaise and cervical lymphadenopathy, whilst the event that precipitated their admission to hospital was an upper respiratory tract infection and secondary lymphadenitis. Presumably the first phase corresponded to the onset of infection with Toxoplasma, producing high titres in the Dye Test. In the second and third cases titres were so high as to make the diagnosis virtually certain but in the first case the highest titre was only 1/64. This was, however, some 6 months after the onset of the disease and the titre would certainly have been much higher during the acute phase.

The development of suppurative cervical adenitis is not characteristic of toxoplasmosis. In Case III suppuration due to tuberculous disease developed and in Case II, at one stage, the left neck was almost explored when the overlying skin became tense and indurated. This was possibly a secondary bacterial infection.

An interesting feature is the finding of positive dye tests in one or more members of the patients' families, indicating a possible source of the infection. Unfortunately nothing is yet known of the mode of transfer of this disease.

As regards treatment, the régime currently advised is a combination of the anti-protozoal drugs Daraprim and Sulphadimidine. This combination has been shown to be effective in experimental infections but its clinical efficacy is less easily proven (Remington *et al.*, 1960). One possible complication of this therapy was demonstrated dramatically in the agranulocytosis that developed in the second case.

The Toxoplasma Dye Test should be performed in children when the clinical picture suggests infectious mononucleosis, yet the characteristic blood film is absent and the Paul Bunnell is negative.

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