ACQUIRED TOXOPLASMOSIS

WITH A REPORT OF A CASE OF LABORATORY
INFECTION

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One of us (S. C. M.) recently became infected with *Toxoplasma gondii* when working in the laboratory. Brief mention was made of this in a recent publication on acquired toxoplasmosis (Skipper *et al.*, 1954) in which two cases of the glandular variety of the disease and one other possible case resembling typhus fever were described. The laboratory infection is now reported because it furnishes yet another example of mild adenopathy, with little constitutional disturbance, due to the toxoplasma.

Case Report

On August 31, 1953, S. C. M., for purposes of animal passage, set out to fill a sterile syringe with mouse peritoneal exudate rich in the Rh strain of toxoplasma. As the needle became blocked he removed it, set it aside point uppermost, and fitted a fresh one. Shortly afterwards he pricked his left third finger on the upturned needle. Realizing what he had done, he tried, unsuccessfully, to make the puncture bleed and applied tincture of iodine.

Nine days later (September 9) he felt shivery and tired, suffered from headache, and discovered an enlarged painful gland in the left axilla. On September 12 his temperature was 102° F. (38.9° C.) and the following day he had a rigor. In spite of a 48-hour course of penicillin, prescribed by his family doctor, his fever continued and ranged between 100 and 103.8° F. (37.8 and 39.9° C.). When examined on September 16 he was sweating and looked ill. The skin of his finger was red where it had been pricked, and two enlarged, tender, discrete glands, each the size of a walnut, were present in the left axilla. Some smaller tender glands were felt in the posterior triangles of the neck. The edge of the liver could be felt, but it was not tender. The blood count showed: Hb, 100%; red cells, 4,900,000 per c.mm.; colour index, 1; platelets, 165,000 per c.mm.; white cells, 11,000 per c.mm. (polymorphs 50%, eosinophils 2%, lymphocytes 26%, monocytes 14%, band cells 8%). Many of the lymphocytes were abnormal, resembling Downey cells types I and II. A Paul-Bunnell test was negative, as were agglutination tests for salmonella and brucella antibodies. A blood culture remained sterile.

On September 16 he was given 2 g. of sulphadimidine, followed by 1 g. six-hourly for five days, at the end of which period his temperature was normal. By September 26 the cervical adenitis had disappeared. On September 30 the total white count was 5,000 per c.mm. (polymorphs 36%, eosinophils 5%, lymphocytes 48%, monocytes 8%, band cells 2%). A few atypical lymphocytes were still present. Further Paul-Bunnell tests (on September 28 and October 23) were negative. By October 5 he felt well and had returned to work, but the enlargement of the axillary glands persisted in a minor degree until January, 1954. On May 5 full clinical examination was negative and x-ray films of the chest and an E.C.G. were normal. A final blood count (May 7) showed: Hb, 120%; red cells, 5,700,000; colour

index, 1.05; white cells, 13,000 per c.mm. (polymorphs 78%, lymphocytes, 16%, monocytes 4%, band cells 2%). No abnormal lymphocytes were seen.

Investigations for Toxoplasmosis.—Previously, S. C. M.'s serum had repeatedly given negative results in the dye and complement-fixation tests for toxoplasmosis. Indeed, it was so free of antibody that it had been regularly used as activator in dye tests, and only four days before the accident it had been satisfactorily employed as a negative control in the rabbit skin neutralization test. Subsequent changes in titre are shown in the Table.

Changes in Titre

Date	Dye Test (Sabin and Feldman, 1948) (Beverley and Beattie, 1952)	Complement- fixation Test (Sabin, 1949)
16/9/53	1: 80	Nil
27/9/53	1: 200	"
9/10/53	1: 600	"
21/10/53	1: 1,560	1: 16
27/10/53	1: 3,200	1: 16
16/11/53	1: 4,200	1: 16
8/12/53	1: 2,400	1: 4
8/1/54	1: 1,150	1: 16
5/2/54	1: 1,600	1: 16
12/3/54	1: 2,000	1: 16

On September 16 inoculation of heparinized blood into six mice, both intraperitoneally and intracerebrally, produced no illness in the animals, and two blind passages of pooled viscera, at intervals of two months, were negative. The toxoplasmin skin test (Frenkel, 1948), which was purposely postponed until February 9, 1954, was strongly positive.

Cases Already Reported

We have been able to find a total of six recorded cases of toxoplasmosis in laboratory workers (Ström, 1951; Sabin *et al.*, 1952; Sexton *et al.*, 1953; Giroud *et al.*, 1953; Franceschetti and Bamatter, 1953). It would seem that Ström's two cases were also briefly reported by Magnusson (1951).

Ström's first case was that of a woman aged 22 who, after working for only 19 days in the laboratory, developed painful adenitis of the neck with fever. She had been employed pipetting toxoplasma exudates, and it was thought infection had been by the mouth. On the third day of her illness she developed conjunctivitis, and on the fourth day a maculo-papular rash on the trunk, which disappeared in two weeks and was followed by desquamation on the hands and feet. Meanwhile the adenopathy had spread to the axillae and groins, and early in her illness the cerebrospinal fluid showed an increase in protein and in mononuclear cells (up to 12 per c.mm.) lasting for three weeks. Three weeks after the onset of the illness transient inversion of the T waves and other slighter changes in the electrocardiograph appeared and she complained of mild anginal symptoms and breathlessness. By this time her temperature was practically normal, but some weeks later severe headaches and attacks reminiscent of petit mal began, these being ascribed to meningo-encephalitis. She gradually improved but still suffered from headaches and from mild angina after six months. The duration of the lymphadenopathy was six to seven weeks. Attempts to demonstrate toxoplasms in an excised lymph node were not successful, and inoculation of mice with cerebrospinal fluid produced no illness. The dye test, at first negative, reached a titre of 1:4,000 three weeks after the onset of the illness.

Ström's second case occurred in a 22-year-old woman who pricked a finger of her left hand with a needle infected with toxoplasma material. Three days later an enlarged gland appeared in the left axilla. Her illness was very mild, and only slight enlargement of the lymph nodes in the neck, axillae, and groins was noted. A blood count was normal except for a relative lymphocytosis of 54%. The dye test was negative two weeks after infection, but gave a titre of 1:2,000 after two months.

Sexton *et al.* (1953) reported a fatal laboratory infection in a 47-year-old woman. She admitted no accident in the laboratory. After a period of four months' vague ill-health, she developed an acute febrile illness and became irrational. On the third day an extensive maculo-papular eruption, which spared the palms, soles, and scalp, appeared. There was no adenopathy. A blood count showed a leucopenia of 2,350 cells per c.mm., but later the white cells rose to 7,850 per c.mm. Moist sounds were present at the base of the right lung and there was rigidity of the limbs and to a less extent of the neck. On the seventh day of her illness convulsions began and she became deeply comatose. The cerebrospinal fluid, previously normal, was now xanthochromic (protein 55 mg. per 100 ml., sugar 48 mg. per 100 ml., culture sterile). Treatment, which included sulphonamides, antibiotics, and, because of low plasma electrolytes, deoxycortone, was unavailing, and she died on the ninth day. The dye test, which was negative before her illness, rose to a titre of 1:256 on the eighth day and the organism was recovered from mice inoculated with whole blood and cerebrospinal fluid taken before death, and with brain, spleen, and liver emulsion obtained at necropsy. Parasites were also seen in the patient's heart muscle, which showed widespread focal myocarditis. There was extensive gelatinous oedema of the lungs with cellular proliferation in the alveoli and in the interstitial tissue.

Giroud *et al.* (1953) briefly describe, in a laboratory technician, a febrile illness accompanied by conjunctivitis, headache, and, on the sixth day, by a facial maculo-papular rash. The complement-fixation test was positive to a titre of 1:32, but a complement-fixation test for Q fever was also positive (1:40).

Sabin *et al.* (1952) mentioned that one of their number was bitten by a toxoplasma-infected rabbit. No fever or other symptoms resulted, but the dye test became positive after 16 days and reached the high titre of 1:16,000 after 30 days, while complement-fixing antibodies appeared later.

Finally, Franceschetti and Bamatter (1953) quote the case of a girl (mentioned to them by Jaeger) whose eye was splashed while manipulating a suspension of toxoplasma. She was said to have developed "relapsing meningo-encephalitis."

Discussion

Skipper *et al.* (1954) point out that acquired toxoplasmosis usually occurs in latent form, no apparent illness resulting. In describing active acquired toxoplasmosis they draw attention to its two main types. In the first, the disease runs a benign course with mild fever and adenopathy, closely simulating glandular fever. In the second, the illness is acute and sometimes fatal. In addition to adenopathy, there are protean manifestations, particularly a maculo-papular rash, pneumonia, myocardial involvement, and infection of the nervous system with the production of meningo-encephalitis. The laboratory infections here described admirably illustrate the different forms the disease may take. Skipper *et al.* (1954) draw particular attention to the glandular variety of acquired toxoplasmosis and state that the disease should be suspected in cases of lymphadenopathy of uncertain aetiology when the Paul-Bunnell test is negative. More recently, Cathie (1954a) has carried out the dye test and complement-fixation test on the sera from 20 children and young adults in whom glandular fever was suspected on clinical grounds and in whom the Paul-Bunnell test was negative. In seven cases the dye test was positive, to titres varying from 1:32 to 1:512, and in six of these the complement-fixation test was positive to a titre of from 1:16 to 1:64.

It is well known that women who bear toxoplasmic infants are latently infected and very rarely show evidence of the disease. It is therefore of interest that Farquhar and Turner (1949) published the case of a woman who during the twenty-sixth week of pregnancy suffered a short influenza-like illness accompanied by enlargement of the cervical, axillary, and inguinal glands and who subsequently bore a toxoplasmic child. In the light of recent knowledge it

seems likely that the adenopathy was a clinical manifestation of active toxoplasmosis occurring during pregnancy.

The diagnostic value of the dye test and of the complement-fixation test is well shown in the case of S. C. M. Although some authorities have expressed doubt about the specificity of the dye test, so far as we are aware high titres such as we obtained in this serum have not been encountered in any other disease. Of particular importance is the rise and fall in the titre, as was emphasized by Sabin *et al.* (1952). As stated, we were unable to recover the organism from the blood by animal inoculation; we did not feel justified in excising a lymph node. Case reports show that direct demonstration of the toxoplasma in sections of affected organs and the transmission of the disease to animals by inoculation of blood, cerebrospinal fluid, or tissue emulsion is by no means always successful. Positive results are more likely to be obtained with severely ill patients. Skipper *et al.* (1954) were unsuccessful with lymph-node tissue, heparinized bone marrow, and citrated blood taken from one of their cases. Cathie (1954b), however, has reported the successful recovery of the organism by animal passage, using saliva and blood taken from a 5-year-old boy suffering from the glandular variety of the disease.

Little is yet known about the source of the infection in acquired toxoplasmosis. Although it has long been realized that the toxoplasma infests many species of animals, including domestic, direct transmission of the disease from animal to human, except, of course, in laboratory infections, has never been conclusively demonstrated. Similarly, transmission from human to human is known to occur only in the case of a woman who bears a toxoplasmic infant. Cathie (1954b) makes the interesting suggestion that one form of transmission may well be by direct contact spread through the saliva.

A large number of compounds have been tried, without success, in the treatment of experimental toxoplasmosis in animals (Eyles, 1953). So far, none of these drugs has been used in the treatment of human infections on a scale large enough to warrant drawing any conclusions. S. C. M. was treated for two days with penicillin without any effect on his pyrexia; it was not possible to ascertain whether there was a response to sulphadimidine.

Summary

A case of toxoplasmosis resulting from a finger-prick sustained in the laboratory is described. After an incubation of nine days a mild illness characterized by fever and lymphadenopathy resulted. The diagnosis was made by means of the dye test, which rose to a high titre (maximum 1:4,200), but the organism could not be recovered by animal passage.

Other published cases of laboratory toxoplasma infection collected from the literature are described. The clinical features of these cases vary, but closely resemble those of the spontaneously acquired disease. One case terminated fatally.

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