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Acute monosymptomatic aseptic meningitis caused by Toxoplasma gondii

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Acute monosymptomatic aseptic meningitis was observed in a 4 year old male patient. Toxoplasma gondii tachyzoites were detected in Giemsa-stained smears prepared from the CSF. Inoculation of mice gave the same result. The patient was cured after the application of pyrimethamine and sulpha drugs. On basis of the smears, the serological results and data in the literature, a direct infection through the nasal cavity has been assumed.

Toxoplasma gondii (T. g.), this obligate intracellular protozoon, is widespread throughout the world and can be found both in humans and in animals. According to surveys conducted in different countries, a large portion of the world's population proved to be infected by T.g. at one time or another [14, 17]. In Hungary the frequency of symptomless toxoplasma infection is between 30 and 50%. The first infection is symptomless in two thirds of the cases, while mild, non-specific manifestation is observed in the rest. There is a great difference in the number of T.g. infections and the number of diseases attributed to T.g., due to the difficulty of diagnosis.

Acquired toxoplasmosis manifests itself with lymphadenitic, cerebrospinal, exanthematous, ocular and myocardial forms [18]. Meningitis caused by T.g. infection is rarely mentioned; even special monographs hardly devote more than a sentence to it [4, 17]. Some papers occasionally mention cases which, considering the changes in antibody titre, could be regarded as T.g. meningitis, although the pathogenic agent was not found in the smears nor was the infection proved by inoculation of mice [1, 7, 8, 9, 10, 11, 13, 15, 19]. Reporting the case of our patient, we aim at providing clinical data to acute, acquired T.g. induced, extremely rare monosymptomatic aseptic meningitis successfully diagnosed, proved and treated.

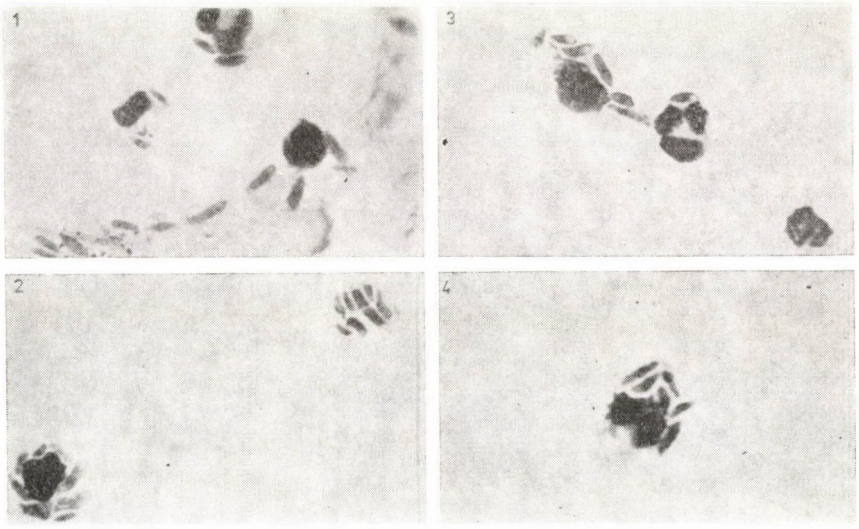
Report of a Case

The history of F.S., a 4 year old boy, did not contain data worth mentioning. On 1st October, 1982, he awoke with a headache, then projectile vomiting and a temperature of 38°C were noted. The doctor found occipital stiffness and positive Kernig sign and sent the child to our hospital with the diagnosis of meningitis. Upon admission the temperature was 38.5°C and the patient complained of mild headache. Physical examination showed no pathological change apart from the mild occipital stiffness. On lumbar puncture water-clear CSF of slightly increased pressure was obtained. It contained 0.24 g/l

TABLE I

Verification of Toxoplasma gondii infection

Examination	Date					
	01.10.	02.10.	04.10.	07.10.	28.10.	03.02.
Demonstration of tachyzoites in smears	positive			positive		
Isolation of the organism				positive		
IgM, IgG/IF		negative				
Complement fixation test			negative		negative	negative
Indirect haemagglutination test					negative	



FIGS 1—4

protein, 3.14 mmol/l glucose and the cell count was 30 n/μl, with 50% granulocytes and 40% lymphocytes. The Giemsa stained smear prepared from the sediment revealed a large number of T.g. tachyzoites extracellularly and a few intracellularly, indicating an acute infection (Figs 1, 2, 3 and 4).

Treatment with pyrimethamine, trimethoprime-sulfamethoxazole and folic acid was administered for a month. In two days the temperature became normal, the complaints and symptoms ceased completely. A second lumbar punture gave a CSF with slightly increased pressure, but this time the cell count was normal and a single T.g. was only discovered.

CFLP strain mice weighing 15—20 g were inoculated with 0.02 ml CSF intracranially and 0.3 ml intraperitoneally; ten days later a large number of T.g. tachyzoites was found in the abdominal exudate. Results and verification of the T.g. infection are summarized in Table I. Further examinations, including X-rays of the head and chest, ECG, EEG, ophthalmologic examination, biochemical tests and quantitative immune electrophoresis did not reveal any pathological change.

DISCUSSION

The positivity of the smear and the inoculation result were regarded as a proof of fresh T.g. infection. On due

treatment and possibly by the protective mechanism of the host immune system the tachyzoites could not invade the tissues and encyst there. This is the explanation why no demonstrable quantity of antibody was produced (Table I).

The ability of the host immune system to protect against T.g. infection has been confirmed by the studies of Hauser and Remington [6] who found that some of the anti-T.g. immune globulins act as opsonin against tachyzoites, most probably by activating the complement system and through the C_{3b} linked to the immune complex. This was a significant observation because phagocytosis of the tachyzoite may occur without opsonization, as indicated by other data, too [20], in that from blood of healthy subjects formerly not infected by T.g. more than 80% of the freshly isolated monocytes and 50% of the polymorphonuclears rapidly destroyed the intracellular T.g.

In our case the linkage of extracellular T.g. tachyzoites to lymphocytes and granulocytes indicated the presence of humoral antibodies (Figs 1, 2, 3 and 4) although cellular immunity to T.g. infection develops only some months after infection [12]. It was remarkable that although the ratio of granulocytes and lymphocytes was nearly equal in the smears, the tachyzoites adhered principally to lymphocytes. A possible explanation of this may have been that while lymphocytes possess mainly IgG_2 receptors, granulocytes and macrophages primarily have IgG_1 and IgG_3 receptors, to which antibodies have the greatest affinity and the anti-T.g. immune globulins belong primarily to the IgG_2 subclass and to a lesser extent to the IgG_3 subclass [5]. In CH_2 and CH_3 domaines the Fc receptors of lymphocytes bind only molecules in the immune complex, therefore the preference of tachyzoites to bind to lymphocytes may be considered an indirect sign of the presence of specific immune globulins. In the smears we have observed several times tachyzoites that formed a bridge-like connection between a granulocyte and a lymphocyte (Fig. 3). An interesting characteristic of tachyzoites is their sporadical clustering around a pole of the cell, thereby capping it (Fig. 4). The same phenomenon was observed in 5—20% of the T.g. tachyzoites by Dzbenski et al [3] who assumed that cap formation and later detachment of the T.g. surface antigen and corresponding antibody from the host cell is an indication of the tachyzoite trying to escape from the host immune system.

The distribution of T.g. in our case pointed to the presence of specific immune globulins. Why was then the IgM IF result negative? We suppose that the infection was discovered in its early stage when only a small quantity of IgM was present and could not be demonstrated by the rather insensitive IF method. Naot and Remington [16] compared the IF methodology with the more sensitive double-sandwich IgM-Elisa test and found that in 25% of the acute cases the IgM IF was negative. Neverthe-

less, in 93% of the examined sera the double-sandwich IgM-Elisa test was definitely positive while the IgM IF result was negative. Recently, McCabe and Remington have concluded that the absence of IgM type antibodies by IF test does not necessarily mean that the infection is not acute [14].

It is conceivable that the pathogenic agent had entered the host organism through the nasal cavity and from here, just like Naegleria and Acantamoeba [2], it passed through the cribriform lamina, reached the meninx along the olfactory nerve and induced meningitis. Infection was possible, for the child often played in the neighbouring sandy playground frequented by cats, and he had a habit of picking his nose.

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