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Toxoplasmosis

Opinions about the incidence of congenital toxoplasmosis in the UK seem to differ between 1 in 10 000,[1] and 1 in 2000.[2] These differences may be due to a wide range of degree of severity.

Diagnosis

The diagnosis of congenital disease in a child is made using the serological tests, notably the dye test, and confirmed by toxoplasma-specific IgM tests. These are carried out at one of the three reference laboratories of the Public Health Laboratory Service, in Leeds, Swansea, or Tooting.

If the dye test titre in a child aged <1-year is high (1:512 or 500 IU), and there is toxoplasma-specific IgM present, congenital disease is likely. Treatment is generally attempted although no treatment can replace damaged brain tissue or even be guaranteed to kill the toxoplasma completely. A combination of pyrimethamine, sulphamerazine, and folinic acid is the most successful.[3]

Prevention of congenital infection

Prevention of congenital infection has been much discussed. The pregnant woman must avoid eating raw meat (considered a common mode of infection on the continent of Europe) and she must not have any contact with faeces from infected cats. Many infected women however deny that they have had contact with infected cat faeces (cats tend to defecate in gardens other than their owner's). Few women in the UK confess to having eaten raw meat regularly. Perhaps there is some other route whereby the oocysts of *Toxoplasma gondii* (a resistant form of the parasite able to survive in soil for at least a year) can reach the pregnant woman—for example in uncooked vegetables.

Is a vaccine needed? Live vaccines would be unsuitable. Most strains of *T. gondii* isolated from the lymph nodes of infected humans are avirulent for mice and would produce considerable damage in the immunologically less competent fetal tissues. Dead vaccines seem to be of limited value.[12] The virulent form of the parasite, notably the RH strain, is able to grow more rapidly inside cells and can break through the immunity offered to mice by killed vaccines.[4] The immunological mechanisms of the protection against *T. gondii* have yet to be worked out.[5] Some work on monoclonal antibodies by Araujo *et al.*[6] is being done and may show which antibodies are protective. Cell-mediated immunity as well as humoral immunity occurs in the infected female and this must protect the fetus from the full effects of toxoplasmic parasitaemia. Why only 30% of infected pregnant women produce infected babies is not known. The placental barrier mechanisms must play a part.

It is the pregnant woman infected in the 1st trimester whose infant is most severely affected, presumably because of low immunological competence in the fetus at this stage.[7] As the pregnancy progresses the damage to the fetus lessens although the chance of infection of the fetus remains the same. At the last trimester there is a high proportion of subclinically infected babies born, although in some of them the manifestations of the disease may take many years (5–10) to appear. More work is needed to delineate the effect of subclinical infection on a child's educational performance.

How should the obstetrician deal with a suspected toxoplasma infection in pregnancy? In France women are tested for toxoplasma antibody when, or even before they get married. If found positive before they have borne children they are declared immune, because recurrent infection in successive pregnancies is rare and requires no further treatment. If found negative they are told to avoid eating raw meat and to avoid contact with cat faeces should they become pregnant. They are tested for toxoplasma antibody every month throughout the pregnancy and if they convert to positivity they are treated throughout pregnancy with spiramycin (2 g a day). Only about 20% of French women are still negative by the time they become pregnant so that the problem of serological testing is only one-fifth of what it would be in the UK.

In the UK if a woman is pregnant and suspected of having toxoplasmosis she is tested for toxoplasma antibody in her serum and if this shows a dye test titre of more than 1:512 (500 units)/ml with toxoplasma-specific IgM at any titre a decision whether to offer termination must be made. The decision should be left to the mother and is obviously only feasible before the 20th week. What are the risks of such a mother producing a clinically damaged baby? Desmonts and Couvreur[7] have

shown that the risk of damage is particularly severe in the 1st trimester, although not all fetuses are infected, so the risk of severe damage is about 8%. Oral doses of 2–3 g spiramycin were given for 3 weeks to women with acquired toxoplasmosis during pregnancy. Cases of congenital toxoplasmosis were appreciably more common (45%) among 82 untreated cases, than in 98 treated women (24%). Clinically apparent disease in newborn infants was the same (11%) in both groups.[8] The control groups in this and other studies have not been entirely satisfactory because maternal infections are not evenly distributed throughout pregnancy.[3] Until further results are available treatment is advisable, especially as some infants born without signs or symptoms subsequently develop serious untoward sequelae of congenital infection.[9] In the 2nd and 3rd trimesters of pregnancy, when termination is impossible, chemotherapy is all that is available and spiramycin 100 mg/kg a day orally for 30 days or pyrimethamine 1 mg/kg a day orally for 30 days, together with sulphadiazine 100 mg/kg a day orally in divided doses for 30 days, and oral folinic acid 5 mg/24h is indicated.

It is doubtful if this treatment will kill the toxoplasma once inside cells. In my experience *T. gondii* was isolated from a case of congenital disease after two successive courses of treatment, one of spiramycin and one of pyrimethamine, each for one month.

Eye manifestation

The paediatrician is faced with a difficult problem with the mildly affected child, usually having retinitis. Although there is some evidence that treating posterior uveitis due to infection with *T. gondii*[10] will arrest the disease, no treatment can replace damaged cells. The uveitis is partly an allergic response to the infection and steroids will help, but whether these alone allow *T. gondii* to spread in ocular tissue in the human as they do in the rabbit is debatable.[11] If there is posterior uveitis with active disease near the macula and the presence of antibodies to *T. gondii*, steroids with pyrimethamine, sulphonamides, and folinic acid are needed. Peripheral white cells and platelets should be examined each week to avoid folate deficiences as a result of this treatment. It would be a tragedy if mild ocular disease were treated with drugs that led to folate deficiency.

Conclusion

The best attack on this disease would seem to be prevention by the pregnant women avoiding contact with the organism.

The cost effectiveness of routine serological screening is currently being investigated for the UK but it seems unlikely that such screening would be worthwhile. If a woman presents in the 2nd or 3rd trimester of pregnancy with signs and symptoms of acquired toxoplasmosis or is found to have a toxoplasma antibody titre of 1:512 or more (500 IU), especially if this is accompanied by IgM antibodies, treatment with spiramycin should be begun.

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