TOXOPLASMOSIS

Two observations and a specification

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Summary: On the basis of two interesting observations of toxoplasmic disease the Authors attempt to interpret the various pathological pictures, comparing two different formulations of toxoplasmic disease: that of Sabin and that of more modern AA.

Some ten years ago we were consulted, in another hospital, by a patient with an obstetric history of 7 consecutive miscarriages between the 2nd and 4th months of pregnancy.

The various tests carried out (hysterosalpingography, listeria, glucose tolerance test, vaginal smear, cervical smear etc.) all proved to be within the norm. The only datum outside the normal scale of values was that of the toxoplasmoses which showed a high level of specific IgG and absence of IgM.

On the hypothesis that this might be an element favouring abortive interruption of pregnancy we undertook a specific antitoxoplasmosic therapy with Pirimethamine and Erbapreline in cycles. Then we advised the patient, who had naturally lost confidence, to try another pregnancy.

This happened after some months, and was carried through to the 38th month an was concluded with the spontaneous delivery of a live and viable foetus, with no signs of illness, at least for the two years during which we were able to check it.

The problem only recently returned to our consideration when another observation of toxoplasmosis in pregnancy called our attention to the illness.

The patient was a woman of 33, who in 1966 had been treated for toxoplasmic corioretinitis. At that time the specific IgM was positive and the antibody title of the IgG was high. The patient was also a carrier of Antigen Au with marked positivity for Anti-HBe.

Her obstetric history indicated two Cesarean sections, one with the podalic presentation of a healthy newborn, the second, in 1974 through feto placentary insufficiency and previous Cesarian section carried out 14 months previously. The newborn was healthy.

In 1984 the patient embarked on another pregnancy and referred to her last menstruation on 12.1. The pregnancy proceeded well in the Ist trimester, gave signs of feto-placentary insufficiency in the 2nd, while at the beginning of the 3rd arterial hypertension appeared. Tests of renal function showed slight changes in clearance and creatininemia reached levels of 2.8 mg/100 ml.

In the meantime fetal growth slowed, while serial hormonal levels of HPL and E_3 did not support echographic data, even at the lower limits.

The sierological situtation remained compared with the Australian antigen; indirect hemoagglutination for toxoplasmosis gave positive values up to 1 : 256.

The oculistic examination indicated: « issue of disseminated toxoplasmosic corioretinitis, diffused miopic dystrophy, slight signs of hypertensive vasculopathy, denoted by the tortuosity of the reflex ab-

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sent from the arteriole. Report sustantially unvaried in respect to previous checks » (fig. 1).

At the end of the 37th week, on the basis of ecographical data of feto-placentary insufficiency and of pressure values, which had only been maintained at levels of 160/100 by hypotensive therapy, it was decided (having performed the Clements test) to proceed to the Cesarean section.

A fetus was delivered weighting 1990 grs/42 cms, with apgar 7-8-9 in three successive evaluations at intervals of 5'-10'-15. The placenta, which weighted 350 grs, was sent to the Pathological Anatomy Institute for histological examination: « Placenta of 300 grs weight (after fixing) which appeared characterised by the presence of large areas of infarctual type sometimes confluent. At the histological examination we observed extensive areas of ischemic necrosis which left only nuclear shadows recognisable peripherically, and which appeared disseminated by numerous calcifications. In the adjacent zones the villi appeared to be associated with the fibrous phenomena which lead to atrophy of the vascular formations and are associated with micro-calceous areas. Finally, we observed phenomena of thrombosis of the intervilli spaces sometimes associated with focal hyperplasia of the syncizio trophoblast. The above mentioned histological samples agree with the diagnosis of toxoplasmosis of placentary localisation ».

This sample is suggestive, inasmuch as it is held (Hall) that in an early phase toxoplasmosis is better diagnosed by sierological methods, and in a later phase by histological methods.

Confirmation is given by the studies of Remington, Saxen, Saxen, Argyle, Schuman, who attribute a notable specificity to the cellular and histological modifications of lymphonodal toxoplasmosis.

The newborn, immediately sent into the care of the Newborn Pathological Centre of our Department, and submitted to a series of enquiries, was considered clinically healthy, apart from the presence of positivity at I : 256 of the toxo-test (IgG transmitted by the mother). The IgM were absent. All the checks were repeated at the 3rd month and at the 6th month, the period of this presente communication.

At the 3rd month the toxo-test was negatived by the disappearance of the passive anti-bodies. At the 6th no changes included in the tetrad of the conatal toxoplasmosis were evident, it being born in mind however, that further tests will be necessary at some future titme. (Henry-Suchet).

COMMENT

The first observation caused us to have some doubt as to the validity of Sabin's rule, according to which toxoplasmotic infection may act negatively only as a recent infection. In fact the pregnancy following the primary infection should be protected by adequate antibody presence. On the other hand the development of the pregnancy up to the 38th week might also be a coincidence, and also for this reason the case was filed.

Undoubtedly more recent research has shown that habitual miscarriage, contravening the above-mentioned concepts, may be related to the persistance of a toxoplasmotic infestation (Cacciapuoti, Cacciapuoti, Langer, Remington etc.). In other words it would pass from infestation to toxoplasmotic disease by a mechanism which might be explained in the following way.

The toxoplasma Gondii is an opportunist parasite, and as such develops its agressive potentiality only in relation to its host's immunity condition.

It penetrates the intestinal epithelium in the merozoit phase of its biological cycle, then effects a haematogenic and lymphatic invasion as a tachyzoit, causing parasitemia.

If the immune defence system of the host is valid, the parasite is eliminated, either as a reaction of neutralising antibodies on the basis of humoural immunity, or, in an immediately following phase, as a cellular-immediated immunity mechanism.

If, however, the host organism is going through a period of immunodepression, related to endogenous or exogenous factors, then it passes on to the formation of so-called "latent cysts" which can be localized in various organs, with prevalent selection of the uterus or muscular apparatus.

In pregnancy the so-called immunological tolerance then takes over, therefore, at the rupture of a cyst, the bradizoits it contains are freed and transform themselves into tachizoits causing parasitemia. This is also favoured by mechanical, humoural and erosive factors of the toxoplasmic cysts on the part of the trophoblast. It is therefore considered that pregnancy generally provokes a reactivation of toxoplasmosis.

The IgM at this point, as an indication of recent infection, should not be found, inasmuch as their synthesis is depressed by the IgG already present (J. Henry-Suchet).

Our first observation would thus be explained, in the sense that treatment for toxoplasmosis would have helped the parasitemic blocking, allowing for the development of the pregnancy.

We know, in fact, that tachizoitic parasitemia in the Ist trimester often leads to the development of miscarriage in pregnancy.

Different observations might be made in considering the second case to which we have referred.

In fact the preceding toxoplasmosis should have blocked the reinfection. Evidently it was not a matter of re-infection but of recidivism through the letting in of the bradizoits due to the rupture of latent cysts. Obviously the IgM did not appear on account of the high title of the IgG present; however the parasitemic phase, thanks to the immunological tolerance, was not immediately hindered and allowed time to give placentary localisation.

At this point another observation has to be made.

The newborn, at least on the basis of tests carried out during the first six months of life, is unaffected by the connatal toxoplasmosis as is shown by the absence of IgM. These, in fact, did not pass through the placentary filter because of their molecular structure, while the presence of IgG in the newborn showed the existance of a maternal - fetal transfer without excluding their fetal production, since in the 3rd trimester the fetus was immunoresponsive (Cacciapuoti, Cacciapuoti).

Then a siero-prophylaxis for antibodies and an autochtonous immunoantibody response took place in the fetus.

We consider that this, presumably is why clinical or instrumental signs of toxoplasmosis did not appear, even in succeeding months, in the unweaned infant.

* * *

The conclusive considerations following the study of these observations might then be:

It is true, as Sabin says, that primary toxoplasmotic infection extends to subsequent pregnancies, but it is also true that there might be recurrences (*) in subsequent pregnancies for the following reasons:

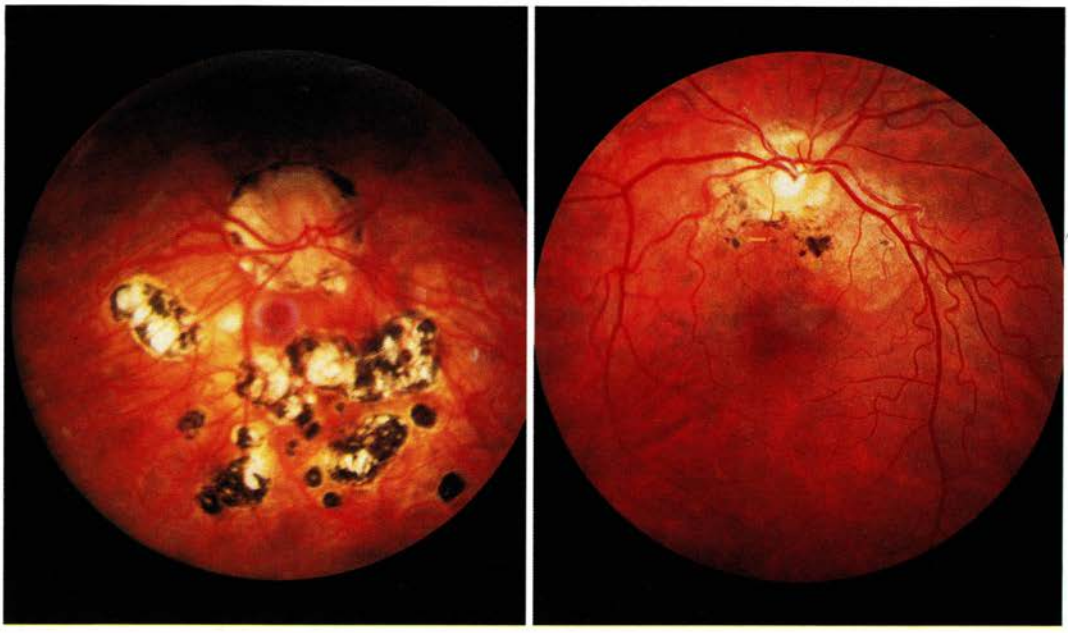
1) pregnancy takes place during a period of immunological tolerance;

2) the biological cycle of the toxoplasma evolves in three particular phases:

a) of merozoits, in the phase of penetration of the intestinal-epithelium;

b) of tachizoits in the phase of hemolymphatic invasion;

(*) Sometimes referred to as reactive or new infection.



left eye

right eye

Fig. 1. — Spots on the papillary maculae site of pigmented disseminated corioretinitis.

c) in the bradizoits in the phase of cystic localization.

The cystic localisation may be maintained for some time and give rise to toxoplasmotic dissemination if, at a time of immunological depression, a rupture of the cysts takes place. If, at that moment the parasitemic presence is blocked within reasonable time, the pregnancy develops normally and the fetus is covered by the passive siero-prophylaxis. If on the other hand the parasitemic is not inhibited by the biohumoral defence of the mother in the 1st trimester, miscarriage may take place because the embryo is not immuno--competent and the passage of IgG is limited to the villous barrier, still in a two- strata structure: syncizic-trophoblast and plasmodic-trophoblast.

But if the parasitemic presence enters during the last stage of the pregnancy, added to the more massive maternal-fetal IgG transfer, there is also the immunitary defence capacity of the fetus, already immuno-competent, then the infection, even if it were transmitted would not be transformed into disease.

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