JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 1999, p. 3423–3424 Vol. 37, No. 10
0095-1137/99/$04.00+0

CASE REPORT

Intravenous Immunoglobulin Therapy: Confounding Effects on Serological Screening for Toxoplasmosis during Pregnancy

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Received 27 January 1999/Returned for modification 26 April 1999/Accepted 24 June 1999

The serological diagnosis of toxoplasmic infection during pregnancy is intended to prevent congenital infection of the fetus. However, in the context of recurrent pregnancy loss intravenous immunoglobulin therapy can create a biological trap for the interpretation of serological results, with potentially serious consequences for the outcome of the pregnancy.

CASE REPORT

At the beginning of November 1998, a private nonspecialized laboratory transferred to our university hospital two sera (obtained on 23 and 30 October 1998) that had been collected from a pregnant woman (date of conception, 21 September 1998) for *Toxoplasma* serology (serological results are reported in Table 1). The medical biologist had noted a slight increase in immunoglobulin G (IgG) levels and had specified that the woman was known to have been negative for *Toxoplasma* as of May 1998. The routine techniques performed on these two sera revealed low levels of IgG (with a slight interim increase) but no IgM. The serological methods used have already been described (1). Briefly, specific IgG antibodies were detected by using both Vidas TXG (bioMérieux, Marcy l'Etoile, France) and indirect immunofluorescence assay (IFA), while IgM antibodies were detected by using Vidas TXM, ImmunoSorbent Agglutination Assay (Toxo-ISAGA; bioMérieux, Marcy l'Etoile, France) and IFA.

The serology profile indicated the likelihood of a past infection. Nevertheless, to complete the serological data, *Toxoplasma* serology was performed, on two sera that had been collected for biological analysis other than *Toxoplasma* serology on 20 June 1998 and 6 October 1998. Surprisingly, these sera were both negative for *Toxoplasma* antibodies. Thus, the two sera collected on 23 and 30 October 1998 clearly indicated a past infection while the serum collected on 6 October 1998 was undoubtedly negative.

At this point, it was necessary to determine whether this woman had seroconverted for *Toxoplasma* during pregnancy or not, and consequently, to decide if a specific treatment and prenatal diagnosis should be performed. Seroconversion could be suggested by the fact that the serology profile changed from negative to positive (which is the strict definition of seroconversion). However, the serological pattern (the IgG titers and the absence of IgM) and the high anti-*Toxoplasma* IgG avidity (the index was 0.55 for the serum collected on 30 October) for the two positive sera strongly suggested that the infection had been acquired before pregnancy (7). Even though the absence of detectable specific IgM is highly compatible with an infection acquired in the distant past, it must be emphasized that even the presence of IgM would not have been an absolute proof of a recent infection (6). Three hypotheses could thus be put forward: (i) there was a true infection with a very unusual serological profile (which could pose quite a challenge to the interpretation of other cases); (ii) there had been an error in the serum identification (this was controlled many times, and no mistake was evidenced); or (iii) immune disorders in the patient could have led to the presence of unusual antibody subsets (which could perhaps explain discrepancies in serology and IgG avidity). Thus, a new serum was requested (collection date, 12 November 1998), and the medical biologist and the obstetrician who monitored the course of the woman's pregnancy were requested several times to attempt to detail all of the medically significant events in the woman's life. Finally, we learned that this woman had a history of recurrent pregnancy loss, which had made the injection of gammaglobulin necessary (4). Intravenous immunoglobulins had been injected on 9 and 30 October 1998, which had led to the appearance of exogenous anti-*Toxoplasma* IgG in the patient's blood.

Congenital toxoplasmosis, which is transmitted from the mother to the fetus in the case of maternal infection with *Toxoplasma gondii*, can cause severe lesions to the fetus, newborn, or child (8). To detect seroconversion linked to maternal infection, some countries have decided that serological testing for *Toxoplasma* antibodies should be mandatory during pregnancy. In France, this screening is conducted on a monthly basis in *Toxoplasma*-negative pregnant women. If the woman is positive for *Toxoplasma* before pregnancy, this screening is not necessary, since there is no risk of transmission of the disease to the fetus. For women with unexplained recurrent pregnancy loss, the use of intravenously administered gammaglobulins allows a better outcome of pregnancies (4). However, the use of such gammaglobulins can cause trouble in the interpretation of serology profile for infectious diseases (5). We have reported here a case in which *Toxoplasma* serology was especially

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TABLE 1. Serial results of serology for *T. gondii*

Date of serum sampling	Specific IgG		Specific IgM		
	Vidas TXG[a]	IFA[b]	Vidas TXM[c]	ISAGA[d]	IFA[e]
20 June 1998	0	0	0	0	0
6 October 1998	0	0	0	0	0
23 October 1998[f]	17	8	0	0	0
30 October 1998[g]	47	8	0	0	0
12 November 1998	15	8	0	0	0

[a] Vidas TXG was scored as positive if ≥10 IU/ml.
[b] IFA for IgG was scored as positive if ≥8 IU/ml.
[c] Vidas TXM was scored as positive for an index of ≥0.65.
[d] ISAGA was scored as positive for an index of ≥9.
[e] IFA for IgM was scored as positive for a titer of ≥1/40.
[f] The patient was intravenously administered immunoglobulins on 9 October 1998.
[g] The patient was intravenously administered immunoglobulins on 30 October 1998.

difficult to interpret, which could have resulted in serious consequences for the woman and her child.

This case illustrates the difficulties in interpreting serological results after intravenous administration of immunoglobulin (5). For toxoplasmosis this problem has already been described, even though the literature on this topic is scant (2). Our case allows us to underline the two main problems that can arise. First, the appearance of anti-*Toxoplasma* antibodies may lead to an erroneous diagnosis of toxoplasmic seroconversion (if the serological data are not carefully interpreted and if complementary tests, such as an IgG avidity test, are not performed) and thus result in unnecessary anxiety, treatment, and perhaps antenatal diagnosis. On the contrary, if the only sera available are those for which the serology result is falsely positive (for instance, the sera collected on 23 and 30 October 1998 from our patient), without having any immunization against *T. gondii*, the woman can be falsely considered immunized. In such a case, the screening during pregnancy might not appear to be necessary. Furthermore, prenatal diagnosis might also not appear to be necessary, even though PCR performed on amniotic fluid is an accurate approach to detecting congenital *T. gondii* infection (3). However, an infection may occur anyway, and the fetus can be infected with severe lesions. In such a case, it is impossible (if sera sampled before pregnancy are not available) for the medical biologist to know whether the antibodies detected are the "real" antibodies of the patient or not. The only solution to this problem is to improve the communication among all the medical staff involved in the follow-up of pregnant women, in order to avoid the occurrence of such cases, which may have dramatic consequences. Furthermore, patients who receive intravenous immunoglobulin should be informed that this therapy may modify some results of laboratory analyses performed on their blood.

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