Prenatal diagnoses of cytomegalovirus (CMV), rubella, toxoplasmosis, varicella, parvovirus, herpes simplex and syphilis. The Lagos programme experience

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Summary

Prenatal diagnosis of infectious diseases has been shown to be indispensable to confirm or exclude in utero infections due to cytomegalovirus, rubella, toxoplasmosis, varicella, parvovirus and herpes simplex, and a multidisciplinary approach is needed. Our report is on data obtained from 236 pregnant women at risk for the above-mentioned conditions. The specific IgM test suggested seroconversion in only 198 of these patients and 162 of them requested prenatal diagnoses by means of fetal blood sampling or amniocentesis, or both. The results are encouraging but more work is required to optimize our diagnostic approach, i.e., monoclonal antibodies and DNA probes with direct identification by means of choronic villi sampling, which we use for prenatal diagnoses of hemoglobinopathy (DNA-genetic).

Key words: Prenatal diagnosis; Cytomegalovirus; Rubella; Toxoplasmosis; Varicella; Parvovirus; Herpes simplex II; Syphilis.

Introduction

The microorganisms most frequently responsible for congenital infertility are rubella virus, cytomegalovirus, and toxoplasmosis gondi whereas hepatitis B, type II herpes virus, parvovirus, varicella and HIV1&2 cause prenatal infections based on the characteristics of transmission [1]. For cytomegalovirus (CMV) the transmission to the fetus may occur with the primary infection but may also result from reaction of a latent infection, and for rubella and toxoplasmosis the involvement of the fetus occurs only in primary maternal infections [2-5]. It should be noted that in utero infection during reinfection, unlike in cases of primary infection, rarely leads to lesions at birth, where the fetus in the case of a formally seropositive mother for CMV is considered "not to be at risk" of pathological lesions related to these infections. As a result, while the findings – prior to pregnancy to toxoplasmosis gondii and rubella virus specific antibodies – appear to suggest that fetal infections are no longer possible (or highly improbable). The findings of maternal CMV antibodies prior to pregnancy do not exclude the likelihood of reactivation with possible fetal infection, which is detectable only through isolation of the virus from the neonatal urine.

In fact, as far as CMV is concerned, prenatal diagnoses are considerably more complex than those seen in rubella and toxoplasmosis. In the case of the latter infection, the finding of specific IgM in the mother during pregnancy may safely be taken as evidence of primary infection.

In such cases, the serological investigation may be extended to include fetal blood sampling by means of fetoscopy or free needle aspiration (cordocentesis). Determination of specific IgM in fetal serum is of critical importance not only on account of the fact that maternal IgM do not cross the placenta but also because the low titre may be there for several months (up to 25 weeks) after the onset of infection [5-13]. Our present report is based on our experience of prenatal diagnoses of infectious disease at the Prenatal Diagnosis and Therapy centre, College of Medicine University of Lagos.

Material and Method

Between December 1994 and December 2004 a total of 236 pregnant women were referred to our centre for confirmation by serological diagnoses of a possible rubella virus, cytomegalovirus, and herpes simplex infections in pregnancy (rubella, CMV, toxoplasmosis, varicella, and herpes simplex type II, parvovirus and syphilis).

Serological diagnosis in all women was carried out using the immunoenzymatic method ELISA for IgG and IgM antibodies and immunofluorescence in those with positive results. Serum titering for specific IgM was always preceeded by serum absorption with IgG carrying latex particles to eliminate the rheumatic factor.

In patients in which the findings of specific IgM indicated the possibility of seroconversion occurring in pregnancy, serological investigations were extended to the fetus with fetal blood sampling, amniotic fluid sampling and sometimes fetal urine. Prior to antibody titering in fetal samples, fetal IgM was separated on columns to eliminate any possible interference in the diagnostic assay of the IgG derived mostly from the mother.

Results

Out of the 236 patients investigated the specific IgM test suggested seroconversion in 162 cases. Seventy of these patients requested prenatal diagnoses by means of fetal blood samples or amniocentesis or both.

There were 21 positive fetal blood IgM samples out of 48 for rubella, 38 positive fetal blood IgM out of 64 for CMV, one positive fetal blood IgM out of six for herpes

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simplex type II, three positive fetal blood IgM out of six for toxoplasmosis, four positive fetal blood IgM out of 12 for varicella, and two positive fetal blood IgM out of 21 for syphilis and one fetal blood IgM out of five for parvovirus. Amniotic fluid IgM was also positive for all those with fetal blood IgM positivity samples (Table 1).

Table 1. — *Prenatal diagnosis of rubella, cytomegalovirus (CMV), toxoplasmosis, varicella, herpes simplex II, syphilis and parvovirus (n = 236).*

	Rubella	CMV	Toxoplasmosis	Varicella	Herpes simplex II	Syphilis	Parvovirus
Total female patients	63	91	18	29	8	21	6
Maternal IgM (+)	48	64	6	12	6	21	5
Fetal IgM (+)	21	38	3	4	1	2	1

Discussion

Our results of the 236 pregnant women investigated to rule out involvement of rubella virus, CMV, varicella virus, herpes simplex type II, toxoplasma gondii, syphilis and parvovirus infections revealed that only 68.64% had a recently acquired maternal infections thus confirming the reports of others [14, 15]. In this report, in cases where infections were demonstrated in pregnant women, further investigations of fetal blood samples and amniotic fluid samples were carried out. It was possible to demonstrate fetal infection in 70 (29.7%) cases and thus allowing continuation of pregnancy in the rest which led to normal condition of the neonates at delivery thus supporting our preliminary results and those of other authors [8, 10-13, 18-21].

Our results show that there is a high occurrence of congenital rubella, CMV, toxoplasmosis, Varicella zoster, Herpes simplex, syphilis and parvovirus in our environment, and antenatal screening programme should be introduced and encouraged.

Our results are encouraging but more work is required to optimize our diagnostic approach, i.e. monoclonal antibodies and DNA/RNA with direct identification by means of cordocentesis, amniocentesis and chorionic villi sampling to rule out possible placentitis involving the pathogens [7, 8].

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