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Amniocentesis for the detection of congenital toxoplasmosis: results from the nationwide Austrian prenatal screening program

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Abstract

Prenatal diagnosis of congenital toxoplasmosis (CT) influences therapeutical management in pregnant women and their offspring. In Austria, a nationwide serological healthcare program to identify potential maternal toxoplasma infections during pregnancy exists. We assessed the clinical use of amniocentesis for toxoplasma-specific polymerase chain reaction (PCR) on amniotic fluid to detect CT. Data on serology, amniocentesis, PCR, complications, treatment, and paediatric clinical outcome were collected retrospectively among the birth cohort 1992–2008. There were 1386 women with amniocentesis, but only in 707 cases (51%) was acute maternal infection confirmed serologically. A high proportion (49%) of amniocenteses with negative PCR results in women with chronic infection or seronegativity were performed without clinical justification for the women or their foetuses. The positive and negative predictive values of PCR were 94.4% and 99.3%, respectively. Thirty-nine foetuses with CT, including four deaths, were reported. The five PCR-negative but infected infants were identified by the serological and clinical follow-up program. Thirty percent of amniocenteses were performed in the third trimester, and gestational age or treatment did not influence PCR sensitivity. Amniocentesis is indicated in women with acute maternal infection, and facilitated targeted therapies in pregnant women and their offspring. In women with late toxoplasma infection, negative amniotic fluid PCR made treatment of infants unnecessary. Serological and clinical follow-up of infants is important to confirm the infection status of the infant. Recommendations, based on our 17-year experience, to improve the current diagnostic strategies and to reduce unnecessary amniocentesis, are given.

Keywords: Amniocentesis, amniotic fluid PCR, congenital toxoplasmosis, polymerase chain reaction, *Toxoplasma gondii*
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Introduction

The clinical severity of congenital toxoplasmosis (CT) varies from no clinical signs to major manifestations with severe central nervous system impairment and death [1]. Even though the symptomatic form of CT is rare, it remains a worldwide health problem.

In Austria, a mandatory screening for toxoplasma-specific antibodies exists [2]. In this healthcare program, seronegative women are retested serologically until birth. Acute maternal infection during pregnancy (AI) might result in materno-foetal transmission, thus, treatment according to the Austrian guidelines is recommended. Several studies have shown the positive effect of treatment on transmission as well as clinical sequelae of CT [3–15].

PCR of amniotic fluid is the standard test for diagnosing CT with high sensitivity [16–19], and can be performed early in pregnancy (starting from week 15 of gestational age) [20]. The importance of PCR has already been described in several studies [17–19,21–27] and is essential for further treatment

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management of both mother and infant. In Austria, amniocentesis is standard practice since 1992, and is an additional investigation during pregnancy.

In this study we assessed the clinical practices of amniocentesis in the context of a mandatory prevention program (Austrian Toxoplasmosis Screening Program). Hereby, a standard program covers serological testing during pregnancy and treatment of women and infected infants. Furthermore, medical care of infants is part of a standard early-childhood program covered by national healthcare providers. Additionally, we collected data on serological testing during pregnancy and treatment of women and infected infants, as well as information on amniocentesis, complications, and clinical follow-up of infants in a database (Austrian Toxoplasmosis Register) over a 17-year observational period.

Materials and methods

This retrospective study included 1386 pregnant women (16 twin pregnancies) with amniocentesis for PCR and their foetuses (n = 1402), 1992–2008 (Fig. 1). In 1362 of these cases, immunoglobulins (Igs) were detected, including women with AI and chronic infection. Six women had known immunodeficiencies or inborn errors of metabolisms, and thus were excluded. In another 24 women, amniocenteses were performed due to pathologies in prenatal ultrasound, and these women were seronegative. Finally, 707 of 1386 (51%) immunocompetent women with AI and 39 infants with CT were included for final statistical analysis.

Austrian prenatal screening program

The mandatory serological screening was standard procedure for all pregnant women and covered by the national healthcare providers in Austria [2]. Routine screening was mandated by the obstetrician within the first visit and performed at clinical laboratories by different automated analysers (IgG, IgM, IgG avidity test). In women with chronic infection, only one test, and in seronegative women, bi-monthly testing, was recommended. In case of undetermined serology, unclear infection status, or AI, confirmatory testing at the Reference Laboratory using in-house Sabin-Feldman dye test and immunosorbent agglutination assay (bioMérieux, Marcy L'Etoile, France) were performed. Moreover, our laboratory offered counselling for physicians and parents as well as an outpatient clinic for follow-up of women and infants.

Serological test results were interpreted retrospectively at the Reference Laboratory in accordance with the criteria of the European Toxoplasmosis Group [28]. The maternal infection status was defined as follows:

1. Suspected acute maternal infection: The first screening test was IgG/IgM positive; serological re-testing was requested to assign infection status.
2. AI: Seroconversions, rising titre, or primary high titre (IgG/IgM positive, IgG avidity).
3. Chronic infection: Stable high IgG and IgM negative, high IgG at beginning of pregnancy.

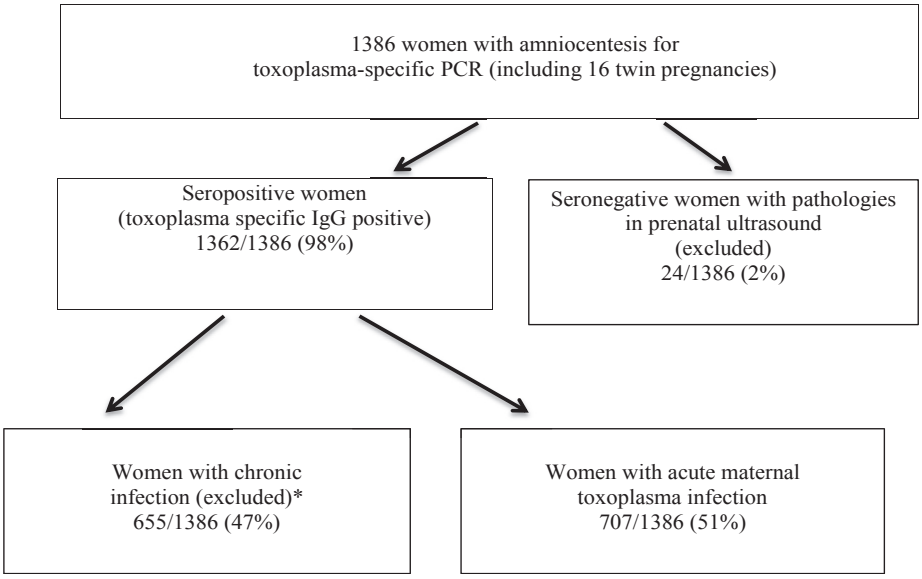

FIG. 1. Flow chart of women enrolled in this study (n = 1386). Amniocenteses were performed on *Toxoplasma gondii* – seropositive pregnant women and in women with pathologies in prenatal ultrasound. The serologic diagnosis was made in accordance with criteria of the European Toxoplasmosis Group. PCR, polymerase chain reaction of amniotic fluid. *Including six women with immunodeficiency or inborn errors of metabolism.

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