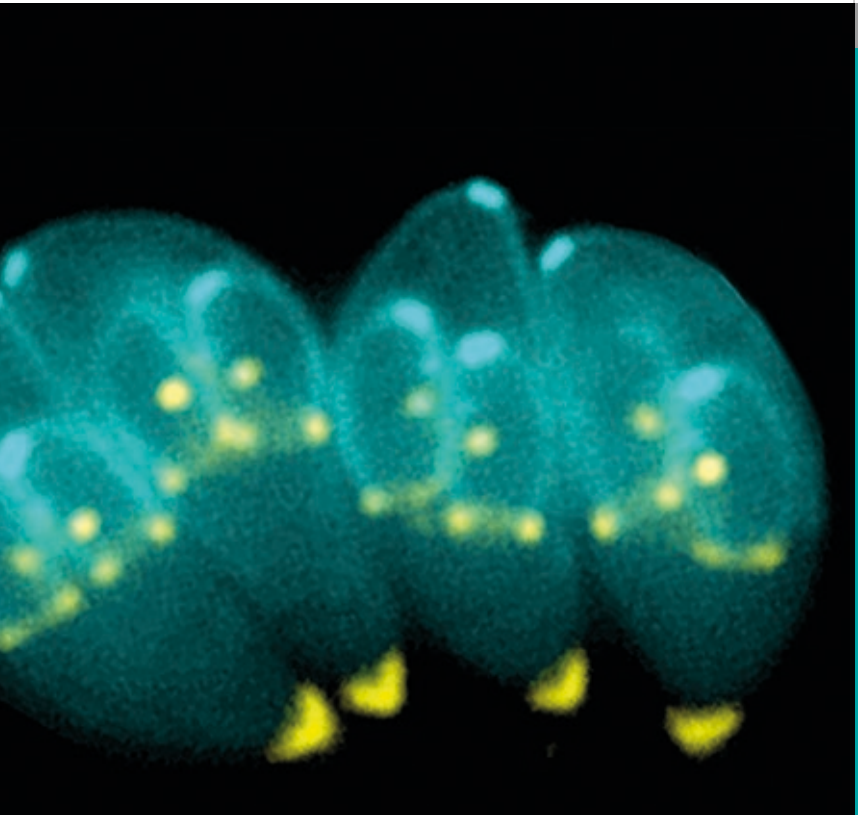
SWISS SOCIETY OF NEONATOLOGY

A rare presentation of a well-known congenital infection



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Source: http://commons.wikimedia.org/wiki/File:Toxoplasma_gondii.jpg

The pregnancy of this 25-year-old G2/P2 had been uneventful until 26 0/7 weeks of gestation when the mother was admitted to an outside hospital because of vaginal bleeding due to placenta praevia. Tocolysis with nifedipin was administered and fetal lung maturation was induced.

At 28 1/7 weeks of gestation, the mother had been transferred to the university hospital for further investigations of ventriculomegaly. Apart from ventriculomegaly (Fig. 1), ultrasound examinations revealed dilatation of the third ventricle, periventricular echodensities, a hyperechogenic matrix zone (Fig. 2), and an elevated peak systolic velocity in the middle cerebral artery (Fig. 3). A fetal MR confirmed the sonographic findings and revealed aqueduct obstruction, hemorrhages in the basal ganglia and thalamus, as well as multiple subcortical cysts (Fig. 4). No calcifications were seen.

At this point, the etiology of these findings remained unclear and further tests were initiated in an attempt to explain the various findings on MRI: tests for maternal anti-platelet antibodies (to explain the hemorrhages) and fetal hemoglobin in maternal blood (to explain the elevated peak systolic velocity in the MAC)) were negative. TORCH serology was performed and was positive for toxoplasmosis IgG and IgM. IgG avidity of 0.249 indicated that the infection must have occurred at least four months ago. The exact point

of infection could not be determined; however, toxoplasmosis serology had been negative during the first pregnancy in 2011. Although the MRI findings could not to be fully explained by the diagnosis, congenital toxoplasmosis was highly suspected. Ventriculomegaly as well as the periventricular echodensities with cyst formation were progressive in the following weeks of the pregnancy; the Doppler abnormalities persisted and mild ascites was diagnosed at 30 3/7 weeks of gestation. One week later, at 31 4/7 weeks of gestation, a Cesarean section was performed because of progressive vaginal bleeding from a placenta praevia.

The Apgar scores were 1, 3, 3 at 1, 5 and 10 minutes, respectively. Arterial cord-pH was 7.20. Because of bradycardia and apnea bag and mask ventilation was started with a maximal FiO2 of 1.0. Intubation was difficult because of hydrops and succeeded not until the age of 20 minutes. Afterwards the FiO2 could be reduced to 0.3 and the baby was transported to the neonatal intensive care unit.

The baby had a birth weight of 2130g (P75-90), a length of 41cm (P25-50) and a head circumference of 36.5cm (P>97). Physical examination on admission showed a severely ill child without any spontaneous movements, generalized edema of the skin most distinct on head and trunk, bilateral pulmonary rales, a 2/6 systolic heart murmur with normal blood pressu-

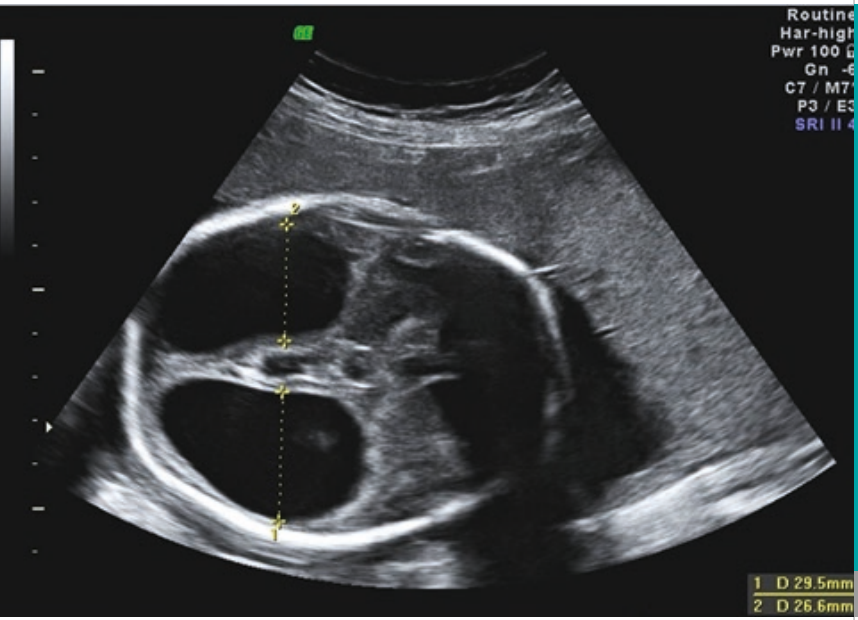


Fig. 1

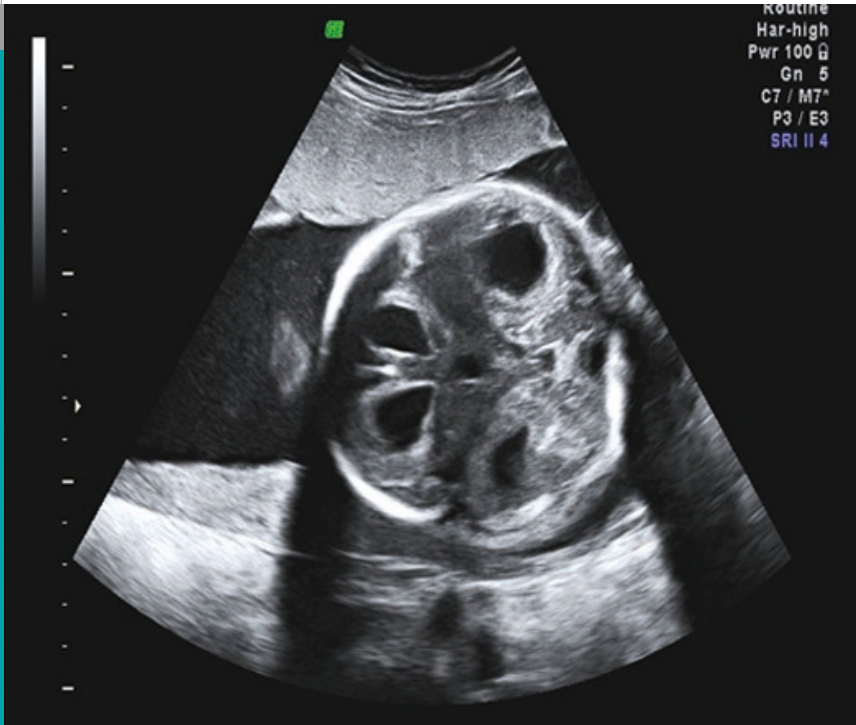
Fetal ultrasound examination at 28 1/7 weeks of gestation: severe ventriculomegaly.

re and palpable pulses, hepatosplenomegaly, bilateral cryptorchidism and disseminated petechiae.

Laboratory investigations revealed mixed acidosis (pH 7.04, a pCO2 9.4 kPa, and a BE -11.7 mmol/l), anemia (hematocrit 23%) and erythroblastosis (82/100 WBC), a WBC of 18.8 G/l, thrombocytopenia (31 G/l) and pathological coagulation parameters (Quick 38%, INR 1.3, aPPT 74 s, TT 45 s, fibrinogen 1.2 g/l).

Fetal ultrasound examination at 28 1/7 weeks of gestation: dilatation of the third ventricle, periventricular echodensities and hyperechogenic matrix zone.

Fig. 2



A babygram showed bilateral pleural effusions and cardiomegaly (Fig. 5). Echocardiography revealed enlarged ventricles with normal contractility, signs of pulmonary hypertension, dilatation of the inferior vena cava, and no pericardial effusions. The prenatal imaging findings were confirmed by cerebral ultrasound: severe hydrocephalus with only a narrow rim of parenchyma with increased echogenicity and multiple cysts. No normal gyri and sulci could be demonstrated. The basal ganglia were small with increased echogenicity (Fig. 6).

In view of the critical clinical condition and extremely poor neurological prognosis, a decision was made to redirect care to comfort measures. After extubation, the infant died at the age of 5 hours.

The symptoms described above were suggestive of a prenatal infection. Based on maternal serology, congenital toxoplasmosis was most likely. This diagnosis was confirmed by histopathology of the placenta and detection of toxoplasmosis DNA in umbilical cord blood. At the request of the parents, no autopsy was performed.

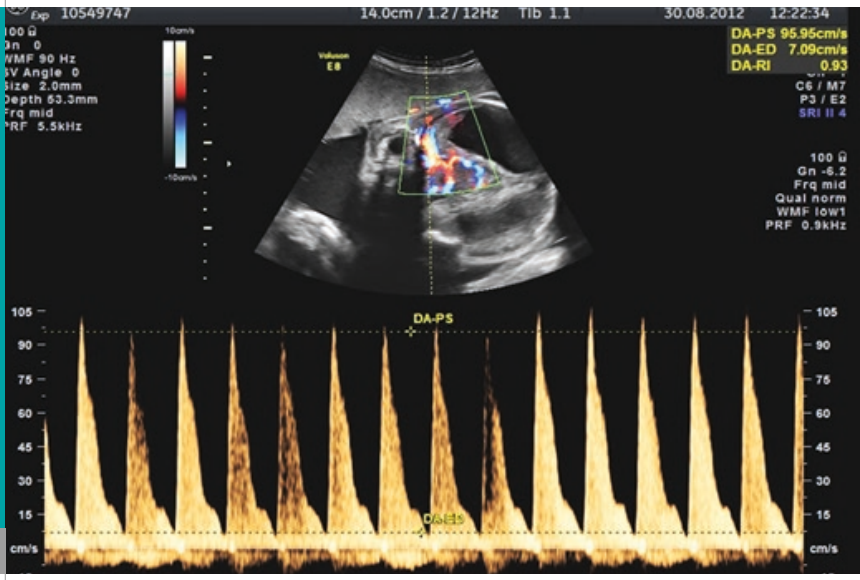


Fig. 3

Fetal color Doppler study: elevated peak systolic velocity in the middle cerebral artery.

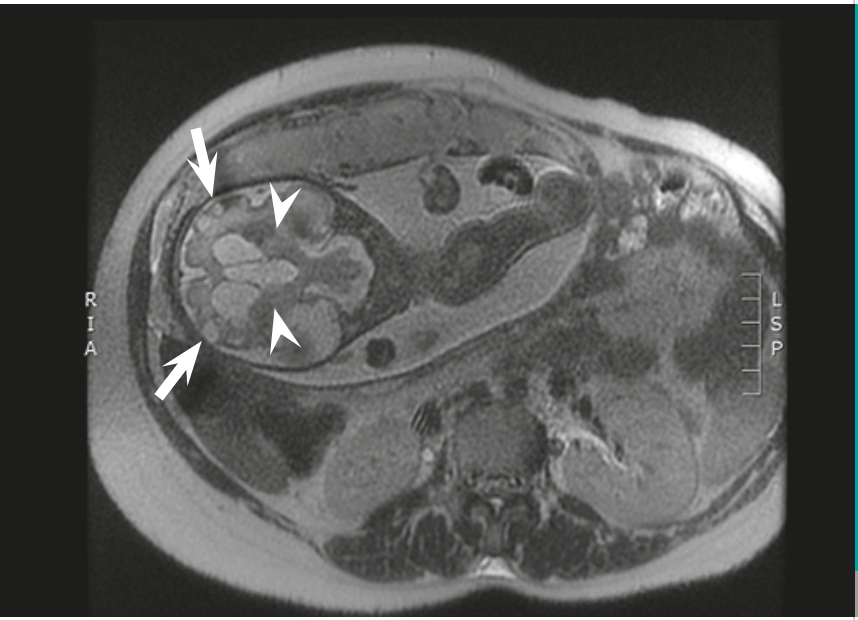


Fig. 4

Fetal MRI: hemorrhages in the basal ganglia (arrowheads) and thalamus and multiple subcortical cysts (arrows).

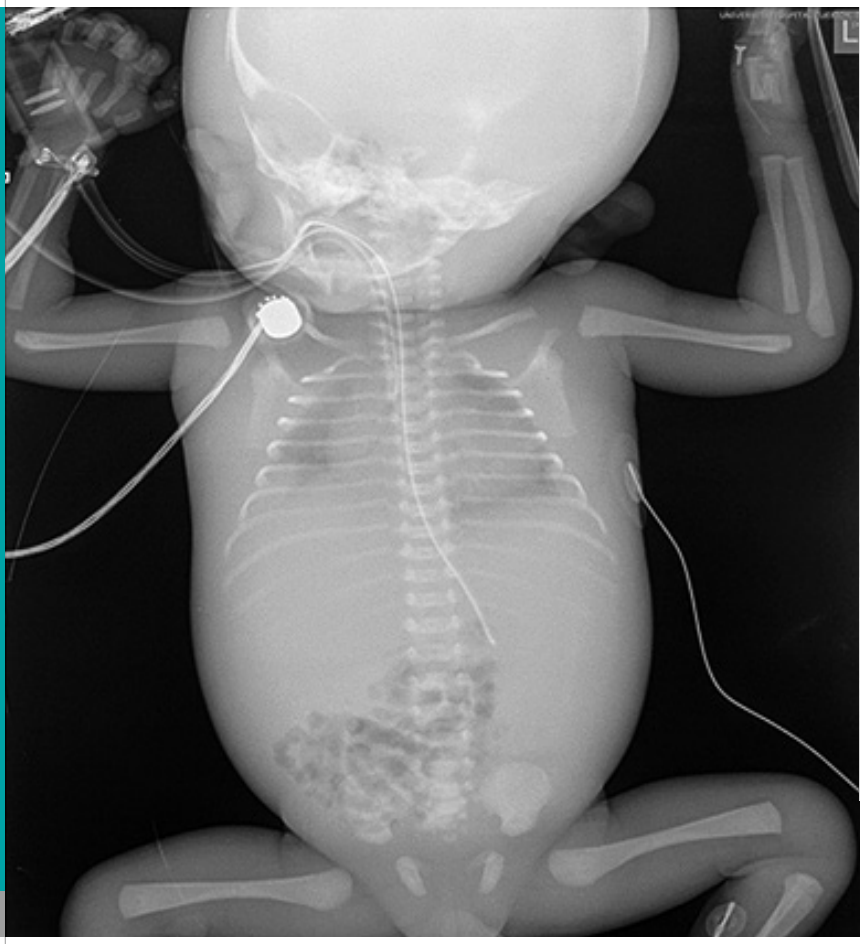


Fig. 3

Babygram: hydrops with bilateral pleural effusions and cardiomegaly.

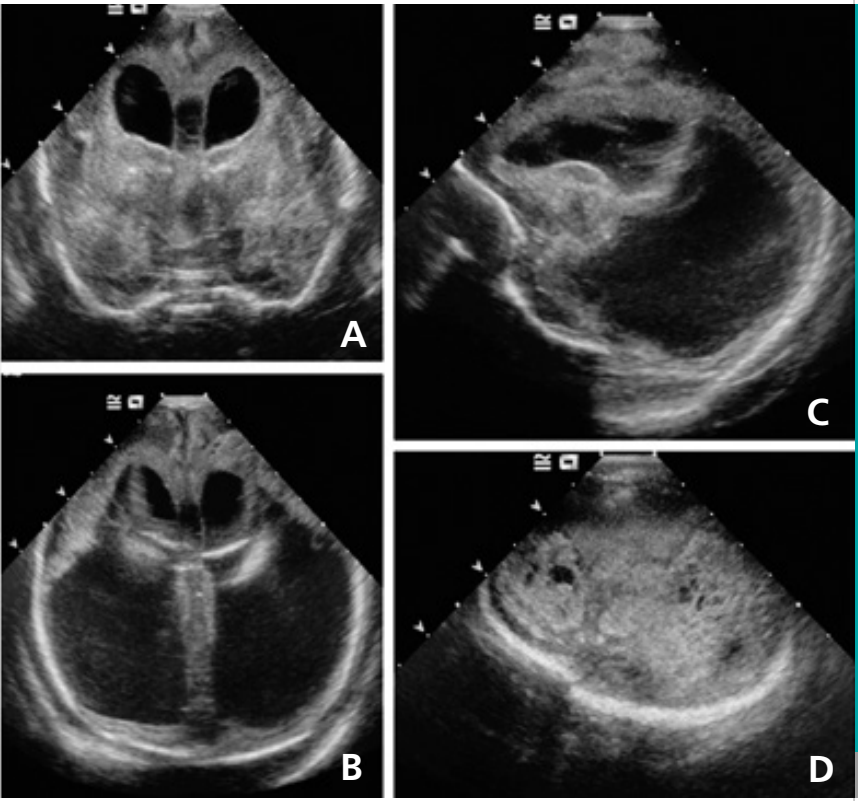


Fig. 6

Postnatal cerebral ultrasound examination: pronounced hydrocephalus on coronal (A, B) and sagittal views (C); increased periventricular echogenicity and cysts.

DISCUSSION

Toxoplasma gondii is a ubiquitous protozoan parasite. Infection can be acquired from contaminated soil or by consumption of undercooked meat or unpasteurized milk. Acute infection with T. gondii is usually asymptomatic in children and adults, but serious clinical disease can result from congenital infection (1). Clinical manifestations largely depend on when the infection is acquired in utero. Vertical transmission rate is lower in early pregnancy than in later pregnancy but results in more severe clinical disease (2). Clinical manifestation of congenital toxoplasmosis includes chorioretinitis, anemia, jaundice, petechiae due to thrombocytopenia, pneumonitis, hepatosplenomegaly, diarrhea and neurological manifestations such as microcephaly, intracranial calcifications, epilepsy, encephalitis and hydrocephalus, resulting in various degrees of psychomotor and/or mental retardation (1, 2).

Ventriculomegaly and multiple intracranial calcifications (periventricular regions, basal ganglia, and corticomedullary junction) are typical findings on cerebral ultrasound. Further characteristic signs, although less well known, include multiple echogenic nodular foci located in the brain parenchyma, periventricular or caudothalamic zones, diffuse periventricular echogenicity and periventricular cysts (3). In severe cases, cerebral toxoplasmosis may produce brain abscesses with cyst formation resembling posthemorrhagic insults (3). Cerebral ultrasound and MRI findings in our

patient are therefore consistent with congenital toxoplasmosis.

The prognosis of children with congenital toxoplasmosis, not surprisingly, correlates with the extent of brain involvement. Ventriculomegaly associated with multiple echodense nodules, as in our case, is characteristic of severe congenital toxoplasmosis and carries a poor prognosis (3). In contrast, children with normal ventricular size and only a few brain nodules can have normal neurological development.

Until 2009, screening for toxoplasmosis during pregnancy was performed in Switzerland, even though no official recommendation existed (4). In 2009, the Swiss Working Group on congenital Toxoplasmosis (SWGT) recommended the cessation of testing for T. gondii antibodies before and during pregnancy (5). The main arguments for this new strategy where the low incidence and morbidity of congenital toxoplasmosis in Switzerland (only 1 case of congenital toxoplasmosis per 2300 live births, and only 1 symptomatic infection per 14'000 live births) (5) and above all, the fact that there is no evidence at all that screening and therapy during pregnancy is effective. A broad review of all available data (EUROTOXO Study) could not provide any scientific proof that maternal treatment during pregnancy would translate into any beneficial effects for the fetus (6, 7). Instead, the SWGT emphasized the importance of primary prophylaxis, the only preventi-

on strategy which showed some effect in the EUROTOXO Study (6, 7).

In our case, maternal serologies indicated that the infection must have taken place in the first trimester of pregnancy with severe fetal consequences. At the time of diagnosis, extensive cerebral injury had already occurred. Based on the evidence from the literature, it is highly doubtful, if earlier diagnosis and therapy would have altered the fate of the child (3, 5-8). Since the mother had a migration background and did not speak any German or another European language, it is likely that she was not informed about risk factors and primary prevention of toxoplasmosis (9).

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