Congenital toxoplasmosis of the brain caused by infection in late pregnancy

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A fetus, on routine growth ultrasound scan, at 36 weeks, was found to have severely enlarged lateral ventricles and a dilated third ventricle, and normal growth (figure). The findings were confirmed by MRI (figure), which also showed signal abnormalities in the caudothalamic grooves, and extensive signals in the periventricular white matter indicating possible oedema, macrocephaly, and hepatosplenomegaly.

The mother, a 33-year-old primigravida, had conceived by in-vitro fertilisation; both parents were carriers for cystic fibrosis, and preimplantation genetic testing of the embryo was negative for aneuploidy and mutations in *CFTR*, the gene encoding the epithelial ion channel. No family history of birth defects, intellectual impairment, genetic disorders, or congenital anomalies was recorded. The previous second-trimester anatomy scan had shown typical growth and no fetal anomalies; and these new findings raised suspicion for a congenitally acquired infection.

Further discussion with the mother found that she had no known exposure to *Toxoplasma gondii* or anyone with toxoplasmosis, but she did report proximity to farm animals, feral cat exposure in the backyard of her home, and ingestion of cooked wild venison multiple times during the pregnancy.

Maternal TORCH (*T gondii*, cytomegalovirus, rubella virus, and herpes simplex virus) titres found elevated IgG and IgM titres for *T gondii* (normal range <7·2 IU/mL and less than arbitrary units per mL, respectively).

Given the late gestational age of the fetus, amniocentesis was deferred and, on discussion with the mother, it was decided to deliver the baby; an uncomplicated elective caesarean section delivered, at 38 weeks' gestational age, a 3410 g neonate (41st percentile for gestational age). Apgar scores were 8 and 9 (typical range: between 7 and 10). Maternal and fetal cord blood samples were collected and sent to a toxoplasmosis reference laboratory. Results confirmed maternal toxoplasmosis: *T gondii* IgG Sabin-Feldman dye test positive 1:8000 (normal <1:16), low IgG avidity testing, *T gondii* IgM ELISA positive 10·0 (normal <2·0), AC/HS 400/400, IgA ELISA positive, and IgE ELISA positive, indicating a diagnosis of an acute infection with *T gondii* acquired during the third trimester of pregnancy.

Examination of the placenta was notable for chronic villous inflammation with multiple cysts identified within the chorionic villi and membranes with positive immunohistochemical stains for *T gondii*.

At delivery, the newborn presented with diffuse hypotonia. Neonatal blood samples showed *T gondii* IgG Sabin-Feldman dye test 1:8000 positive, *T gondii* IgM ELISA immunosorbent agglutination assay positive, and *T gondii* IgA positive. *T gondii* PCR on whole blood and cerebrospinal fluid were also positive, confirming congenital toxoplasmosis.

Neonatal brain MRIs showed severe dilatation bilaterally of the lateral and third ventricules, cortical thinning, aqueductal stenosis, and bilateral periventricular and basal ganglia calcifications. Ocular involvement was also noted with bilateral peripheral retinal lesions and vitritis. The infant was admitted to our neonatal intensive care unit for 45 days receiving pyrimethamine and sulfadiazine with folinic acid, steroids, supportive measures, and feeding therapy. Due to symptomatic hydrocephalus, a ventriculoperitoneal shunt was put in place after 35 days of life.

At follow-up 6 months later, the infant was recovering well, still on antiparasitic therapy with the ventriculoperitoneal shunt in place; he was meeting his milestones appropriately, although there was a concern for congenital palsy of the right upper arm.

Toxoplasmosis is an endemic disease caused by *T gondii* and an estimated 170 infants are born with congenital toxoplasmosis yearly in the USA. The protozoan infection is transmitted to humans by ingesting undercooked meats containing the parasite's cysts, contaminated vegetables, or by contact with cat faeces. Primary maternal infection is asymptomatic in about two-thirds of patients. When symptomatic, it typically presents with mild malaise, headache, and lymphadenopathies. The overall risk for congenital toxoplasmosis following maternal primary infection ranges from 20% to 50% without treatment. The risk of transmission increases with gestational age and can be as high as 60% if acquired by greater than 36 weeks of gestation; the earlier the infection is, the more severe the impact on the fetus. Even though most infected infants do not have clinical signs of infection at birth, up to 90% will develop sequelae later in

Lancet 2024; 403: 1081–82

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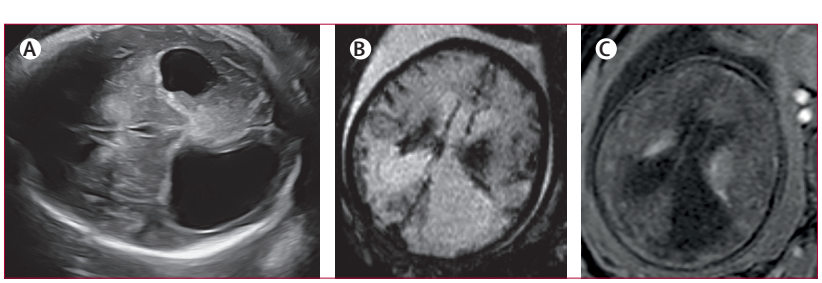

Figure: **In utero and congenital toxoplasmosis of the brain caused by infection in late pregnancy**
(A) Axial ultrasound of the fetal brain, at 36 weeks' gestation, shows asymmetric severe lateral ventriculomegaly and increased echogenicity of the deep grey matter nuclei—suggestive of parenchymal calcifications. Axial echoplanar (B) and T1 weighted (C) MRIs of the fetal brain, at 36 weeks' gestation, show ventriculomegaly and findings suggestive of parenchymal calcifications.

life. Diagnosis of maternal toxoplasmosis is usually confirmed serologically. Given the high false-positive rates of commercially available IgM-based testing kits, confirmatory testing at a reference laboratory should always be done.

Contributors
We were all involved in providing care for the patient and his mother, and in reviewing and editing the manuscript. SD wrote the original draft and administered the project. MSC conceptualised the project and supervised the case. Written consent for publication was obtained from the baby's mother.

Declaration of interests
We declare no competing interests.