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Case Report

Microcephaly Resulting From Congenital Toxoplasmosis: What the Radiologist can Expect to See? A Case Report ☆

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ABSTRACT

Microcephaly is defined as an occipitofrontal head circumference two standard deviations (2SD) below average for age and sex, with severe microcephaly below three standard deviations (3SD). Congenital toxoplasmosis is one of the congenital infections that can potentially lead to microcephaly. It reflects neurotropism for fetal central nervous system (CNS) cells from toxoplasma, causing massive destruction of neural tissue, resulting in serious neurological damage. We present a case of severe microcephaly observed at birth in a newborn from an unmonitored pregnancy with an unknown maternal serological profile. The mother, aged 25 years, had no prior medical history. Imaging investigations revealed significant neurological lesions, while serological tests confirmed congenital toxoplasmosis. This case report illustrates the radiological semiology of neurological involvement in congenital toxoplasmosis and serves as a reference for radiologists, highlighting the importance of recognizing the radiological features of congenital toxoplasmosis.

Introduction

In spite of the lack of a standardized definition, microcephaly is generally defined as an occipitofrontal circumference (OFC) of the head ≤2 standard deviations (SD) below the mean for age-matched (or gestational age, if identified prenatally) and sex-matched curves [1]. Severe microcephaly is considered when the OFC is ≤3 standard deviations below the average. Primary microcephaly is diagnosed shortly after delivery or in utero during ultrasound screening [2], whereas secondary microcephaly develops during infancy after normal head circumference at birth [3]. It's essential to note that microcephaly itself is not a diagnosis [4], but rather a clinical sign that can result from various etiologies, with congenital infections representing a major risk factor. Congenital toxoplasmosis is one of the congenital infections that can potentially lead to microcephaly. The pathogens responsible for these infec-

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tions are known as "TORCH" (Toxoplasma gondii, Rubella, Cytomegalovirus (CMV), Herpes simplex virus (HSV), and Other agents). Microcephaly is noted in 5%-15% of severely symptomatic congenitally infected infants. Congenital toxoplasmosis is subclinical in approximately 75% of infected infants [5]. Therefore, it may go unrecognized at birth and may be recognized between 12 and 24 months of age [6], but the process may be slower if ocular lesions are included. We present a clinical case illustrating the severe neurological consequences of congenital toxoplasmosis, highlighting the role of the radiologist in diagnostic assessment.

Case Report

We report the case of a newborn male infant, only a few minutes old, with a birth weight of 2400 g, gestational age of 39 weeks, from a nonconsanguineous couple, with an unmonitored pregnancy. The 25-year-old mother (Pregnancy 1, parity 1) had no significant medical history, drug or toxic intake, and an unknown serological profile during pregnancy. She reported no infectious symptoms throughout her pregnancy. After delivery, the routine pediatric examination identified a cranial perimeter of 25 cm (<3 SD), estimated size at 40 cm (<3 SD), and redundant scalp skin overlying (Fig. 1), with no other abnormalities observed.

A transfontanellar ultrasound scan was performed, showing a small portion of frontal brain parenchyma that was atrophic with ventriculomegaly (Fig. 2). Due to the overriding of the cranial bones, the anterior fontanel was squeezed and did not offer a good acoustic window. For better characterization, and due to difficult access to MRI, a nonenhanced cerebral CT scan was performed. It showed microcephaly, overriding of the cranial bones, and overlying redundant scalp skin, but also lissencephaly (the absence of gyri), cerebral atrophy with a reactive appearance of ventriculomegaly, and agenesis of the corpus callosum. Cerebral calcifications were found in the cortex, subcortical white matter, and basal ganglia. The posterior cerebral fossa was without anomalies, and there were no ophthalmologic abnormalities (Fig. 3).

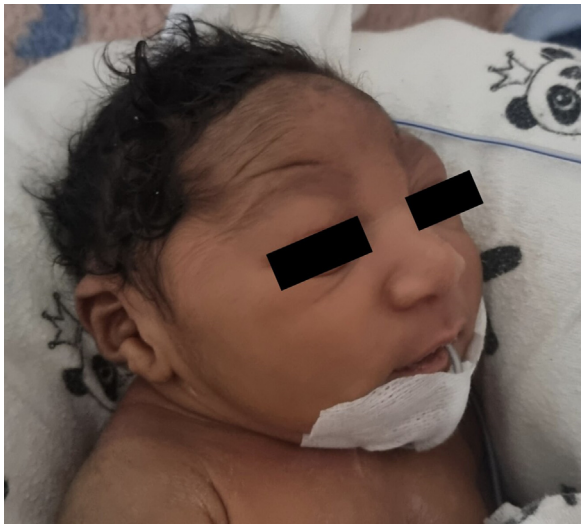

Fig. 1 – Photograph of the newborn displaying microcephaly. It illustrates the reduced cranial volume, measured at 25 cm (<3 SD), with overlying redundant scalp skin.

Serological tests were conducted on peripheral blood samples of both the mother and the newborn to screen for various pathogens: Toxoplasma gondii, Rubella, Cytomegalovirus (CMV), Herpes simplex virus (HSV), and Other agents. All results returned negative except for toxoplasmosis. Specifically, the newborn exhibited the presence of specific IgM antibodies in 2 separate samples taken 2 weeks apart. The initial test showed IgM levels at 8.1 index, while the subsequent sample indicated a value of 6.3 index, indicative of an active infection. The mother showed positive specific IgG without detectable IgM, signifying maternal immunity acquired from a prior infection that occurred early during pregnancy or just before. Additionally, specific IgG antibodies were detected in the newborn on 2 samples, showing an increase in their levels on the second sample, with values of 81 IU/ml and 98 IU/ml, respectively. This suggests the transfer of antibodies across the placenta from the mother's bloodstream. The microparticle chemiluminescent immunoassay (CMIA) technique, validated for both adults and newborns, on the Abbott Alinity automated system, was utilized for the analysis of all samples.

A diagnosis of congenital toxoplasmosis was established, and to mitigate the progression of the infection, the newborn was initiated on antimicrobial treatment consisting of pyrimethamine, sulfadiazine, and leucovorin. This treatment was administered continuously for one year with clinical, ophthalmological, and serological monitoring.

Discussion

Toxoplasmosis is 1 of the most prevalent parasitic infections worldwide [7]. The causative agent, Toxoplasma gondii, can be transmitted to humans either orally or congenitally [5]. Oral transmission typically occurs through exposure to cat feces or by eating undercooked meat [6], as well as through ingestion of contaminated soil, food, or water containing mature oocysts.

Congenital infection generally results from a primary maternal T. gondii infection acquired during or just before pregnancy, leading to parasitemia that subsequently infects the placenta and the fetus. The risk of fetal lesions is inversely related to the gestational age at which the maternal infection occurs [5].

The incidence of congenital toxoplasmosis is influenced by the seroprevalence in the population, with higher risks observed in seronegative women. Although most infections in pregnant women are asymptomatic [8], they can lead to severe neurological and ophthalmologic complications with significant sequelae. Epidemiological studies on microcephaly resulting from congenital toxoplasmosis are limited [9,10]. However, infants with microcephaly have a high

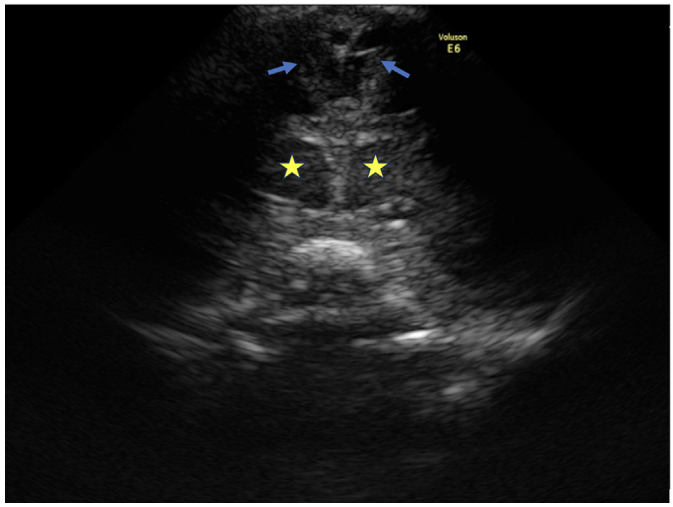

Fig. 2 – Transfontanellar ultrasound scan with coronal section, revealing brain atrophy in frontal portion (Blue arrows) with ventriculomegaly (Yellow stars). (The challenging acoustic window due to the overriding of cranial bones is evident, emphasizing the need for complementary imaging techniques for accurate characterization.).

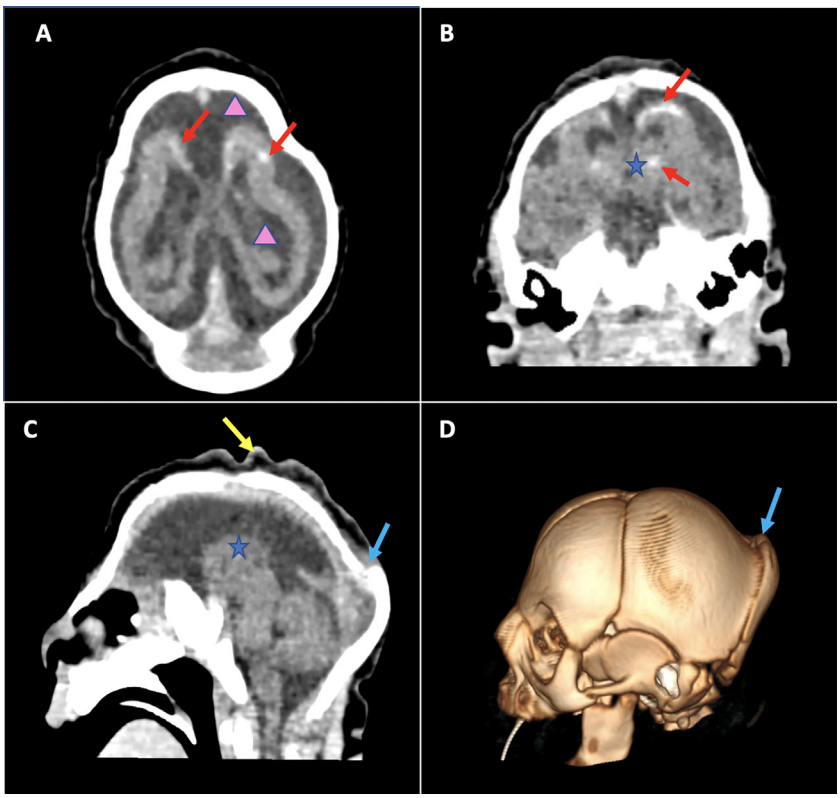

Fig. 3 – Brain- nonenhanced CT scan with axial (A), coronal (B), sagittal (C), and 3D reformatted images (D) showing a reduction in cranial volume (Microcephaly) related to Cerebral hemisphere atrophy with the absence of gyri (lissencephaly) contrasting with normal appearance of posterior cerebral fossa. Bilateral brain calcifications nodular in the basal ganglia, nodular and both linear in subcortical white matter (Red arrows, Fig. 3.A and B). Ventriculomegaly with increased fluid surrounding the brain (Pink arrowheads, Fig. 1.A), associated to the absence visualization of the corpus callosum, related to a c corpus callosum aplasia (Blue star, Fig. 3.B and C). Overriding of the cranial bones more pronounced at the parieto-occipital level (Blue arrows, Fig. 3.C and D). The whole is covered by overlying redundant scalp skin (Yellow arrow, Fig. 3.C).

morbidity due to associated neurological sequelae and severe extraneurological damage, potentially increasing mortality [11].

Congenital toxoplasmosis frequently presents with microcephaly along with other clinical manifestations typical of vertically transmitted "TORCH" infections [12]. Microcephaly associated with congenital infections reflects the neurotropism of Toxoplasma gondii for fetal CNS cells [13], causing extensive destruction of neural tissue during the first and early second trimesters of pregnancy [14,15].

The destruction caused by the pathogen and the associated inflammatory responses leads to neuronal loss, reducing brain tissue mass (volume) and consequently decreasing head size. This reduction in brain mass contributes to an increase in intracranial fluid, which may manifest as ventriculomegaly, hydrocephalus, hydranencephaly, or dilation of the subarachnoid spaces. Additionally, TORCH infections can lead to hydrocephalus due to obstruction of the aqueduct of Sylvius or the foramen of Monro [16].

Tissue necrosis and infarction contribute to the development of cerebral calcifications. These lesions can be focal or more extensive, leading to cortical thinning or the development of hypoplastic or aplastic regions within the brain, such as the cerebellum and corpus callosum [6]. Infections early in gestation can result in severe, disseminated fetal infection characterized by cerebral calcifications, abscesses, hydrocephalus, microcephalus, and ascites, potentially leading to in utero death. When fetal infection occurs during the third trimester, clinical manifestations may be absent at birth, with diagnosis made antenatally or postnatally.

Given the often asymptomatic nature of Toxoplasma infection, prenatal screening with repeated serological testing is performed in several regions and countries for non-immune pregnant women to identify maternal seroconversions [17]. The biological diagnosis of fetal infection typically involves PCR assays on amniotic fluid to detect T. gondii DNA [17].

Antenatal ultrasound may not detect fetal abnormalities in approximately two-thirds of cases [17]. Cerebral calcifications are the most frequent and distinctive lesions associated with congenital toxoplasmosis, often observed during the third trimester, though they may appear earlier. Symmetrical cerebral ventricular dilatation generally indicates an unfavorable prognosis. While microcephaly is less commonly detected, it can be identified earlier in some cases.

Intrauterine growth retardation (IUGR) associated with reduced intrauterine fetal movement has also been described [6]. Other nonspecific signs, such as hepatomegaly, ascites, pericardial effusion, hyperechogenic fetal bowel, and increased placental thickness, can also be present [17]. Clinical examination is usually unremarkable but may reveal nonspecific signs of evolving conditions, such as hepatomegaly, splenomegaly, jaundice, thrombocytopenic purpura, or anemia [17]. Microcephaly may be evident at birth, as in our patient, but it more commonly develops postnatally [18]. It is characterized by a reduction in cranial volume, with a superiorly flattened cranium and overlying redundant, rugose scalp skin. Imaging modalities such as transfontanellar ultrasound or sectional imaging (CT and MRI) are essential in diagnosing neurological damage. Transfontanellar ultrasound can reveal nodular or curvilinear calcifications, ventriculomegaly, or hydrocephalus. However, it may be limited by an insufficient acoustic window due to overlapping cranial bones, as seen in our patient's case. CT scans, and ideally MRI, provide more detailed lesion mapping, including findings such as microcephaly with overriding cranial bones and overlying redundant scalp skin [6], corpus callosum and cerebellar vermis aplasia. These radiological signs, observed in our clinical case, underscore the severity of neurological involvement in the patient. Schizencephaly (deep cortical clefts or grooves) was reported in a few cases in the literature. Other findings include a reduced number of thick, flat gyri (pachygyria) or complete absence of gyri (lissencephaly). Ventriculomegaly, hydrocephalus, hydranencephaly (partial or complete absence of cerebral hemispheres), and increased fluid surrounding the brain are also observed. Neuron-shaped calcifications in congenitally infected patients are typically found in the cortex and subcortical white matter [19,20], with dissemination to periventricular areas or confinement to the basal ganglia [21]. In our case, calcifications were noted in both the cortex and basal ganglia.

Ophthalmological anomalies, including optic nerve atrophy and microphthalmia, may also be present [22]. Indirect ophthalmoscopy is ideally used to detect retinochoroiditis [17]. Positive biological diagnosis is based on the detection of specific IgM and/or IgA in peripheral blood or cord blood, as IgG is the only immunoglobulin that crosses the placenta [17]. Maternal-infant immunological profiles can be compared to identify IgG, IgM, and IgA synthesized by the neonate. Proven congenital infection (diagnosed antenatally, at birth, or postnatally) necessitates prenatal and/or postnatal treatment to mitigate the risk and severity of long-term sequelae.

Postnatal treatment typically involves a combination of pyrimethamine and sulfadiazine or sulfadoxine, with variable efficacy reported. Spiramycin or a combination of pyrimethamine and sulfonamide is administered during pregnancy to prevent mother-to-child transmission [17].

Conclusion

Despite the absence of specific radiological signs, imaging remains an indispensable tool in the diagnosis of congenital toxoplasmosis. The radiologist can anticipate and identify several characteristic radiological features indicative of neurological involvement. Recognizing these findings is crucial for the prompt diagnosis and appropriate management of congenital toxoplasmosis.

Ethical Approval and Informed Consent

Ethics approval does not need to be obtained: This is a case report, based on the editor Guidelines-Ethics Approval and Informed Consent Statements: Ethics committee/IRB approval is often not required.

Patient consent

Written informed consent was obtained from the legal authorized representative (LAR) of the patient for the publication of this case report.

Author's Contribution

All authors contributed to this work. All authors have read and approved the final version of the manuscript.

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