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MINISYMPOSIUM: FETAL/NEONATAL IMAGING

Imaging of congenital central nervous system infections

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Abstract
Congenital central nervous system (CNS) infections are a cause of significant morbidity and mortality. The recent Zika virus outbreak raised awareness of congenital CNS infections. Imaging can be effective in diagnosing the presence and severity of infection. In this paper we review the clinical presentations and imaging characteristics of several common and less common congenital CNS infections.

Keywords Brain · Central nervous system · Computed tomography · Congenital · Fetus · Infant · Infection · Magnetic resonance imaging · Virus

Introduction

Central nervous system (CNS) infections acquired in utero are a significant cause of morbidity and mortality. The TORCH acronym denotes a group of common perinatal infections with similar presentations — rash and ocular findings — that includes toxoplasmosis, other (syphilis), rubella, cytomegalovirus and herpes simplex virus. However, other well-described perinatal infections exist, expanding the "other" category to include enteroviruses, Varicella-Zoster virus and parvovirus B19. More recently, Zika virus, an arthropod-borne Flavivirus, has received much attention because of the outbreak in the Americas, the Caribbean, and the Pacific.

Tissue damage by CNS infections is related both to the primary insult caused by the pathogen-specific endotoxins and the host's inflammatory response. The risk of damage differs significantly from those infections acquired in utero to those acquired in childhood and adulthood. The developing brain is particularly sensitive to neurotropic organisms. Infections acquired in early pregnancy, particularly the first and early second trimesters, can interfere with normal brain development and result in migration abnormalities, cortical disorganization and altered white matter myelination.

Different pathogens have a predilection for specific anatomical regions based on the method by which the organism gains access to the CNS and causes tissue damage. To that end, imaging might be effective in not only diagnosing the presence of CNS infection but also in identifying the specific infectious agent. Here we review the clinical and imaging attributes of several common and less common fetal CNS infections.

Cytomegalovirus

Clinical findings

Cytomegalovirus (CMV) is the most common intrauterine infection in the United States, with a prevalence of 0.48–1.3%. Transmission of the virus to the fetus occurs across the placenta. Risk of fetal infection is higher in women who initially acquire the virus during pregnancy (primary) than in those who acquire it prior to pregnancy (nonprimary or reactivation). That risk increases with advancing gestational age [1]. Approximately 10% of infected fetuses in the U.S., 3,000 to 4,000 births per year, are symptomatic at birth, and this is termed congenital

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CMV disease. Most infected neonates, approximately 35,000 births per year, are asymptomatic [2]. Symptomatic infants have a high risk of epilepsy, neurodevelopmental delay, cerebral palsy, vision loss and sensorineural hearing loss [3]. Among those who are asymptomatic, up to 25% still develop sequelae by age 2, such as sensorineural hearing loss.

Prenatal diagnosis is possible by amniocentesis performed after 6 weeks of maternal infection and after 21 weeks of gestation. Postnatally the diagnosis is ideally made prior to 3 weeks of age by detecting CMV in the urine or saliva. After 3 weeks of age, detection of CMV could indicate either a congenital or a postnatal CMV infection, making an accurate diagnosis more challenging. Early recognition is important because treatment with ganciclovir in the first 30 days after birth has been shown to improve long-term audiologic and neurodevelopmental outcomes [4, 5].

Imaging findings

CMV is a neurotropic virus that hematogenously seeds the choroid plexus and replicates in the ependyma, germinal matrix and capillary endothelium. Involvement of the germinal matrix can result in disruption of neuronal migration from the ventricular region, leading to malformations of development. Capillary involvement can lead to thrombosis and ultimately brain ischemia [6].

The brain imaging findings of congenital CMV are heterogeneous and include cerebral calcification (Fig. 1), ventriculomegaly, white matter disease, neuronal migrational disorders and microcephaly [7–10]. The presence and severity of these findings vary widely based on the timing of infection during pregnancy. In utero infection in early pregnancy generally results in more devastating brain damage and worse clinical outcomes than late-gestation infection.

Infection acquired in the first half of the second trimester can result in severe abnormalities such as agyria/pachygyria, cerebellar hypoplasia and ventriculomegaly [8, 9]. Less severe migrational abnormalities such as polymicrogyria (Fig. 2), and occasionally schizencephaly, can be seen with infection in the mid to late second trimester [8, 9, 11]. The ventriculomegaly is often less severe. Infections acquired in the third trimester do not result in migrational abnormalities. However, myelin delay or destruction might be seen. The white matter abnormality can be focal, patchy or confluent [12] (Fig. 2). A pattern of white matter signal abnormality in a predominantly posterior distribution, with sparing of the periventricular and subcortical white matter, is common in congenital CMV infection [9] (Fig. 3).

Cerebral calcifications are the most commonly reported neuroimaging finding of congenital CMV infection, seen in up to 70% of cases. Best identified on CT imaging, they are classically described as thick and chunky, occurring within the periventricular regions [13] (Fig. 1). In practice, they can be fine or punctate and occur throughout any region of the brain parenchyma, including the deep gray nuclei. While calcifications are quite common in congenital CMV, they are nonspecific and can be seen in a wide variety of pathologies including other infections, ischemia and metabolic disorders.

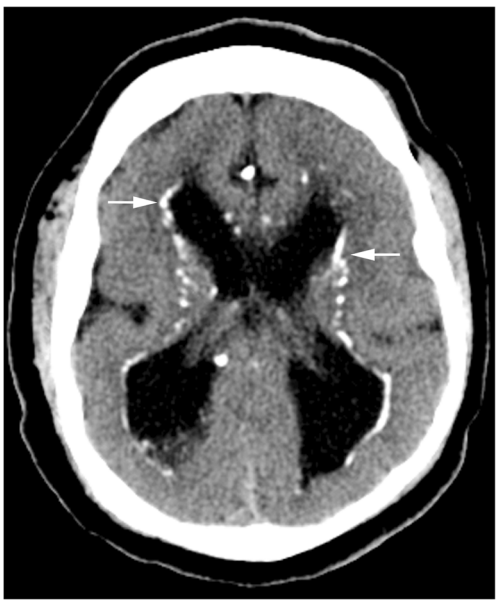

Fig. 1 Congenital cytomegalovirus infection in a 14-year-old girl. Axial non-contrast head CT image demonstrates chunky calcifications (*arrows*) throughout the periventricular regions

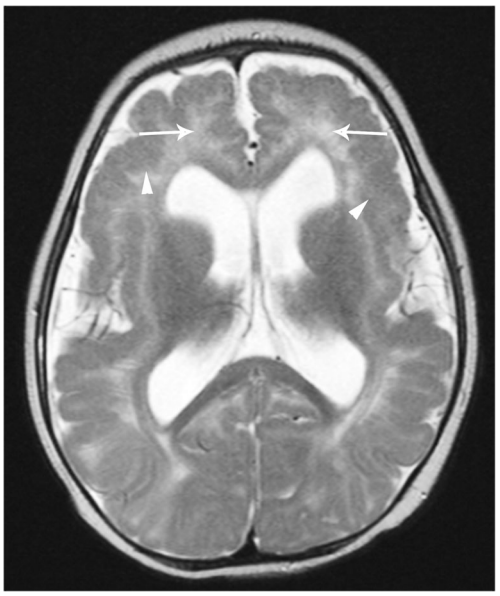

Fig. 2 Congenital cytomegalovirus infection transmitted during the late second trimester in a 6-month-old boy. Axial T2-weighted head MR image illustrates diffuse white matter signal abnormality (*arrows*) with extensive overlying polymicrogyria (*arrowheads*)

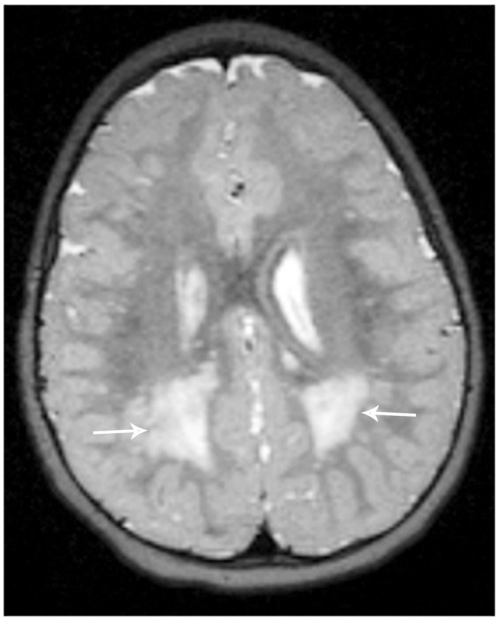

Fig. 3 Cytomegalovirus infection transmitted in the third trimester in a 1-month-old girl. Axial T2-weighted head MR image reveals posterior white matter signal abnormality (*arrows*) that spares the periventricular and subcortical regions

Periventricular cysts in congenital CMV have been described in a variety of locations [13]. They are most commonly identified in the anterior temporal lobes in association with white matter abnormalities [7, 9] (Fig. 4). Cysts can occur in and around the ventricular system secondary to necrosis or hemorrhage of the germinal matrix. In isolation, cerebral calcifications, migrational abnormalities, white matter disease and anterior temporal cysts are nonspecific, though in combination these findings raise concern for congenital CMV disease.

Toxoplasmosis

Clinical findings

Toxoplasma gondii is a protozoan parasite that infects animals and humans. Human infection is thought to be caused by the ingestion of undercooked or cured meats containing viable tissue cysts, though contaminated soil or water is a source of infection in humid climates. Infection is often asymptomatic in immunocompetent hosts. Disease can occur in the setting of immunosuppression or congenital infection [14]. The fetus, newborn and young infant with congenital infection are particularly at risk of complications, specifically neurologic and ophthalmologic [15]. The pathogenesis of congenital brain infection is poorly understood.

Congenital infection ranges from 1 in 10,000 U.S. births to 1 in 1,000 births in endemic areas [16, 17]. Transmission to the fetus is via the blood–placental barrier following primary maternal infection. The risk of fetal infection increases steeply with advancing gestational age, but the clinical severity decreases [18]. The classic triad of chorioretinitis, hydrocephalus and intracranial calcifications occurs in fewer than 10% of cases. Most infants (70–90%) have a subclinical infection with a normal routine neonatal examination. Detailed evaluation with ophthalmologic and cerebrospinal fluid (CSF) examination, however, does reveal abnormalities in about 40% [16]. The minority of infants with symptomatic congenital toxoplasmosis have a clinical profile similar to that of congenital CMV disease, including hepatosplenomegaly, jaundice, seizures, lymphadenopathy, abnormal CSF and anemia. Congenital toxoplasmosis distinguishes itself from CMV with its high rates of chorioretinitis (85%) and hydrocephalus.

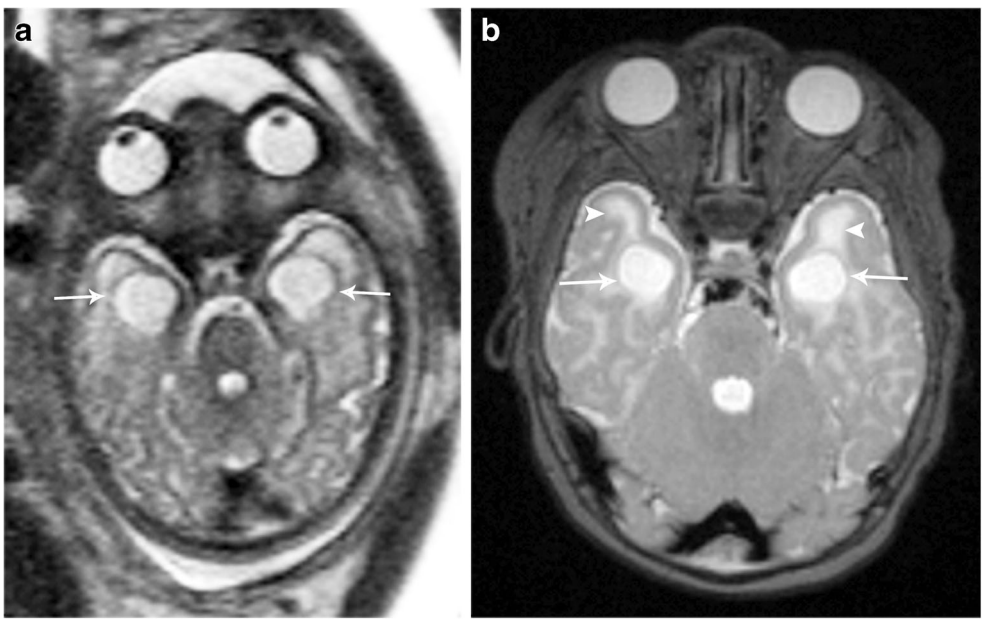

Fig. 4 Prenatal findings in a 34-week gestational age fetus suspicious for cytomegalovirus, and at 1-month postnatal follow-up. **a** Axial single-shot turbo spin echo fetal MR image demonstrates periventricular temporal lobe cysts (*arrows*). **b** Postnatal follow-up axial T2-weighted MR image at 1 month of age confirms presence of cysts (*arrows*) and illustrates adjacent white matter signal abnormality (*arrowheads*)

Without treatment, symptomatic patients have a mortality of 12%. There is a high rate of intellectual disability, seizures and spasticity/palsies in surviving infants [19, 20].

Diagnosis is usually established serologically and might require serial samples and comparison with maternal serology. Timely diagnosis facilitates early initiation of therapy and improves long-term prognosis [16].

Imaging findings

Brain imaging is characterized by calcifications, large ventricles, macrocephalus or microcephalus, hydrocephalus, parenchymal destruction/volume loss, and orbital abnormalities such as microphthalmia (Fig. 5). The severity is dependent upon time of in utero infection, ranging from mild atrophy and small periventricular calcifications to near-complete parenchymal destruction and large diffuse calcifications [21]. Areas of in utero necrosis are thought to result in dystrophic calcification because of the immature immune system's ability to perform phagocytosis. These calcifications are larger with earlier infections and sometimes resolve slowly with treatment [22].

Infection before 20 weeks results in hydrocephalus, volume loss/porencephaly, and large diffuse calcification (Fig. 5). Later infection during the first half of the second trimester leads to hydrocephalus and less diffuse calcification. Hydrocephalus is rarely found with infections after the second half of the second trimester, and smaller calcifications might be scattered in a periventricular and parenchymal distribution [21–23].

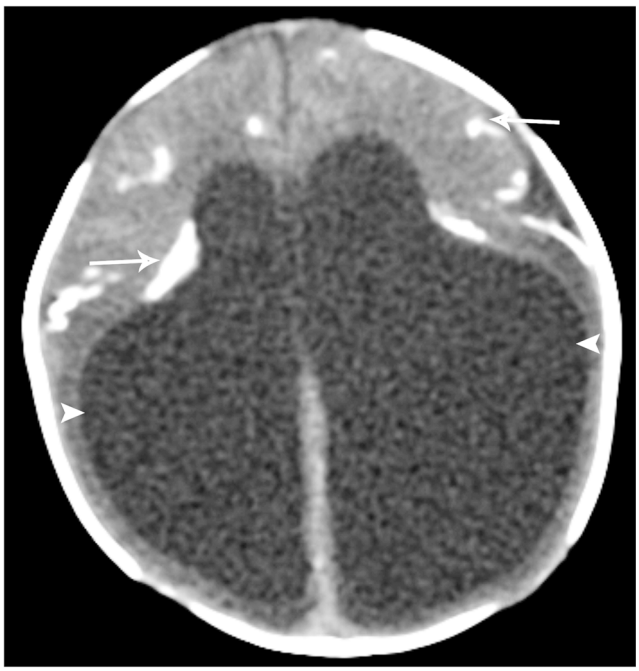

Fig. 5 Congenital toxoplasmosis infection acquired early in the second trimester in a 1-day-old girl. Axial non-contrast head CT image shows coarse calcifications (*arrows*) throughout the periventricular and subcortical white matter in this girl, who also has ventriculomegaly (*arrowheads*)

In contrast to congenital CMV disease, hydrocephalus is frequently associated with congenital toxoplasmosis, while migrational abnormality is very rare.

Herpes simplex virus

Clinical findings

Herpes simplex virus (HSV) infection occurs in 1 in 3,000–10,000 births annually, with 1,500 cases annually in the United States [24]. As a member of the Herpesviridae family, HSV has similar properties of latency and reactivation. It enters the host through mucosal surfaces and skin breaks to infect sensory nerve endings, and remains lifelong as a latent virus in the dorsal root ganglia. Both HSV-1 and HSV-2 can cause neonatal infection [25].

HSV can be acquired by the fetus during the intrauterine, perinatal and postnatal time periods. Intrauterine, or congenital infection, is rare and occurs in only 5% of cases, with the greatest risk during primary maternal infection. It can result in in utero fetal hydrops and demise. The most common route of infection is in the perinatal period from contact by the fetus with the infected maternal genital tract (85%) [26].

Neonatal HSV usually presents in the first 3 weeks after birth and is grouped into three clinical forms: localized to the skin, eyes and mouth; central nervous system involvement with or without skin, eyes and mouth; and disseminated disease. Disease of the skin, eyes and mouth occurs in 45% of cases and can progress to disseminated disease if left untreated, but has a better outcome if diagnosed and treated early. The infants with central nervous system involvement with or without skin, eyes and mouth (30%) can have encephalitis, seizures, lethargy, irritability, tremors, poor feeding and temperature liability. Last, neonates sometimes present with a sepsis-like condition, or dissemination (25%), resulting from multi-organ failure. The mortality of untreated disseminated disease exceeds 80% [26].

Diagnosis is usually established by identifying HSV deoxyribonucleic acid in the serum or CSF. Acyclovir therapy should be started empirically because it improves survival and outcomes, particularly if begun early in the course of illness. Survivors of neonatal HSV, even with therapy, are frequently left with significant neurologic sequelae, including cerebral palsy, epilepsy and developmental delay [27].

Imaging findings

Intrauterine HSV infection causes encephalomalacia (Fig. 6), ventricular enlargement, scattered calcifications and microcephaly [28]. Perinatal/postnatal HSV encephalitis has a more variable imaging appearance, and is dependent upon image timing with

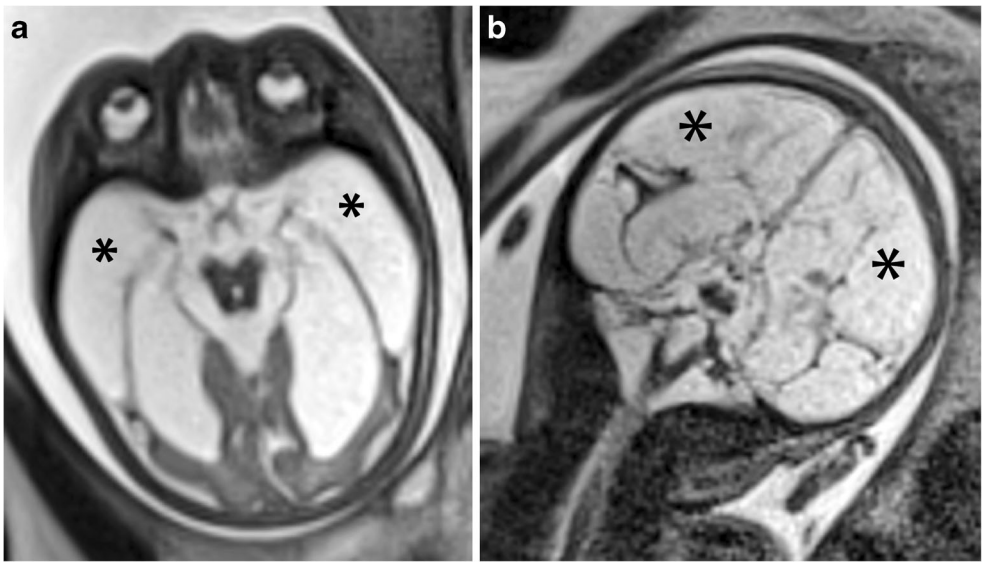

Fig. 6 Intrauterine herpes simplex virus infection in a 33-week gestation age fetus. **a**, **b** Axial (**a**) and coronal (**b**) single-shot turbo spin echo fetal MR images illustrate widespread encephalomalacia throughout the supratentorial brain (*asterisks*)

respect to the disease course. Early on, imaging might be normal, especially with ultrasound evaluation. Within the first week of infection, MR imaging might demonstrate edema and multifocal diffusion restriction with or without associated hemorrhage (Fig. 7). After the initial week, diffusion-weighted imaging becomes less useful, and severe parenchymal destruction rapidly develops [29, 30]. This is evidenced by diffuse cystic encephalomalacia, cortical thinning, atrophy, scattered calcifications, and ventricular enlargement (Fig. 7). Very early imaging might underestimate the degree of injury, and repeat imaging can be helpful to visualize the true extent of injury.

Unlike HSV encephalitis in older children and adults, neonatal HSV does not have a predilection for the temporal lobe and insular cortex. Instead, neonatal HSV has a more variable multifocal appearance and can involve the white matter, cortical gray matter, basal ganglia, temporal lobes, watershed areas and occasionally the brainstem and cerebellum. Patchy parenchymal and meningeal enhancement might also be seen acutely [28, 31].

Human immunodeficiency virus (HIV)

Clinical findings

The incidence of perinatal HIV is dramatically decreasing in the United States, with 1,650 new diagnoses in 1991 and 107 new diagnoses in 2013 [32]. While the incidence is decreasing worldwide, prevention remains a significant challenge,

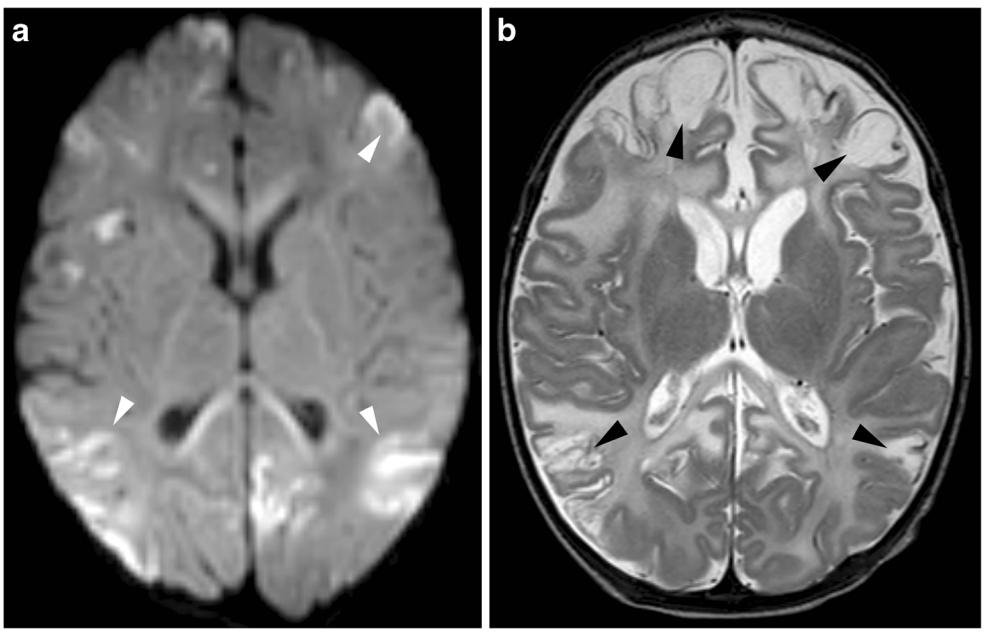

Fig. 7 Perinatal herpes simplex virus encephalitis in a 2-month-old boy. **a** Axial trace diffusion-weighted MR image reveals multifocal areas of restricted diffusion (*arrowheads*). **b** Follow-up axial T2-weighted MR image, several months later, demonstrates evolution of the acute injury into areas of encephalomalacia (*arrowheads*)

particularly in sub-Saharan Africa, with 240,000 perinatal HIV cases diagnosed worldwide in 2013 [33]. Most perinatal HIV infections are thought to occur during delivery, although the virus can be acquired by vertical transmission at any time during gestation and delivery, as well as during breastfeeding. By preventing mother-to-child transmission through universal screening, reducing maternal viral load, administering neonatal antiretroviral prophylaxis, and eliminating breastfeeding, the risk of HIV transmission decreases from approximately 25% to 1% [34, 35].

Children with congenital HIV are often asymptomatic at birth. Symptoms, including lymphadenopathy, hepatomegaly, oral candidiasis, failure to thrive and developmental delay, typically develop after 3 months, though this ranges up to 10 years. Opportunistic infections are less frequent as compared with adult-acquired HIV, with *Pneumocystis jirovecii* and CMV being the most common. Neurologic symptoms from HIV encephalitis include spasticity, extremity weakness, microcephalus and seizures. If left untreated, severe developmental delay and milestone regression develop, and there are high mortality rates, with most children dying by the age of 5 [36, 37].

Imaging findings

The most frequently encountered intracranial imaging findings are calcifications and global atrophy (Fig. 8). Calcifications favor the frontal lobe subcortical white matter and are commonly identified with in utero HIV infection. The burden of calcification positively correlates with HIV viral load [38]. Extracranially, lymphadenopathy and parotid gland lymphoepithelial cysts are frequently identified [39].

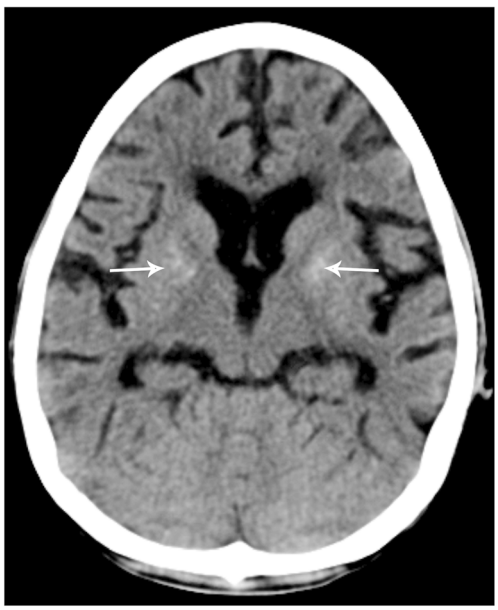

Fig. 8 Congenital human immunodeficiency virus infection in a 1-year-old girl. Axial non-contrast head CT image illustrates faint calcifications of the basal ganglia (*arrows*) and diffuse cerebral volume loss

Later in the disease course, children can develop a fusiform vasculopathy manifested by intracranial arterial ectasia and fusiform aneurysmal dilation [40]. This is thought to result in hemorrhage and infarction, with approximately 1% of children with congenital HIV/AIDS (acquired immune deficiency syndrome) manifesting a clinical stroke [41, 42].

Secondary infections are less common, but changes related to CMV encephalitis, fungal infection, Varicella-Zoster virus and progressive multifocal leukoencephalopathy are sometimes identified. Intracranial neoplasms also rarely occur, with CNS lymphoma occurring in less than 5% [43].

Zika virus

Clinical findings

Zika virus is an arthropod-borne Flavivirus that is most commonly transmitted to humans by the bite of an infected mosquito (Aedes species) [44, 45]. The first case was identified in 1952. Outbreaks of Zika virus infection have since occurred throughout Africa, Latin America, Southeast Asia and the Pacific Islands. In early 2016, Zika virus was declared a global health emergency by the World Health Organization (WHO) after the outbreak in the Americas, the Caribbean and the Pacific. The main risk of infection is to pregnant women, potentially causing a variety of severe fetal brain defects.

Maternal–fetal transmission can occur any time throughout pregnancy, though the greatest risk of serious fetal sequelae is with first-trimester infection. In utero Zika virus infection can result in fetal growth restriction and serious sequelae related to the central nervous system. The virus is both neurotropic and gliotropic, preferentially targeting neural progenitor cells [46, 47]. Neuronal growth, proliferation, migration and differentiation are disrupted, thus slowing and impairing normal brain development in utero and in infancy [46]. The main clinical features of congenital Zika infection include microcephaly, hypertonia and hyperreflexia, seizures, arthrogryposis, ocular abnormalities and sensorineural hearing loss. However the full spectrum of the syndrome is still evolving.

Diagnosis of congenital Zika virus infection is confirmed by the presence of the virus ribonucleic acid in infant serum, urine or cerebrospinal fluid collected within the first 2 days of age [48]. To date, there is no specific treatment for Zika virus infection and no vaccine for prevention. More than a dozen drug companies and the National Institutes of Health are focusing their efforts on developing a vaccine. While the current outbreak has dissipated and the WHO no longer considers Zika a global health emergency, it remains an important pathogen with serious complications to those infected.

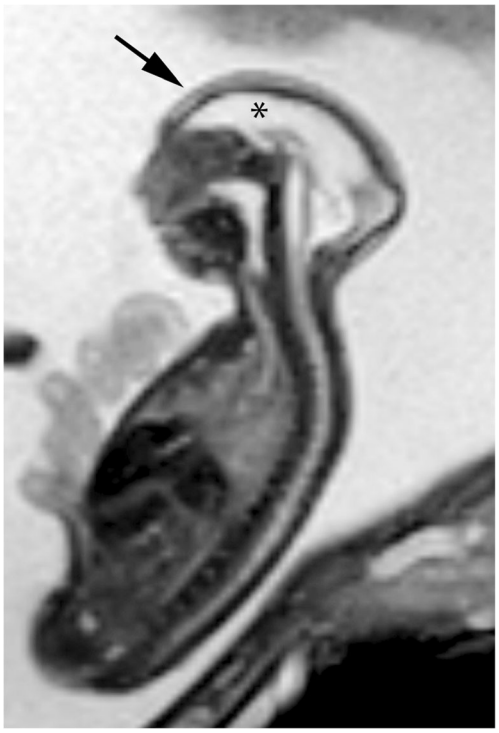

Fig. 9 Zika virus in a 22-week gestational age fetus. Sagittal balanced turbo field echo MR image demonstrates profound microcephaly (*arrow*) with severe cerebral volume loss (*asterisk*)

Imaging findings

Zika virus can disrupt normal brain development at any stage. As a result, there is a spectrum of findings on neuroimaging. Microcephaly is the hallmark of the disease and appears to be a consequence of infection early in pregnancy; however, it has also been observed in infection during the third trimester of pregnancy (Fig. 9). Brain atrophy with ventriculomegaly, unilateral or bilateral, is common and sometimes associated with subependymal pseudocysts at the occipital horns [49–51]. Other brain findings include malformations of cortical development, such as polymicrogyria, gyral simplification, pachygyria-lissencephaly and opercular dysplasia [52–55]. Abnormalities of the posterior fossa include cerebellar hemisphere hypoplasia, vermian hypoplasia and enlarged cisterna magna. Corpus callosum abnormalities include thinning, dysgenesis, hypoplasia and even absence [49, 53]. Abnormal white matter signal is present in the majority of patients and is likely caused by delayed myelination or dysmyelination [49] (Fig. 10).

Intraparenchymal calcifications have been reported in almost all infants with proven congenital Zika infection. They are mainly located at the corticomedullary junction within the frontal and parietal lobes, though can be present in the thalamus, basal ganglia, cortex and periventricular regions [56]. Calcifications at the gray–white matter junction are not classically described in other congenital infections, suggesting a possible vascular component of its pathophysiology. Calcifications of the brainstem are a common finding on autopsy.

Orbital abnormalities include asymmetrical microphthalmia, cataracts and herniation of the orbital fat into the cranial vault.

It is important to note that normal head circumference does not exclude infection and, to that end, neonates can have severe brain abnormalities with a normal head circumference. With time, the full spectrum of the disease is expected to be more fully understood.

Less common congenital central nervous system infections

Rubella

Rubella virus is the only member of the genus Ribivirus, a family of the Togaviridae. Prior to the establishment of vaccination programs, rubella occurred worldwide every 6–9 years, with the last U.S. pandemic in the 1960s. Congenital rubella syndrome is now rare in developed countries and is rapidly decreasing in developing countries [57].

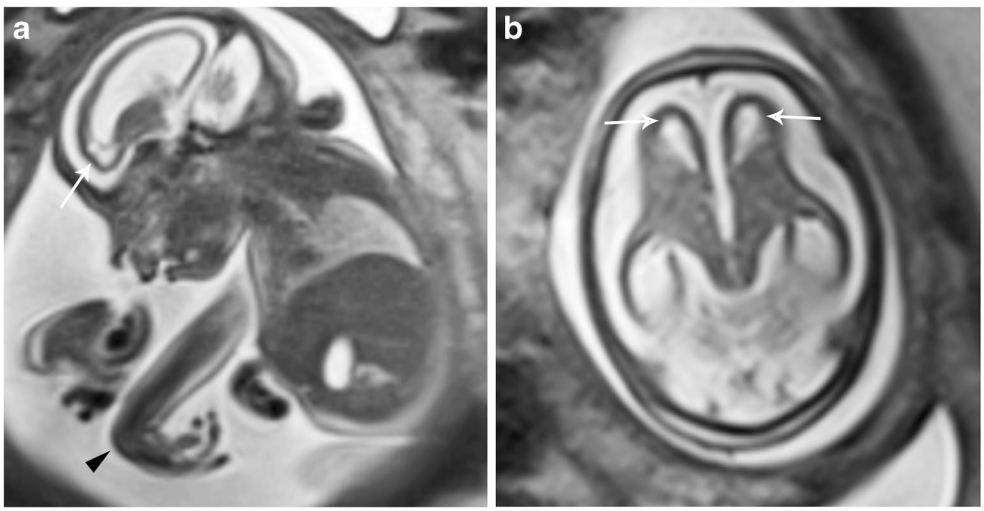

Fig. 10 Zika virus in a 32-week gestational age fetus. **a, b** Sagittal (**a**) and axial (**b**) single-shot turbo spin echo fetal MR images demonstrate microcephaly with cerebral volume loss (*arrows*). Patient was also noted to have contractures of the extremities (*arrowhead* in **a**)

Rubella is transmitted via blood–placental barrier during maternal viremia, and has the highest risk of congenital defects when infection occurs in the first 10 weeks of gestation. Hearing loss, cataracts/glaucoma, and cardiac disease are the most frequently encountered manifestations [58, 59]. A classic "blueberry muffin" rash, a reflection of extramedullary hematopoiesis, is often described. No directed therapy exists, and survivors sometimes develop microcephaly and learning disabilities, presumably the sequelae of meningoencephalitis and vasculitis [60].

Brain imaging is not specific and has a wide range of appearances. Later infections can result in enlarged ventricles, myelination abnormalities and patchy frontal predominant periventricular signal abnormality, similar to that of congenital CMV [61, 62]. Periventricular and basal ganglia calcifications and cystic change have also been described. Earlier infections can lead to near-total brain destruction and microcephaly [62].

Syphilis

Transplacental infection from maternal *Treponema pallidum* infection causes fetal spirochetemia, which is disseminated to all fetal organs [63, 64]. Most infants are asymptomatic at birth. Early congenital syphilis is defined as symptom onset before 2 years of age, most frequently with hepatomegaly, jaundice, rash, skeletal abnormalities, rhinitis and adenopathy. Although less common, involvement of the gastrointestinal tract, lungs, eyes and kidneys has also been described [65]. Characteristic radiographic long-bone abnormalities might be the sole manifestation of congenital syphilis infection in the neonatal period [66, 67]. Late congenital syphilis with clinical onset after 2 years of age is related to chronic inflammatory changes and persistent infection. These children might demonstrate facial deformities, hearing loss, and ocular, cutaneous and skeletal abnormalities [64, 65].

CNS involvement can be characterized as asymptomatic or symptomatic. Symptomatic CNS syphilis is rare with the appropriate penicillin therapy, and might result from ongoing dissemination. Acute syphilitic leptomeningitis usually presents at 3–6 months, and chronic meningovascular more often presents at the end of the first year of age. Clinically these children have hydrocephalus, cranial nerve palsies, optic nerve atrophy, neurodevelopmental regression and seizure [65, 68]. Endocrine abnormalities can result from exudative involvement of the pituitary gland/infundibulum, and infarcts can develop from syphilitic endarteritis [69, 70]. Brain imaging reflects the meningoencephalitis with leptomeningeal enhancement, hydrocephalus and infarcts.

Lymphocytic choriomeningitis virus (LCMV)

LCMV is a prevalent Arenavirus with a rodent reservoir. The incidence and spectrum of congenital infection is unknown, likely because of infrequent testing. Most congenital cases are transmitted transplacentally, with the virus preferentially replicating in the meninges, choroid plexus and ependyma [71–73]. Severe neurologic sequelae develop in more than half of survivors, with spastic quadriparesis, intellectual impairment and epilepsy. Unlike other congenital infections, LCMV does not result in systemic findings, such as hepatosplenomegaly, jaundice or rash. In other respects, it is very similar to congenital toxoplasmosis. Almost all affected neonates have chorioretinitis, and there is a high association with hydrocephalus [73].

The imaging appearance has significant overlap with both congenital CMV and toxoplasmosis, including microcephaly, periventricular calcification, cerebellar hypoplasia, parenchymal destruction and gyral abnormalities suggestive of polymicrogyria [73] (Fig. 11). Hydrocephalus develops in more than half of

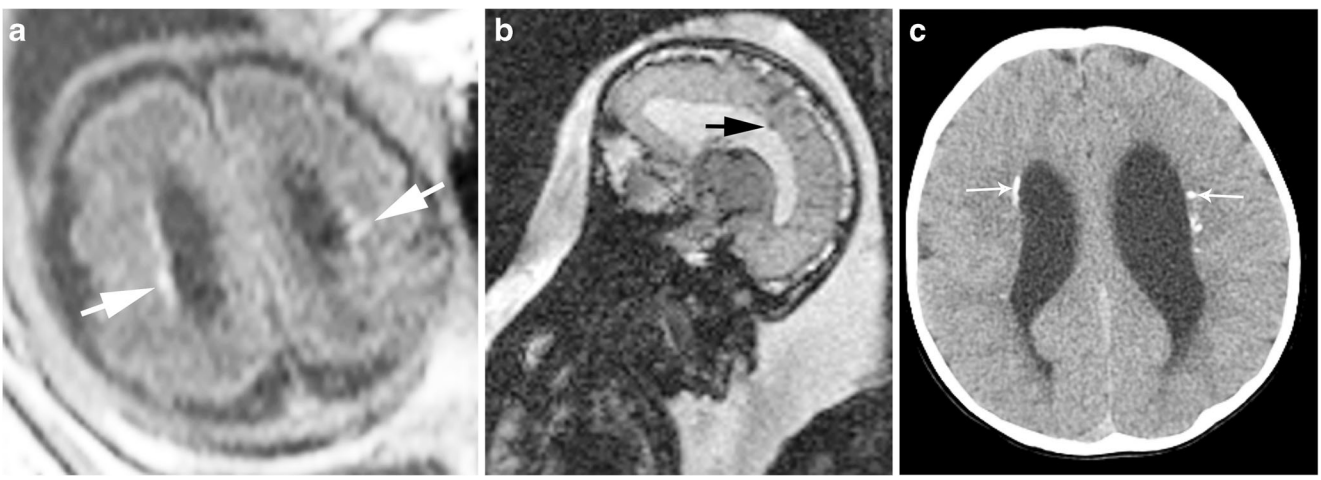

Fig. 11 Lymphocytic choriomeningitis virus in a 30-week gestational age fetus and post-natal follow-up. **a, b** Axial T1-weighted fetal MR image (**a**) shows fine areas of hyperintensity throughout the periventricular regions (*white arrows*) that demonstrate susceptibility effect on (**b**) sagittal echoplanar fetal MR image (*black arrow*). **c** Postnatal follow-up axial non-contrast CT image confirms the presence of periventricular calcifications (*arrows*)

affected infants from necrotizing ependymitis obstructing the cerebral aqueduct [73, 74].

Varicella

Varicella-Zoster virus is a Herpesvirus that can be transmitted in utero, perinatally or postnatally to the infant, resulting in congenital varicella infection. The transmission rate is low, with a risk of approximately 2% if the infection occurs before 20 weeks' gestation [75, 76]. The incidence of maternal and fetal infections has also decreased since introduction of the vaccine in 1995.

Like LCMV, varicella infections lack the typical signs of congenital infection, such as hepatosplenomegaly and jaundice. Characteristic cicatricial skin scarring might be seen at birth. Neurologic sequelae, ocular defects, limb hypoplasia and gastrointestinal abnormalities might also be present [75, 77].

Imaging findings are variable and not well defined, possibly reflecting gestational age at infection. Lobar parenchymal destruction, basal ganglia necrosis, cerebellar hypoplasia/aplasia, polymicrogyria and hydrocephalus have been described [78, 79].

Differential diagnoses

If serology is negative for TORCH (or other) congenital infection, several other diagnoses have imaging findings that mimic congenital CNS infection. Some of these diagnoses to consider include pseudo-TORCH syndrome (i.e. *OCLN* gene mutation), Cockayne syndrome, metabolic disorders (such as biotinidase deficiency and carbonic anhydrase II deficiency) and Aicardi-Gouti res syndrome.

Conclusion

Congenital infections are a serious cause of central nervous system injury. Imaging can be effective in diagnosing the presence and severity of infection. Early diagnosis can help determine prognosis and guide prenatal counseling and postnatal therapy.

Compliance with ethical standards

Conflicts of interest None

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