Intracranial Hemorrhage, Destructive Pathologies, and Infection

11

11.1 Intracranial Hemorrhage

Definition Hemorrhage occurring within the fetal cranium. It is commonly diagnosed at 26–33 weeks.

Causes
- Alteration in fetal/maternal blood pressure.
  - Drug induced—e.g., Aspirin
  - Pre-eclampsia
  - Monochorionic twin demise
- Trauma
- Infection
- Maternal thrombocytopenia, coagulation disorders
- Placental abnormalities-insufficiency, abruption
- Fetal arteriovenous malformation

Pathology
The germinal matrix cells appear by 20 weeks. They are prone to hemorrhage due to fragile capillaries. Secondary venous infarct can also occur.

Imaging Features
Sonography: The hemorrhage appears echogenic in the hyperacute stage without color flow, isoechoic in subacute stage and later hypoechoic. There may be debris and sometimes septations within the lateral ventricles.

MR imaging: Intracranial hemorrhage can be intraparenchymal, periventricular, intraventricular, or extra-axial. Sonographic appearances of hemorrhage may sometimes be confusing and may resemble a mass. MRI is sensitive in detecting the different phases of hemorrhage from acute to chronic. MRI is useful in depicting the intraventricular/subarachnoid/intraparenchymal extensions and also the associated cyst formation, parenchymal ischemia and hydrocephalus. GRE (or EPI GRE), b0 diffusion, HASTE are important sequences to identify hemorrhage in the descending order and it is seen showing dark signal on these sequences [1]. Hemorrhage may appear hyperintense T1 and b800 sequences in subacute stage. By a combination of sequences, the age of hemorrhage can be predicted (Table 11.1) [1].

Grading of Intracranial Hemorrhage in Fetuses and Prognosis
Grade 1—isolated germinal matrix hemorrhage. Good outcome in 100% cases.

Grade 2—periventricular hemorrhage with ventricular extension. Good outcome in majority of cases (Fig. 11.1).

Grade 3—periventricular hemorrhage with ventricular extension + ventriculomegaly. Grade 4- Grade 3 hemorrhage with intraparenchymal extension (Fig. 11.2). Poor outcome in majority of cases with grade 3 and grade 4 hemorrhage.

Complications and Long-Term Effects
The complications of fetal intracranial hemorrhage are hydrocephalus intrauterine death and neonatal death. The long-term effects include developmental delay. Seizure disorder, cerebral and palsy [2, 3].

11.2 Encephalomalacia

There is focal/regional damage to the brain.

Etiology
- Ischaemia–monochorionic twin demise and ischemia in the surviving twin
- Infection–TORCH
- Placental abruption
- Arteriovenous malformation/vein of Galen malformation (vascular steal).
- Following laser treatment of twin–twin transfusion (4–7% incidence)
- Maternal trauma, hypotension

R. Rajeswaran, *MR Imaging of the Fetus*, https://doi.org/10.1007/978-981-16-9209-3_11

Table 11.1 The appearances of various stages of intracranial hemorrhage in different sequences

Stage	Duration	Hemoglobin	T1	T2	GRE
Hyperacute	<24 h	Intracellular oxyhemoglobin	Iso	Iso to hyper	Hypointense rim
Acute	1–3 days	Intracellular deoxyhemoglobin	Iso	Hypo	Hypo
Early subacute	3–7 days	Intracellular methemoglobin	Hyper	Hypo	Hypo
Late subacute	1–4 weeks	Extracellular methemoglobin	Hyper	Hyper	Central hyperintensity and peripheral hypointensity
Chronic	>4 weeks	Hemosiderin	Iso or hypo	Hypo	Hypo

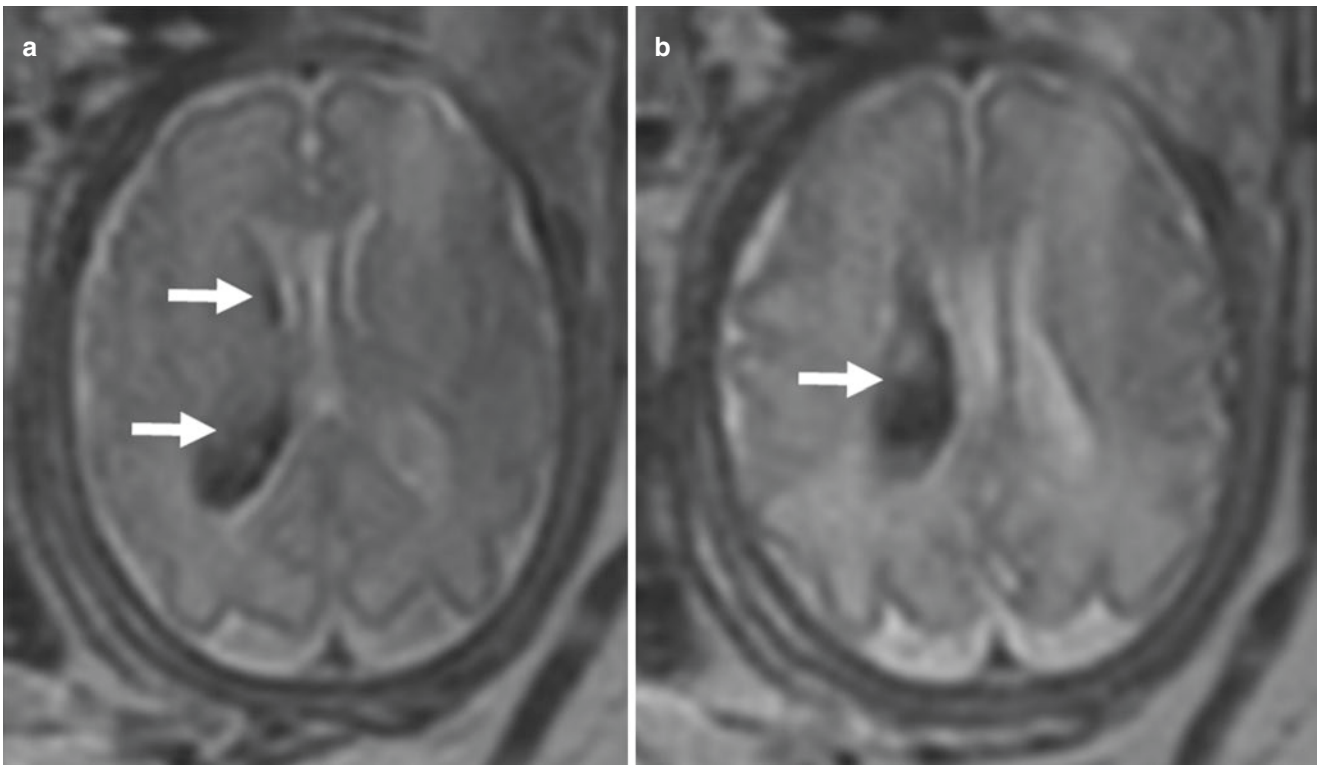

Fig. 11.1 Axial (**a**, **b**) T2W HASTE images of a 31-week fetus show a hypointense lesion in the right germinal matrix—intraventricular region (arrows)—Grade 2 Germinal matrix hemorrhage

Pathology

Following the regional/diffuse brain insult, there is astrocytic proliferation and glial septations.

Imaging Features

Sonography: In acute phase, the ultrasound may look normal. Later there may be echogenic area with irregular borders. Associated ex vacuo dilatation of the adjacent ventricle is seen.

MRI: To be done in suspected and at high-risk fetuses. There is hyperintensity in the affected brain parenchyma on T2-weighted images. There may be a hyperintensity on diffusion-weighted images in acute ischemia. Areas of hemorrhage/calcifications may be seen as hypointensities on T2-weighted images. There is associated dilatation of the adjacent ventricle.

Prognosis

- Depends on the size of the affected brain
- May be associated with developmental delay, seizures

11.3 In Utero Infections

The common in utero infections are due to TORCH (Toxoplasmosis, Other [Varicella-Zoster, syphilis], Rubella, Cytomegalovirus, Herpes), zika and parvovirus and brain abnormalities may be present. The fetus is more likely to get

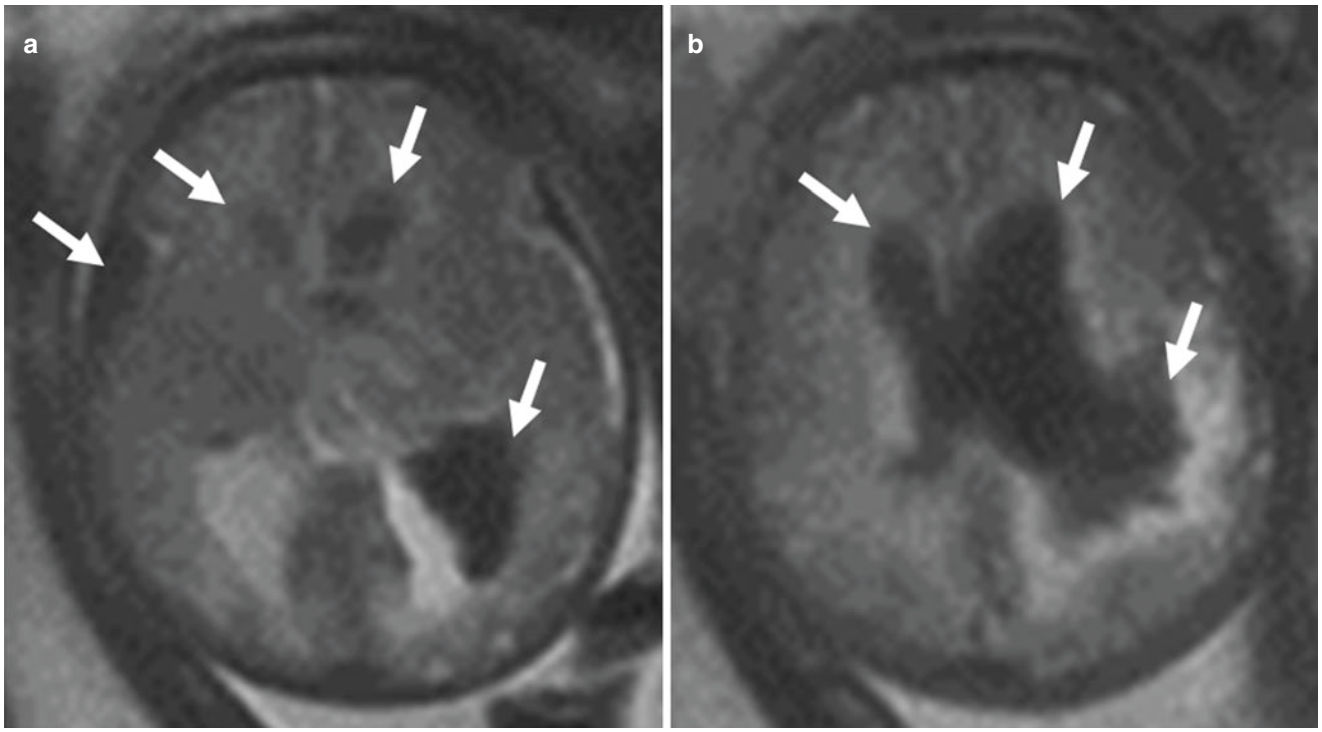

Fig. 11.2 Axial (**a**, **b**) T2W HASTE images show hemorrhage in the left germinal matrix with intraventricular/subarachnoid and intraparenchymal extension (arrows)—Grade 4 hemorrhage. There is associated mild ventriculomegaly

infected if the maternal infection happens early in gestation [4]. Once a maternal infection has been confirmed, the possibility of infection in the fetus needs to be worked up. Confirmation of fetal infection is possible by invasive testing like amniocentesis and cordocentesis. Generally, the amniotic fluid polymerase chain reaction (PCR) test will become positive after 6 weeks after the maternal infection. Fetal urination is not fully developed until 18–20 weeks' gestation, and hence amniocentesis should be delayed till 18–20 weeks' gestation, so that the virus will be present in urine (amniotic fluid) in sufficient concentrations.

Pregnant women who present with rashes, malaise, and/or other symptoms or signs suggestive of viral infection need to be investigated. The important tests utilized for diagnosing maternal infection are ELISA (enzyme-linked immunosorbent assay), paired serology tests for virus-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies.

Fetal congenital infection may be suspected when some of these findings are visualized on ultrasound—microcephaly, cerebellar abnormalities, polymicrogyria, white matter signal abnormality. Multiple calcifications, parenchymal destructive lesions, cortical dysplasia, lissencephaly ventriculomegaly, hepatomegaly, splenomegaly, periventricular pseudo-cysts, and placentomegaly. Fetal MRI is extremely useful in demonstrating the brain parenchymal changes though the calcifications may not be well depicted.

Differential diagnosis: Fetal infections can be mimicked by pseudo-TORCH syndrome/Aicardi-Goutiere syndrome, a familial autosomal recessive disease that manifests with cortical malformations and calcifications.

11.3.1 Cytomegalovirus

It belongs to the human herpesvirus family and is the most common cause of congenital viral infection. It can affect multiple fetal organs.

Incidence—Approximately 0.2–2.2% of live births [5–7].

Pathology—It affects the fetus transplacentally from the mother.

Imaging Features [8–11]
Brain:

- Ventriculomegaly (Fig. 11.3a, b) can be mild to severe, the latter carrying a bad prognosis. Sometimes it can mimic aqueduct stenosis. Ventriculitis may be seen as irregularity and T1/T2 hyperintensity along the ventricular walls There may be associated intraventricular strands due to adhesions.
- Parenchymal—T2 hyperintensities in white matter and periventricular pseudocysts can occur. There may be

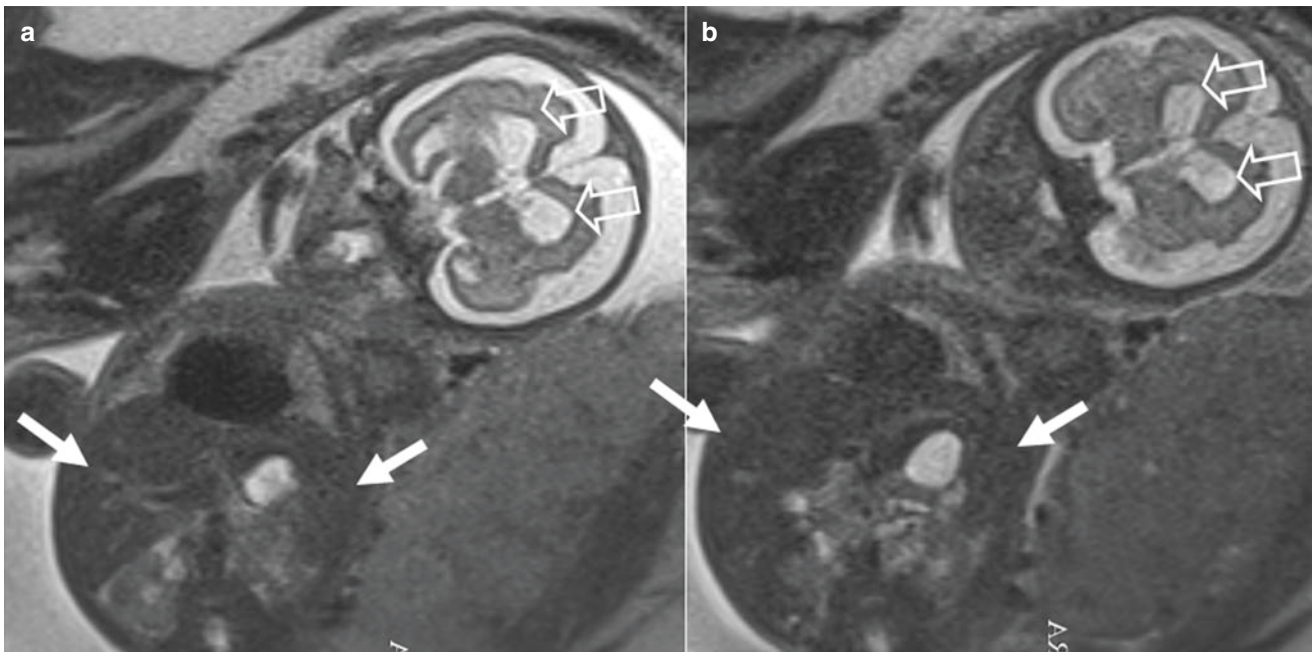

Fig. 11.3 Coronal T2W images (**a**, **b**) showing hepatosplenomegaly (arrows) in a 29-week fetus who was positive for CMV infection. Bilateral ventriculomegaly (open arrows) and cerebral atrophy are also seen in brain images

associated cortical malformations like cortical dysplasia, polymicrogyria, lissencephaly (Fig. 11.4a, b, d, e), pachygyria, and schizencephaly. Other findings include intraparenchymal calcifications (Fig. 11.4c, f), porencephaly, microcephaly, cerebellar atrophy.

- Microcephaly is associated with a poor prognosis, with the affected children having mental retardation.

Hepatosplenomegaly (Fig. 11.3a, b) may be present and low signal on T1 and T2WI may signify fibrosis.

Fetal growth retardation, Cardiomyopathy, nonimmune hydrops may be present besides poly or oligohydramnios.

The diagnosis is confirmed if the mother shows IgM antibodies or IgG antibodies (if she had been sero negative before the pregnancy). Amniocentesis can be performed to see viral secretion. However, it may take 5–7 weeks to become positive, after the infection.

Prognosis

It is important to note that the fetus need not be affected by the infection though it may have a confirmed infection. So, some of the infected fetuses may never develop structural abnormalities. Similarly, some normal-appearing infected fetuses on imaging can still manifest long-term sequelae. Seizures, neurological impairment, behavioral problems, sensorineural deafness, intellectual disability, and physical handicaps may be present postnatally. Termination is an option once the CMV infection is confirmed as it carries a bad prognosis.

11.3.2 Toxoplasmosis

This infection occurs in the mother when there is ingestion of infected meat/food due to improper cooking. The infection then spreads transplacentally and affects the fetus.

Imaging Features [12, 13]

- Brain—Ventriculomegaly may be present with intraventricular adhesions
- Intraparenchymal calcifications may be present in the basal ganglia or corticomedullary junction or periventricular locations. Sometimes obstructive hydrocephalus may be present. The other findings described are encephalomalacia, cerebral/cerebellar atrophy, microcephaly or macrocephaly due to hydrocephalus, cortical malformations, and chorioretinitis.
- Hepatic calcifications
- Fetal growth retardation

Amniocentesis can be performed and PCR test on the amniotic fluid is diagnostic.

Prognosis

For those affected fetuses, the severity of infection is related to the trimester of pregnancy when the transmission had occurred [14]. Infection during the first trimester may result in intrauterine death. Infection during the second trimester may be manifested with microcephaly, retinochoroiditis, and intellectual disability. Infection during the third trimester

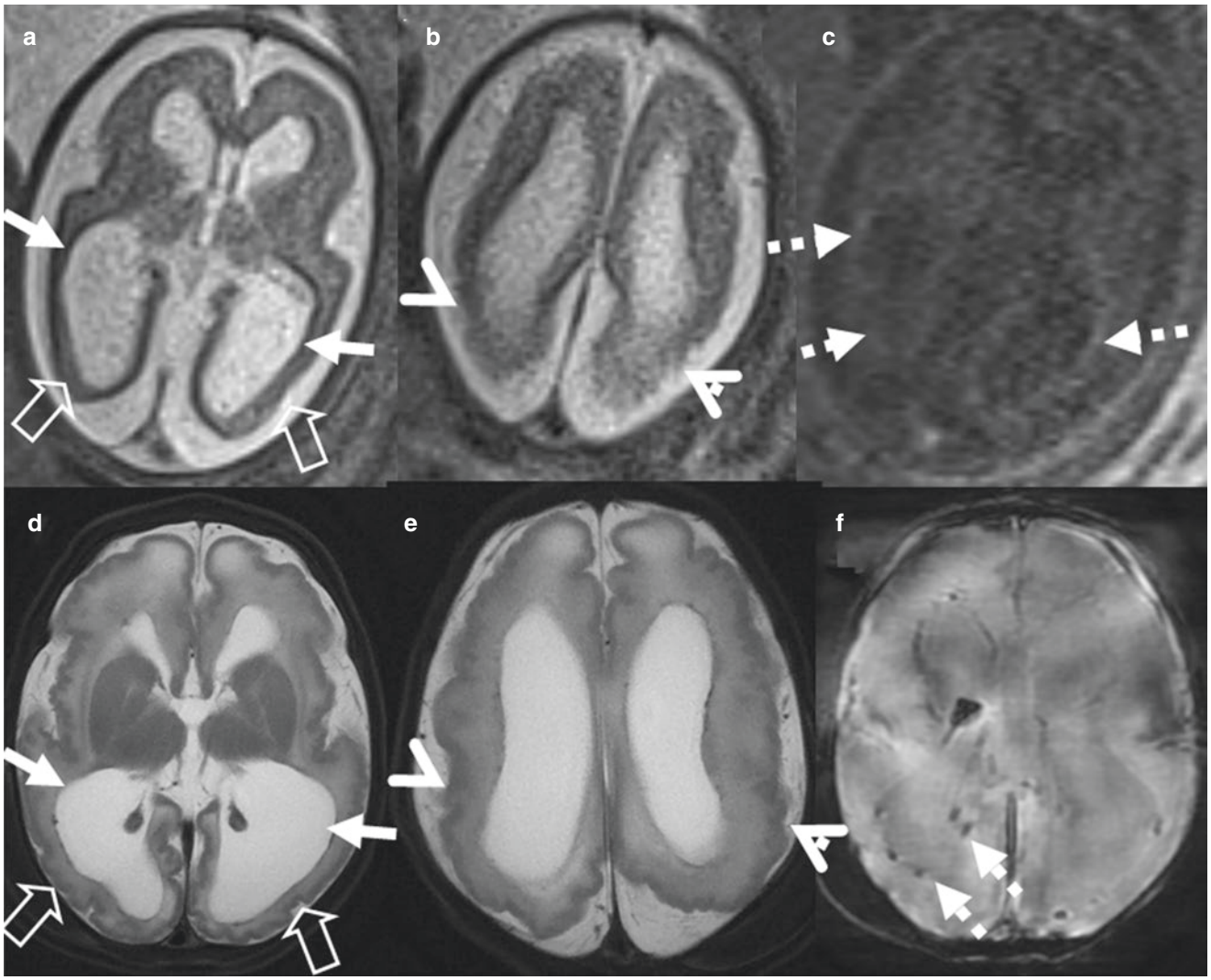

Fig. 11.4 Axial (**a**, **b**) T2W images of a 31-week CMV infected fetus shows ventriculomegaly, diffuse cerebral cortical thinning with generalized reduced sulcation and polymicrogyria (arrowheads). Axial (**c**) T1W image shows numerous small periventricular hyperintense foci (broken arrows) suggesting calcifications. Postnatal axial (**d**, **e**) T2W and GRE axial (**f**) images showing similar findings

may be manifested with lymphadenopathy, hepatosplenomegaly, ophthalmic pathologies, and brain calcifications.

Termination is an option once the infection is confirmed as it carries a bad prognosis.

11.3.3 Rubella

The imaging findings are similar to other infections and non-specific.

Imaging Features [15–17]
The important features are—Periventricular calcifications, white matter T2 hyperintensities, intraparenchymal cysts within brain, ventriculomegaly, microcephaly, congenital cataract, cardiac anomalies (especially tetralogy of Fallot and ventricular septal defect), and fetal growth restriction.

Prognosis
The affected child may have neurological/learning disabilities and sensorineural deafness.

11.3.4 Human Parvovirus B19

It is a type of in utero infection associated with fetal anemia, myocarditis, and intrauterine death. It is an inhibitor of erythropoiesis and attacks fetal erythroid progenitor cells.

Imaging Features [18, 19]
The important features are—fetal ascites, cardiomegaly, hydrops fetalis, hepatomegaly, polyhydramnios, and placentomegaly. Low resistance waveform may be seen on fetal MCA Doppler due to the presence of a fetal anemia.

Prognosis

Management consists of treating the fetal anemia, and in appropriate cases, by packed red cells transfusion into the umbilical vein. The development of hydrops fetalis carries a poor prognosis.

11.3.5 Zika Virus (ZIKV)

ZIKV belongs to the flavivirus family and is transmitted by Aedes mosquitoes or through human-to-human sexual contact. Zika virus commonly causes multiple teratogenic malformations. The developing brain is predominantly affected.

Imaging Features [20–23]

The important features are—Microcephaly, reduced cortical gyration and white-matter myelination abnormalities and cerebellar hypoplasia.

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