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## Intracranial Hemorrhage on Prenatal MR Imaging

While intracranial hemorrhage (ICH) is a relatively common finding in preterm neonates, found in 40%–60% of those born before the gestational age of 32 weeks, it is considered rare in the prenatal period, with a reported incidence of no more than 0.1%,<sup>1</sup> particularly when estimated mostly on sonography (US) and in relatively small groups of patients. However, when MR imaging is used for prenatal diagnosis and larger cohorts of patients are reviewed, ICH (meant as all forms of bleeding, ie, germinal matrix hemorrhage [GMH] and all non-GMHs: intraventricular, intraparenchymal cerebral and cerebellar, subarachnoid, and subdural) occurs in 1% of pregnancies<sup>2</sup> or even in approximately 3% as shown in the article in this issue of the *American Journal of Neuroradiology* by Epstein et al,<sup>3</sup> who reviewed 6179 MR imaging scans and found 177 diagnostic-quality fetal MR images demonstrating intracranial hemorrhage. Taking into account one of the limitations of this study listed by the authors that T1, DWI, and EPI blood sequences were performed only in some of the MR imaging examinations since 2016 (the report includes MR imaging scans performed during 2004–2020) and that some subtle ICHs could have been missed, it becomes clear that, in fact, an even higher incidence of ICH in the prenatal period can be expected. This is in accordance with the results of 433 consecutive stillbirth postmortem examinations, in which there was intrauterine hemorrhagic brain injury in 4.6%.<sup>4</sup>

This is an important observation for the following reasons: 1) It confirms the importance of performing fetal MR imaging as an adjunct to prenatal US, enabling detection of the abnormalities that are not picked up on US, ICH being one of these; 2) in some cases, ICH might be the cause and not the result of preterm birth, or at least it precedes it; 3) it has severe medicolegal implications if the family sues the obstetricians and/or neonatologists for inadequate perinatal care; 4) in view of the expected posthemorrhagic hydrocephalus that carries an additional risk of adverse outcomes, follow-up imaging should be undertaken and ventriculo-amniotic shunting is an option for the management in severe cases; and 5) the correct diagnosis should imply cesarean delivery to avoid additional hemorrhage or injury during vaginal delivery.

Although most fetuses from the above-mentioned study (60.5%) showed GMHs, there was also a significant group with non-GMH in the report of Epstein et al,<sup>3</sup> including cerebellar bleeding, which constituted 6.2% of the cohort (11/177) and is

usually more difficult to visualize on US both in fetuses and in neonates. Cerebellar hemorrhages have been attributed in the literature to birth-related trauma so far, and this study shows that the insult may be prenatal. This finding, though not entirely new as the authors themselves state, may be significant in the attempt to explain the causes of autism spectrum disorder (ASD) and various additional behavioral disorders that have been found in extremely premature infants, >10 times more often than in term neonates (8% versus 0.6%); an increased risk of ASD has been found using the Screening Tool for Autism in Toddlers and Young Children (<https://www.ocali.org/project/stat>) in most cases of prematurity associated with cerebellar hemorrhage.<sup>5</sup>

Epstein et al<sup>3</sup> confirmed the results of a previous large study,<sup>2</sup> which showed statistically significantly poorer neurologic outcome of non-GMH than of GMH, including neonatal death and an increased necessity for ventricular shunting.

In utero shunting remains controversial. It was attempted in the 1980s and was abandoned due to lack of encouraging results. Currently, some active fetal therapy research groups are working on new devices, materials, and strategies to improve outcomes of these fetuses, and they encourage fetal MR imaging as providing more accurate information, allowing a more reliable diagnosis and exclusion of other anomalies.<sup>6</sup> Obviously, the procedure of shunting, curative by assumption, can cause complications, including secondary hemorrhages. In the records of my center, we have examples of ICH after shunting that was performed due to nonhemorrhagic hydrocephalus, eg, in congenital aqueductal stenosis.

Most interesting, there was a large representation of multiple pregnancies in the cohort examined by Epstein et al<sup>3</sup> (29.9%, 53/177), and in 34/53 cases, twin-twin transfusion syndrome (TTTS) was confirmed. It is not surprising because monochorionic twins are at high risk for adverse outcome due to complications related to placental vascular anastomoses, and these include both hemorrhagic and ischemic brain injury. Moreover, both kinds of brain damage are also observed in these patients with TTTS who are treated with fetoscopic laser surgery.<sup>7</sup>


Not surprising, it is crucial not only to diagnose ICH but also to rule it out because ICH belongs in the exclusion criteria for fetal surgery, open neural tube defect, and laser therapy for TTTS.<sup>8</sup> Consequently, a complete and reliable evaluation is necessary to qualify the fetus for various types of prenatal interventions. Fetal

MR imaging is usually one of the required procedures before deciding on the intrauterine treatment.

The already wide and still-growing spectrum of the capabilities of fetal MR imaging, including the use of 3T scanners, as well as the ever-expanding range of questions that have to be answered, including in cases of intracranial hemorrhage, means that we will certainly be dealing with more and more fetal observations using MR imaging.

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