The corpus callosum is the largest white matter tract connecting the 2 cerebral hemispheres. Its embryologic development has been studied extensively. At 11 to 12 weeks' gestation, axons begin to cross the lamina terminalis to form the corpus callosum. Development generally proceeds anterior to posterior (from genu to body to splenium) with the exception of the rostrum, which forms last. The mature crescentic shape of the corpus callosum is essentially complete by 18 to 20 weeks. As the brain matures, thickening of the corpus continues until after birth.

Basic knowledge of normal callosal development is essential to the understanding of callosal abnormalities. If the normal developmental process is disturbed, the corpus callosum may be completely absent (agenetic) or partially formed (hypogenetic). Because of the anterior-to-posterior development process, when the corpus callosum is hypogenetic, it is the posterior portion that is most affected. Developmental abnormalities of the corpus callosum may be isolated but more often are associated with other central nervous system anomalies, including Dandy-Walker malformation, holoprosencephaly, Chiari malformation, chromosomal abnormalities, and many other syndrome complexes.

In addition to developmental abnormalities of the corpus callosum, abnormalities of the corpus callosum in the fetus can be destructive in origin. A recent unfortunate case of attempted in utero treatment of a fetus with a large sacrococcygeal teratoma proved that the finding of complete absence of the corpus callosum can be secondary, occurring in the setting of extensive brain injury.

**Case Report**

A 29-year-old woman, gravida 1, para 0, was referred to our institution for further evaluation and consideration of fetal treatment for a sacrococcygeal teratoma. Obstetric sonography showed a living fetus at 22 weeks' gestational age with a predominantly solid, highly vascular sacrococcygeal teratoma associated with mild polyhydramnios and placental thickening but no hydrops (Fig. 1). A detailed anatomic survey of the fetus showed no other morphologic abnormalities; specifically, the brain appeared normal, and the corpus callosum was intact (Fig. 2).
Because rapid growth of the tumor was observed on sequential studies, the decision was made to proceed to fetal intervention. Percutaneous sonographically guided radio frequency ablation of the teratoma was performed. Despite apparent initial success, postoperatively the fetus had a large hemorrhage into the mass. In utero transfusion was therefore performed.

Subsequent sonograms obtained within 2 weeks of the procedure showed progressive ventriculomegaly, bilateral subependymal hemorrhages, and intraventricular hemorrhage (Figs. 3 and 4). In addition, patchy areas of increased echogenicity and progressive cystic changes developed in the periventricular white matter, findings consistent with extensive periventricular leukomalacia related to extensive brain ischemia (Fig. 5).

Magnetic resonance imaging performed approximately 4 weeks after the procedure corroborated these findings, showing marked cystic periventricular leukomalacia, ventriculomegaly, and loss of the normal hypointensity of the germinal matrix; these findings suggested ischemic injury (Fig. 6). In addition, no corpus callosum was found. This absence was presumed to be secondary to degeneration from the extensive white matter injury.

At autopsy, extensive cystic leukomalacia was confirmed throughout the cerebral white matter. Large bilateral subependymal cysts were identified, consistent with previous germinal matrix hemorrhages. The corpus callosum was completely degenerated and pathologically absent (Fig. 7).

Discussion

This unfortunate case of a fetus who incurred extensive brain injury after attempted fetal treatment of a large sacrococcygeal teratoma documents an important cause of absence of the corpus callosum. Other investigators have reported the correlation of white matter injury with volume loss of the corpus callosum. In the mature brain, Wallerian degeneration is a well-described mechanism for explaining how this volume loss can occur. Wallerian degeneration

Figure 1. Initial obstetric sonogram revealing a large, predominantly solid mass arising from the fetus, consistent with a sacrococcygeal teratoma (arrow).

Figure 2. Initial obstetric sonogram showing normal intracranial anatomic characteristics at the level of the head circumference. The cavum septum pellucidum is present, and the visualized corpus callosum (arrow) is intact.

Figure 3. Coronal sonogram of the brain 12 days after the fetal intervention showing the development of small bilateral subependymal hemorrhages (arrows).
also plays a role in the fetal brain. In addition, because of the limited capacity for the immature brain to incite an astrocytic response, brain injury leads to complete resorption of necrotic tissue (i.e., liquefactive necrosis). We postulate that the process of complete liquefactive necrosis was the explanation for the absent corpus callosum diagnosed pathologically.

Prenatal diagnosis of agenesis of the corpus callosum rests on knowledge of associated anatomic findings. In fetal sonography, searching for the cavum septum pellucidum on a routine obstetric sonogram is helpful. When the cavum septum pellucidum is identified, it can be inferred that the corpus callosum is present because the formation of one is integrally related to the formation of the other. A number of additional sonographic findings may be seen when the corpus callosum is absent. Specifically, these findings include elevation and enlargement of the third ventricle, widely spaced frontal horns of the lateral ventricles giving a “steer horn” appearance, dilatation of the posterior horns of the lateral ventricles (colpocephaly), and an abnormal radial sulcal pattern along the interhemispheric fissure.

With enough experience and focused effort, direct sonographic visualization of the corpus callosum in both the sagittal and coronal planes is often possible by 20 weeks’ gestational age. Nevertheless, the in utero sonographic diagnosis of callosal agenesis is almost always made by inference from the indirect signs. Magnetic resonance imaging is very helpful in confirmation of the diagnosis.

This case directly shows the findings of destruction of the fetal corpus callosum, resulting in a radiologic and pathologic appearance indistinguishable from that of developmental callosal agenesis. When complete absence of the corpus callosum is observed in utero, developmental as well as destructive causes must be considered.

Figure 4. Sonogram 3 weeks after the intervention showing moderate ventriculomegaly. Hemorrhage fills the downside ventricle and adheres to the wall of the upside ventricle (arrow).

Figure 5. Coronal (A) and sagittal (B) images of the fetal brain showing increased echogenicity of the periventricular white matter and developing cysts (arrows). Findings are consistent with periventricular leukomalacia.
Disappearance of Corpus Callosum Secondary to Brain Injury

Figure 6. Coronal T2-weighted in utero fetal magnetic resonance image showing increased signal in the periventricular white matter consistent with leukomalacia (arrows). In addition, there is now complete absence of the corpus callosum. The arrowhead points to the expected location of the corpus callosum.

Figure 7. Gross pathologic specimen of the fetal brain confirming extensive periventricular leukomalacia (arrows). No corpus callosum can be identified. Arrowheads point to the lateral ventricles.

References


