Dural sinus malformation (DSM) is a congenital malformation characterized by the presence of a dilated dural sinus pouch that communicates with other sinuses and drains cerebral veins. In postnatal angiography, DSMs are often associated with multiple slow flow mural arteriovenous shunts, and may have additional shunts distant to the DSM.1-4 There are two anatomic types of DSM: 1) Midline, involving the confluens sinuum (torcular Herophili) and adjacent posterior sinuses and 2) lateral involving the jugular bulb with otherwise normal sinuses. In postnatal case series, the midline type has a worse postnatal prognosis, as the lateral type benefits from collateral drainage via the contralateral jugular vein.1,3 and therefore has important clinical implications if identified in fetal life. Dural sinus malformation is a rare entity, and prenatal diagnosis has been reported in roughly 30 cases. Fetal MRI is well described5-10, and there is a brief mention of the autopsy pathology in one case report and in a large radiological series2-9 which confirm the presence of a suspected thrombus within a DSM.

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Prenatal Ultrasound (US) diagnosis of DSM has been described as early as 20 weeks. Ultrasound findings include a cystic structure in the posterior fossa representing a dilated confluence sinus, posterior superior sagittal sinus, straight sinus and transverse sinuses. Color Doppler imaging may fail to detect flow in the lumen because of low velocity. Rossi et al described vascularity at the margin of the DSM and postulated that this might represent multiple mural arteriovenous shunts associated with DSMs. The MRI is a useful modality for diagnosis of suspected DSM. Antenatal MRI identifies a T1 hypointense lesion centered on the confluence sinus: if the DSM is complicated by thrombus it may demonstrate high T1 signal intensity. Associated shunts are usually diagnosed postnatally. Post-natal MRI including MR angiography and venography is the best radiological technique to characterize the arteriovenous shunts and the anatomy of the cerebral veins and venous sinuses.

In this paper we examine the natural history of dural sinus malformations in fetal life. In particular we document, by pathology the fetal vascular abnormalities accompanying malformations of the dural sinus, demonstrate the salience of vascular thrombosis in utero in the evolution of these malformations, and present evidence of significant vascular remodeling.

**Materials and Methods**

A retrospective review of the autopsy series and fetal MRI at our institutions was performed to identify cases with DSM: cases were included if there was an autopsy with ultrasound or MRI correlation. The clinical, imaging and pathologic features were examined.

**Results**

Three patients were identified whose findings were compatible with DSM. In no case was there a history of trauma or maternal coagulopathy, and in all cases cytogenetic studies were performed, and were normal.

Case 1: A 35-year-old woman, gravida 4 para 1, was referred for a routine anatomic US at 22 weeks. She had two prior pregnancy losses due to cervical incompetence and one healthy child. A cervical cerclage was performed at 12 weeks gestation. First trimester screening was normal. Ultrasound performed at 22 weeks demonstrated a posterior, midline intracranial mass with low level echoes, displacing the cerebellum inferiorly (Figure 1a). It was continuous with a dilated superior sagittal sinus and no flow could be detected within it on color Doppler studies. A 1 cm hyperechoic mass was present in the left Sylvian fissure (Figure 1b). Elective termination of the pregnancy was performed at 23 weeks. Postmortem examination demonstrated massive aneurysmal dilation of the confluens sinuum, posterior straight, superior sagittal and transverse sinuses that did not contain thrombus (Figure 1c). A dural arteriovenous fistula (AVF) was identified in the left Sylvian fissure, distended by organizing thrombus (Figure 1d). The brain was otherwise normal, as was the systemic autopsy.

Case 2: A 25-year-old woman, gravida 2, para 1, with one healthy child was referred for evaluation at 21 weeks gestation because of ventriculomegaly and a posterior fossa abnormality detected by ultrasound at another institution. No first trimester screening was performed. Ultrasound performed at 21 weeks demonstrated severe ventriculomegaly and an apparently avascular, complex midline posterior intracranial mass compressing the cerebellum (Figure 2a). Magnetic resonance imaging performed at 22 weeks demonstrated a heterogeneous extra-axial mass with variable T1 (Figure 2b,c) and T2 signal intensity components. The areas of high T1 signal intensity were compatible with areas of thrombus. This mass was centered on the confluens sinuum and was compressing the cerebellum inferiorly, with ventriculomegaly of the third and lateral ventricles. Shunt vessels were not identified. Elective termination of the pregnancy was performed at 22 weeks. The postmortem examination confirmed the presence of a large thrombus occupying a massively dilated confluens sinuum, posterior straight, sagittal and transverse sinuses (Figure 2d).
Figure 2: (Case 2) a) Ultrasound performed at 21 weeks gestational age. Sagittal image shows a 3 x 2.7 cm heterogeneous mass in the posterior cranium (*) with mass effect on the cerebellum (CB) and ventricular dilation (V). b) T2 MR images obtained at 22 weeks, demonstrating a heterogeneous mass in the posterior cranium, with ventriculomegaly. c) High signal on Sagittal T1SPGR image confirms thrombosis (arrow). d) Postmortem at 22 weeks shows a posterior view of the skull with the dura removed. There is massive dilation of the confluens sinuum and posterior sinuses containing organized thrombus (arrows). The curvilinear white marks on the thrombus are artifacts of illumination. Note the discoloration of the cerebellum by hemosiderin, indicative of old haemorrhage. e) Brain with dural sinuses removed, demonstrating splaying of the cerebral hemispheres and flattening of the collicular plate and cerebellum with a dilated, though not aneurysmal vein of Galen (*). f) The removed dural sinuses: anteriorly the falk contains a dilated superior sagittal sinus (ss), and posteriorly the confluens sinuum, straight sinuses and transverse sinuses comprise an enlarged space containing an irregular ball of organizing thrombus posteriorly (t). Anteriorly this space is bounded by the orifice of the great vein of Galen (arrow). g) Photomicrographs of the dorsal thalamus and epithalamus demonstrate dilated veins (v) and clusters of calcified neurons (arrowheads) (Hematoxylin and Eosin x 50). h) Many of the small dilated vessels have organized, albeit thin muscular walls (a) characteristic of fetal arteries. These are occasionally mineralized and embedded in a gliotic stroma with residual germinal matrix and old hemorrhage (Hematoxylin and Eosin x100).
The vein of Galen was ectatic (Figure 2e,f). Dilated dorsal thalamic and epithalamic veins and tangled small arteries with associated mineralization, hemorrhage and reactive gliosis were identified, probably representing a midline arteriovenous malformation (Figure 2g,h), and there was massive hydrocephalus and focal transcortical injury. The remainder of the autopsy disclosed no other abnormalities.

Case 3: A 37-year-old G3P2 woman presented at 19 weeks gestation for routine antenatal ultrasound, which demonstrated a large anechoic left frontal mass: Five days later MRI (Figure 3a,b) demonstrated an extra axial frontal mass, with hypointense signal on T2 weighted sequence, with large vessels draining into a dilated superior sagittal sinus (Figure 3c); a diagnosis of arteriovenous fistula with haematoma or enlarging varix was postulated. The confluens sinus and straight sinus were not dilated. The pregnancy was electively terminated at 23 weeks gestational age. At autopsy the frontal mass was demonstrated to be a large varix compressing the frontal lobe and draining a pial arteriovenous fistula, with draining veins passing to the superior sagittal sinus (Figure 3d,e). The anterior sagittal sinus was mildly dilated, but the confluens sinus and straight sinus were now massively dilated (Figure 3f). The systemic autopsy was normal except for the presence of small mesenteric hemangiomas.

**DISCUSSION**

To our knowledge, this series of cases of fetal DSM represents the first published autopsy series. There is a single case report and a radiological series which briefly mention autopsy findings, but both reports simply confirmed at autopsy the presence of thrombosis in a DSM, without further comment. DSM is a rare entity and is traditionally the realm of pediatric and interventional neuroradiology, whereas fetal ultrasound is performed by radiologists and obstetricians who likely do not have in-depth exposure to neuroradiology: as a diagnostic entity it deserves specific attention by fetal neuropathologists. Dural sinus malformation is a relatively new term in the literature; as the first large case series was published in 1996. Furthermore, publication in a journal indexed in PUBMED, the database preferred by most clinicians, did not occur until 2004. Some recent publications describe DSM using different terms such as fetal or infantile dural AVF, which can lead to some confusion. Our cases aid the understanding of the natural history of fetal DSM. Sinus thrombosis in DSM is thought to represent a secondary, not a causative phenomenon. Grangé et al lend support to this theory as they document a patent DSM complicated by thrombosis on subsequent imaging. Similarly, our Cases 1 and 3 lacked any thrombus in the DSM. In Case 2, thrombus nearly filled the DSM, and was accompanied by hydrocephalus and parenchymal injury. Spontaneous resolution of fetal venous sinus thrombosis has been described in one large series, but postnatal spontaneous thrombosis of DSM is a poor prognostic indicator.
The etiology of DSM is not fully understood. According to one hypothesis, DSM is thought to arise from the normal ballooning of the sinuses which occurs between the 4th and 6th months of gestation.1,8,10,16 It is speculated that this relative dilation might in some instances lead to venous hypertension, and development of secondary dural AVF. Venous hyper-tension has been shown in animal models to be associated with the elaboration of Hypoxia-Inducible Factor-1 (HIF-1), an angiogenic signal, and vascular endothelial growth factor (VEGF), the downstream signal of HIF-1.1,12 However, to our knowledge there are no serial antenatal imaging studies, autopsy series or animal models that establish this hypothetical sequence (i.e. abnormal dilation of venous sinuses leading to dural arteriovenous fistulae), and it remains speculative.

In these cases, the dilation of the confluens sinuum per se did not always precede the AVF; in Case 3, a frontal AVF was associated first with a mildly dilated sagittal sinus, yet over the space of weeks, the principal sinus dilation evolved to affect the confluens sinuum. Clearly the venous anatomy is dynamic. If venous hypertension is a primary cause of this AVF; the original venous anatomy cannot be easily inferred from the anatomy of the consequent dural sinus malformation, and is only evident on serial imaging. High flow through the pre-existing AVF appears to have contributed to the morphology of the dural sinus malformation. The AVF may not be simply a passive consequence of venous sinus dilation, but may substantially contribute to the dural sinus malformation. In one published case report, a post-natally identified dural sinus malformation consisting of a dilated confluens sinuum and dural AVFs evolved over three months to result in a massively dilated left lateral sinus as well,18 demonstrating that even post-natally, the dural sinus anatomy is dynamic and responds to high flow. None of the other published pathological descriptions of this entity explore the AVF well described in the radiological literature, and only further careful in utero and post mortem examinations can definitely establish the developmental sequences of the arterial and venous components associated with this malformation.

Our cases depict the varied presentation of arteriovenous shunts associated with DSM. Shunt vessels were not identified on Doppler sonography in any case and were identified antenatally as possible shunt vessels in only one case. Hence, careful autopsy examination of the brain and dural vasculature is essential to identifying the nature of the disease. In Case 1 the dural AVF in the left Sylvian fissure was seen on imaging, but was not identified as a vascular structure. That fistula was thrombosed and organizing by the time of autopsy, and flow through it may have been minimal. The arteriovenous shunt in Case 2 was occult on both US and MR and was only inferred at autopsy. The venous anatomy of Case 2 was that of a DSM, but the associated arteriovenous shunt was midline, of the type typically associated with vein of Galen malformations (VGAMs)19 and while developmental obstruction of the posterior sinuses has been postulated as an event preceding aneurysmal dilation of the vein of Galen,5,20 here the sinuses are dilated, not chronically obstructed. Dural sinus malformations occur at the level of the confluens sinuum-transverse sinus, while VGAMs are centered more anteriorly and superiorly at the vein of Galen, and may show (unlike our case) prominent blood flow with Doppler evaluation.5,14 Finally, in Case 3 the AVF was the dominant feature on radiology at presentation, and the dilated confluens sinuum and straight sinus developed subsequently. In this material, it is clear that either dural, midline, or frontal arteriovenous fistulas can all be associated with radiologically similar venous sinus anatomy.

Accurate prenatal diagnosis of DSM is essential to providing parents with information upon which to base decisions. The current prognosis of DSM identified postnatally is generally unfavorable. Two large series of 19 and 30 patients have documented poor outcomes: 26-37% died, 3-26% had poor neurological outcome, 30-37% had mild neurological deficit and only 7-10% had no neurological deficit.1,3 The more favorable DSM cases, however, had DSM away from the confluens sinuum1,21 and postnatally diagnosed midline DSM had a very poor outcome. Other poor prognostic indicators include large size of pouch and postnatal thrombosis of the pouch: spontaneous thrombosis can compromise the venous drainage of the brain with subsequent venous infarction and intraparenchymal hemorrhage.3,21 Postnatally, DSM and its associated AVF can cause complications including cardiac failure, macrocrania, venous thrombosis and cerebral atrophy.10 However, antenatal thrombosis is not invariably associated with poor prognosis, and in one series seven of ten cases diagnosed in utero had a good neurological outcome;13 complete regression of the malformation with normal infantile neurological function has been described in several cases.9,14,15 In this paper, Case 2 demonstrated significant antenatal injury, with superficial hemosiderosis, massive hydrocephalus, transcortical injury, and gliosis. The brain in Case 3 showed compression of the left frontal lobe by the AVF, but no ischemic or hemorrhagic injury to the brain. By contrast, antenatal injury was not present in Case 1 at autopsy.

Dural sinus malformation is amenable to characterization by prenatal US and MR. As the shunt vessels may be occult on imaging, the presence of a dilated or thrombosed dural pouch in the region of the confluens sinuum and/or superior sagittal or transverse sinuses should alert to the presence of a midline DSM, and an associated AVF should be sought at autopsy. Serial imaging may clarify the behavior of these malformations, and morphological evolution of both the sinuses and feeding fistulas can be documented. Antenatal brain injury can occur, but is not invariably.

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REFERENCES


