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Fetal intracranial tumors: a review of 27 cases

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Abstract Fetal intracranial tumors are rare. The diagnosis is generally made on histology after birth. The aim of this study was to analyze clinical and imaging data in a series of fetal intracranial tumors and emphasize the findings that may help approach the diagnosis antenatally. We retrospectively analyzed imaging and clinical findings in 27 cases of fetal intracranial tumors assessed by ultrasound (27/27) and MR imaging (24/27). A histological diagnosis was always obtained. Main diagnoses included 15 germinal tumors (13 teratomas), 4 glial tumors, 2 craniopharyngiomas and 3 hamartomas. Average gestational age at diagnosis was 27 weeks for teratomas, 21 weeks for hamartomas and 34 weeks for glial tumors. All tumors but one were supra tentorial, and the lesion extended in the posterior fossa in two teratomas. A heterogeneous pattern, which was more frequently seen in teratomas, was better visualized by MR than US imaging. In addition, in two cases of teratomas, MR imaging better assessed the extension of the tumor. Teratomas and gliomas are the most frequent brain tumors in the fetus. US and MR imagings appear complementary in the prenatal assessment of these lesions.

Keywords Fetus · Intracranial tumors · Ultrasound · MRI

Introduction

Intracranial tumors develop rarely during fetal life, accounting for only 0.5–1.9% of all pediatric tumors [1–4]. Over the last 10 years, progress in prenatal ultrasound (US) has improved the detection and diagnosis of this serious disease [5–7]. Fetal intracranial tumors are usually reported during the third trimester and carry a poor prognosis with a global postnatal survival of only 28% [8, 9]. The definite diagnosis of these lesions is generally made after birth based on histology. Yet making a tentative diagnosis during fetal life using imaging techniques may be clinically important to provide the parents with information regarding the prognosis and discuss the management of pregnancy.

The aim of this retrospective study was therefore to analyze clinical and imaging data in 27 cases of fetal intracranial tumors and emphasize the findings that may help approach the diagnosis antenatally.

Patients and methods

We retrospectively reviewed 27 cases of fetal intracranial tumors that were collected through a survey conducted in 11 institutions in France and Belgium by a research group on fetal imaging (the "Groupe de Recherche en Radiopédiatrie et Imagerie Foetale"-GRRIF). The inclusion criteria were the presence of an intracranial mass that was diagnosed as a tumor by obstetrical US and for which a definite histological diagnosis was obtained either on fetopathology or after surgery. Cases of tuberous sclerosis, arachnoid cysts, pericallosal lipomas and vascular malformations were excluded as they did not require surgical

resection and therefore missed histological confirmation. All sonographic examinations were performed by experienced fetal radiologists. Because this is a retrospective study that included cases followed at different institutions over a 14-year period, different equipment and protocols were used for MR imaging; all acquisitions were performed on a 0.5- or a 1.5-T magnet including at least T2- and T1-weighted sequences.

The indication of fetal MR imaging was discussed for each patient by a pluridisciplinary group, and verbal informed consent was obtained from the parents. As requested in multicentric retrospective studies, all data were anonymized for review and publication. The procedure was in accordance with the recommendations of each local institutional board. The Ethics Committee of the Erasme University Hospital gave consent for the whole procedure.

Results

Antenatal US was obtained in all cases and MR imaging in 24/27 cases; in three cases, termination of pregnancy rapidly followed the US diagnosis without any complementary imaging. Main results are summarized in Tables 1 and 2.

Clinical findings

Tumors were detected by US at a mean gestational age (GA) of 28 weeks (range 18–36 weeks), and MR imaging was obtained at 29 weeks of GA (range 22–37 weeks). Histological diagnoses were very variable, including 15 germinal tumors (of which 13 were teratomas), 4 glial tumors, 2 craniopharyngiomas and 3 hamartomas. Three

Table 1 Clinical and imaging findings in 27 cases of fetal brain tumors

Type		Localization (n)	US aspect (n)	MRI aspect (n)	Mean age at diagnosis (weeks)
Germinal tumors (cases1–15)	Teratomas (cases 1–13)	Supratentorial (11)	Heterogeneous: 9	Heterogeneous: 10	27
		Supra+infra tentorial (2)	Homogeneous: 1	Homogen+cystic: 1	
		Intraparenchymal (13)	Homogen+cystic: 3	Cysts: 10	
			Cysts: 12		
			Calcifications: 2	No data: 2	
	Yolk sac tumor (case 14)	Supratentorial and intraparenchymal	Heterogeneous	Heterogeneous	31
	Pineal germinal tumor (case 15)	Supratentorial	Homogeneous	Homogeneous	35
Cranio pharyngiomas (cases 16,17)		Sellar midline	Hyperechogenic: 2	Heterogeneous:1	28
			Heterogeneous: 1	Homogeneous:1	
			Homogeneous: 1		
Hamartomas (cases 18–20)		Supratentorial: 2	Heterogeneous: 1	Heterogeneous:2	21
		Supra–infra tentorial: 1	Homogeneous: 1	Cysts:0	
		Intraparenchymal: 3	Homogen+cystic: 1	No data: 1	
			Cysts: 1		
Glial tumors (cases 21–24)			Hyperechogenic: 2	Heterogeneous:2	34
		Supratentorial: 4	Heterogeneous: 3	Homogeneous:2	
		Intraventricular: 1	Homogeneous: 1		
			Cysts: 1		
Others (cases 25–27)	Choroïd plexus papilloma (case 25)	Supratentorial	Hyperechogenic	Homogeneous	31.5
		Intraventricular	Homogeneous		
	Hemangio-blastoma (case 26)	Posterior fossa	Hyperechogenic		24
			Homogeneous	Heterogeneous	
	Hemorrhagic unspecified tumor (case 27)	Supratentorial	Heterogeneous	Heterogeneous	32

Table 2 Histologic types of tumors

Type of tumors		n
Germinal tumors	Teratomas	13
	Yolk sac tumor	1
	Pineal germinal tumor	1
Glial tumors	Glioblastoma	1
	Malignant astrocytoma	1
	Optical nerve glioma	1
	Oligodendroglioma	1
Craniopharyngioma		2
Hamartomas		3
Others	Choroïd plexus papilloma	1
	Hemangioblastoma	1
	Undifferentiated hemorrhagic tumor	1

cases included miscellaneous diagnoses detailed in Table 2. Five tumors were discovered before 22 weeks of GA, including 2 teratomas (Figs. 1, 2) and 3 hamartomas. Seventeen tumors were detected between 22 and 32 weeks, including 12 germinal tumors (11 teratomas and one yolk sac tumor), 2 craniopharyngiomas, 1 choroid plexus papilloma, 1 hemangioblastoma and 1 unspecified hemorrhagic tumor. Finally, five tumors were diagnosed after 32 weeks, including the four glial tumors and one germinal pineal tumor.

All tumors but one originated from the supra-tentorial part of the brain, and the lesion extended in the posterior fossa in two cases of teratomas. The hemangioblastoma was the only tumor limited to the posterior fossa. Two tumors (one choroïd plexus papilloma and one intraventricular glioma) developed within the lateral ventricules, and the two craniopharyngiomas developed in the supra-sellar region (Fig. 3). The average size of the tumors was 4.6 cm (range 1 to 10 cm) at diagnosis; this value was 7 cm for the teratoma group (range 2.5 to 13 cm).

US imaging

Most tumors had a heterogeneous US pattern (16/27); this was particularly common in teratomas (9/13), but was also seen in craniopharyngiomas, hamartomas and glial tumors. On the contrary, a homogeneous US pattern was less frequent (11/27). Homogeneous solid lesions (5/27) were encountered in a hamartoma, a craniopharyngioma, a pineal tumor, the choroïd plexus papilloma and the hemangioblastoma. The presence of calcifications was unusual, being present in only two teratomas. Cystic components were seen in 12/13 teratomas, but they were also observed in the optical nerve glioma and in 1/3 hamartomas. A fully cystic content was found in only three teratomas and one hamartoma. Doppler investigations were performed in 14 fetuses, with 10 demonstrating vascularization in the lesion and 4 showing no Doppler signal.

MR imaging

In 17 cases, MR and US imaging provided concordant findings regarding the aspect and extension of the lesions. On the other hand, MR and US showed different tumoral patterns in four cases. In three cases, a teratoma, a hamartoma and the hemangioblastoma, the US described a homogeneous lesion that appeared heterogeneous on MR imaging; the converse was observed in the fetus with optical nerve glioma. Furthermore, MR imaging demonstrated unsuspected tumoral extension in three fetuses. In two cases of very large teratomas, MR imaging revealed in one fetus an orbital extension unsuspected on US, and in the other a submeningeal, but extracerebral, lesion which was described as exclusively intra-cerebral on US. In the third case, the hemangioblastoma, the lesion was suspected to be limited to the posterior fossa on US, but MR imaging detected an extension to the pons and medulla.

In our series, the presence of associated anomalies was rare. We found a cleft lip in one fetus with a teratoma and

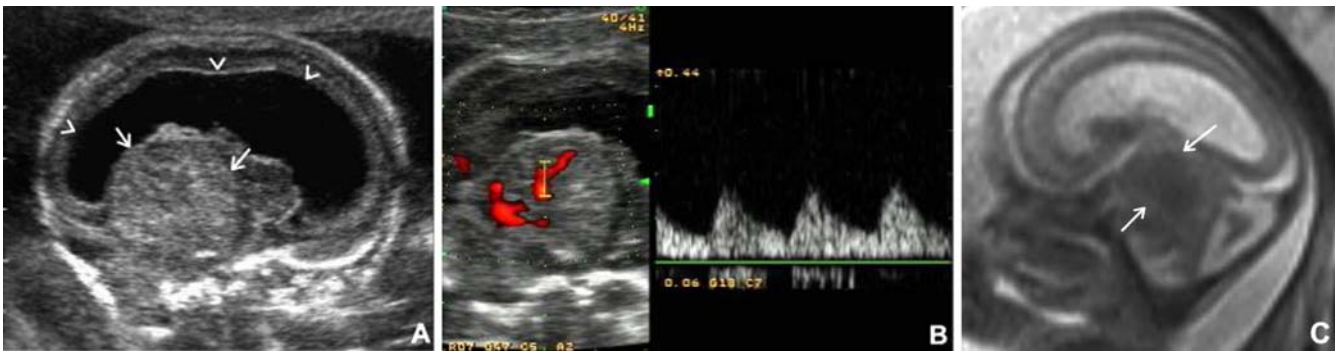

Fig. 1 **A** Sagittal ultrasound scan performed on a 21-week-old fetus showing a homogeneous apparently supra tentorial mass (arrows) inducing marked hydrocephalus (arrowheads). **B** The mass presents arterial flow on Doppler scan. **C** Sagittal T2-weighted MR imaging performed at 22 weeks of GA on the same fetus. The mass (arrows) is slightly heterogeneous and presents in fact a supra- and infra-tentorial extension. Histology confirmed the diagnosis of solid teratoma

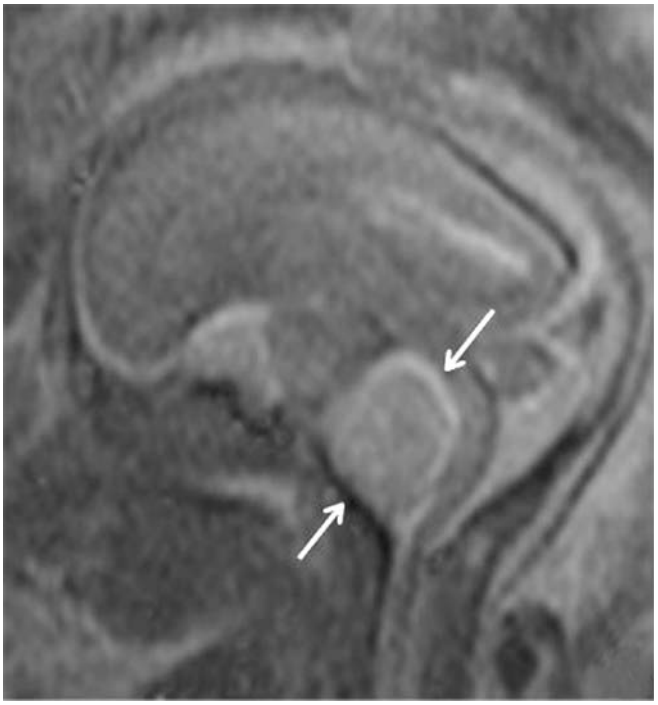

Fig. 2 Sagittal T2-weighted sequence performed on a 22-week-old fetus with a completely cystic supra- and infra-tentorial teratoma (arrows). The differential diagnosis with arachnoïd cyst should be considered

one fetus with a hamartoma; in the latter, there was also a unilateral anophtalmia.

The discovery of fetal brain tumor led to termination of the pregnancy in 23/27 cases; 4 fetuses were delivered at a mean GA of 36.5 weeks. The fetus with a craniopharyngioma is 4 years old at the present time and has panhypopituitarism, growth failure and seizures. The fetus with optic nerve glioma is presently 6 years old and has anomalies in ocular motricity. Finally, the fetuses with glioblastoma and pineal tumor died at 1 day and 2 months, respectively.

Discussion

Because intracranial fetal tumors are very rare, the literature includes primarily single case reports [10–12]. To the best of our knowledge, we provide in this study the largest series ever reported. In our patients, the frequency of the different types of tumors varied with gestational age. Before 22 weeks, the histological diagnoses we encountered more frequently were teratomas [13] and hamartomas [14]. The germinal tumors were frequent (13/17) between 22 and 32 weeks, and glial tumors after 32 weeks (4/5). On average, gestational age at diagnosis was 27 weeks for teratomas, 21 weeks for hamartomas and 34 weeks for glial tumors. Although various histological types were found, germinal tumors were by far the most frequent (15/27), with a predominance of teratomas (13/15) as reported in previous publications [15–19]. The second more frequent diagnosis was gliomas (4/27) [20–23]. We did not encounter neuro-ectodermal tumors (PNET), though these tumors have been described perinatally [8, 9].

Imaging

Tumoral appearance In teratomas, a heterogeneous pattern with cystic lesions on both US and MR imaging was a frequent finding (Fig. 4). We found, however, that due to its better contrast resolution, MR imaging was more sensitive than US for the detection of this heterogeneity. The rapid growth of these tumors and their propensity to contain necrotic parts probably explain this observation [12]. An additional factor is that these tumors contain tissue from the three different germ cell layers. Cysts are

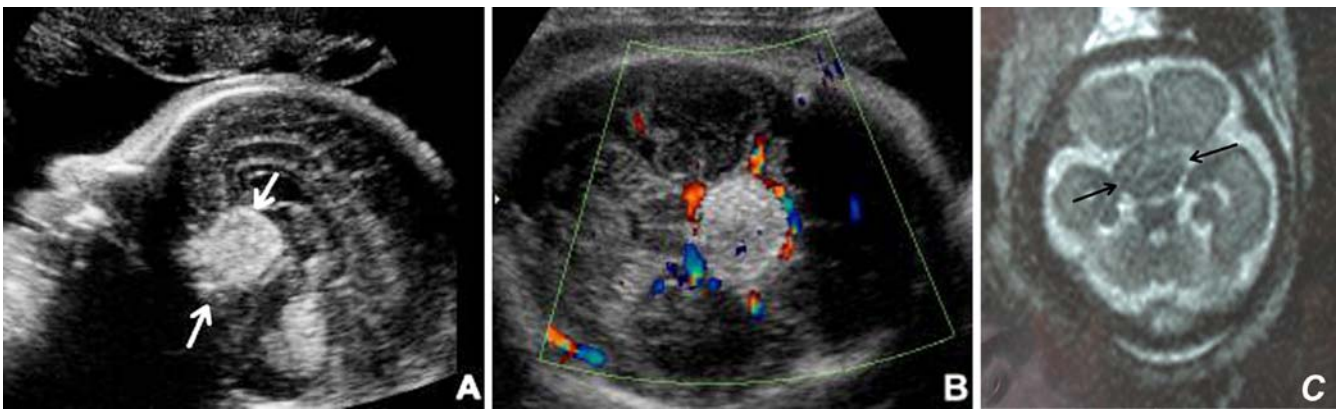

Fig. 3 **A** Midsagittal ultrasound scan of a 29-week-old fetus with an homogeneous supra-sellar mass (arrows). **B** The mass presents Doppler flow in its periphery. **C** Axial T2-weighted sequences performed at 30 weeks of GA. The mass appears well delineated and homogeneous (arrows). A craniopharyngioma was diagnosed at histology

frequent in teratomas (12/13), which may sometimes be completely cystic (Fig. 2). These cysts correspond to necrotic lesions and are uncommon in other types of tumors (3/14). In addition to the cysts, the heterogeneous appearance of the tumor may relate to hemorrhagic components (Fig. 5); these, however, are more frequent in gliomas. These components can be easily detected on T1 and T2* sequences, but it may be difficult to make the differential diagnosis with extensive intraparenchymal hemorrhages. Although the Doppler studies performed in our cases were not informative in this regard, we think a Doppler study should always be performed as it can be helpful to differentiate solid vascularized [24] from hemorrhagic lesions.

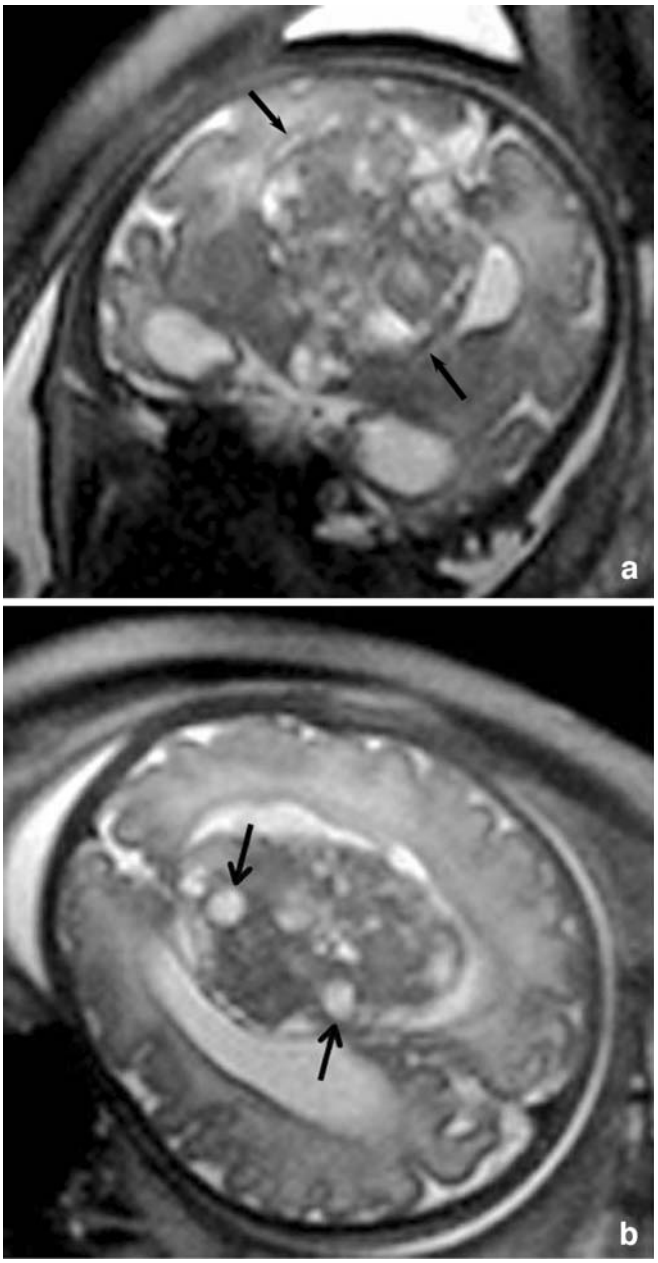

Fig. 4 A,B Coronal and axial T2-weighted MR sequences performed on a 32-week-old fetus with typical heterogeneous supratentorial teratoma. Cystic lesions are classical (arrows)

Tumoral extension Because teratomas and gliomas are often large lesions, US may not be optimal to assess tumoral extension. In two cases of teratomas, MR imaging better assessed the extension of the tumor due to its larger field of view and contrast resolution. Determining precisely the extension of the tumor and the degree of involvement of adjacent structures is obviously of primary importance as far as the prognosis, the potential of the lesion for surgical resection and the possible sequels of surgery are concerned.

Protocols Based on the present report, we suggest that MR imaging should be included in the assessment of fetal intracranial lesions [25, 26]. We propose the following protocol, which will require validation in a prospective study. Acquisitions are made using a 1.5-T magnet with a phased-array body coil and include 12 to 20 slices in the coronal, sagittal, and axial planes relative to the fetal head; these are T2-weighted turbo spin-echo sequences (TR/TE, 5324/140 ms; duration, 19 s) without mother respiratory triggering. In addition, T1-weighted images are acquired with a turbo field echo sequence with inversion prepulse to enhance the T1 contrast (TR/TE, 18/6.9 ms; angle, 22°, inversion time, 1354 ms, duration, 4 min). Furthermore, whenever a hemorrhagic lesion is suspected on T1 sequences, T2* sequences (TR, 3,000 ms, TE, 270 ms, duration, 15 s) should be added as they are particularly sensitive in detecting blood degradation components [27, 28]. The field of view is of 340 mm in order to avoid wrap-around artifacts, and slice thickness is 3 to 4 mm.

Impact on the management of pregnancy

In this series, the diagnosis of brain tumor led to termination of the pregnancy in 23/27 cases. Only four fetuses were delivered, and two of them died in the neonatal period. This gives rise to the difficult ethical question of when it is legitimate to consider medical termination of pregnancy. Legal issues may limit the practical relevance of this question. Medical termination of pregnancy is authorized under restricted conditions whatever the gestational age by the Belgian and French laws, but the legislation is more restrictive in many countries and prohibits termination of pregnancy after the second trimester. In Belgium and France, termination of pregnancy is always discussed with the parents in the dramatic context of fetal brain tumors. This is why it is critical to have the most precise information regarding the tumoral nature and the extension of the lesion. In addition, even when the

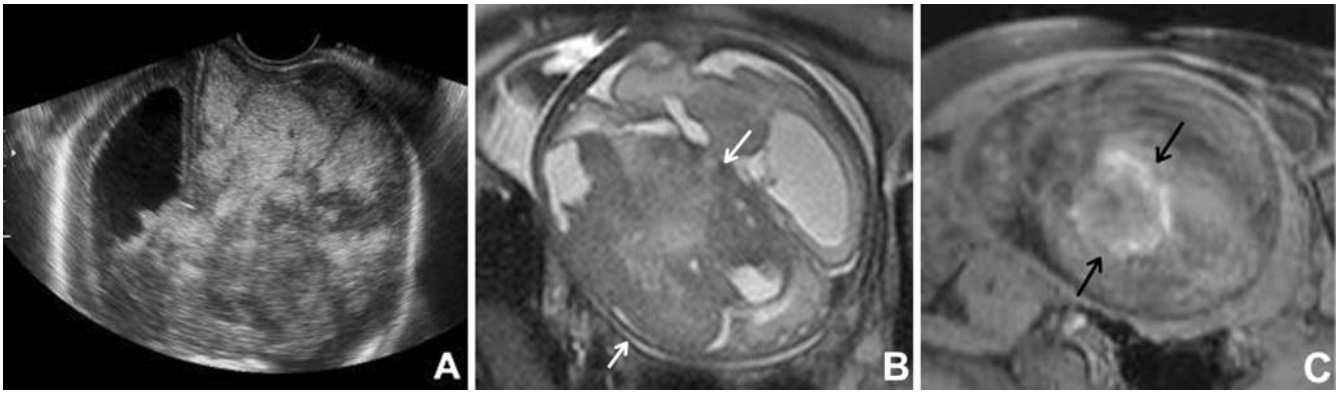

Fig. 5 **A** A coronal ultrasound scan of a 32-week-old fetus with an heterogeneous supratentorial hemispheric mass responsible for complete loss of the normal brain architecture. **B** Axial T2-weighted sequence shows intra- and extra-cerebral development of the mass (arrows). **C** T1-weighted sequence shows hyperintense portions (arrows) attesting of hemorrhagic components in the mass. An hemorrhagic and necrotic tumor of unspecified nature was confirmed on histology

parents do not opt to terminate pregnancy, the precise diagnosis provided by antenatal imaging may help health-care professionals prepare them for the neonatal outcome.

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