Case report - **Extracardiac Malformation**

MALIGNANT FETAL BRAIN TUMOR - DIAGNOSIS, MANAGEMENT, PROGNOSIS. CASE REPORT AND LITERATURE REVIEW

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Abstract

A case of the rare fetal brain tumor is presented. This initally was observed as bleeding and ventriculomegaly and it was diagnosed at 28th week gestation by 2D, 3D and TUI ultrasound. The patient remained under the perinatal care until the end of pregnancy: cesarean section was performed at 37th week of gestation. Despite neurosurgery, the baby died on the 3rd day of postnatal life. On the basis of histopathological examination the diagnosis was established such as highly malignant tumor with focal ependymal and neuronal differentation that expands the current histopathology tumors classification.

Key words: *brain tumor, ventriculomegalia, 3D, TUI*

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Congenital malignant brain tumors are very rare. The prognosis is difficult to assess because it depends on tumor size, location and histologic type, which cannot be predicted on the basis of imaging techniques alone. Final diagnosis of the tumor type is possible postnatally after biopsy and neuropathology. A longitudinal observation of prenatal changes of a fetal brain tumor with its unusual histopathology has not been previously reported.

CASE REPORT

A 32-year-old healthy woman with an uncomplicated first half of prenatal course. Medical history: First pregnancy - blighted ovum, second pregnancy - postnatally diagnosed craniostenosis. In this 3rd pregnancy, the ultrasound (US) at 12th and 22nd week was described as normal. At the 28th week, US revealed ventriculomegaly and two masses: the first in anterior cranial fossa around the frontal right corner of the lateral ventricle which was heterogeneous and irregular, and the second, a hypoechogennic, regular, oval shape located below the central part of the left lateral ventricle leading to asymmetric ventriculomegaly (Vp left 20mm, Vp right 16mm) with enlargement of the IIIrd ventricle (7mm). The ependymal lining of the lateral ventricle was hyperechogenic with an irregular surface (Fig. 1, 2). On the tumor surface, vessels were visualized by HD power Doppler imaging. The fetal head circumference was adequate for gestational age. In the middle cerebral artery (MCA), the blood flow had reduced resistance. The circulatory system of the fetus was otherwise normal, as well as the amniotic fluid index. The pregnant woman was directed to the reference center. Fetal MRI and echocardiography confirmed the presence of a fetal brain tumor and normal heart anatomy with no functional anomalies in the circulatory system. Testings for intrauterine infection and for bleeding disorders were negative. Fetal brain US performed at 30 wk of gestation revealed further ventricular dilatation possibly due to bleeding (Fig 1). At the 36th week of gestation, the tumor size was twice as big as that in the 28th week of gestation. The brain tumor was established as possibly malignant. Due to spontaneous contractile activity at the 37th week, the infant was born via caesarean section at the local hospital, close to the place of maternal residence. The male newborn had a birth weight of 2730g and an Apgar score of 2/4/4 in 1/5/10 min, and was transferred to the Neurosurgical Department of the University Children's Hospital in Krakow in severe condition. After a CT head scan, neurosurgical treatment was attempted, but the infant died on the 3rd day of life. Neuropathological evaluation (see also figure 6).

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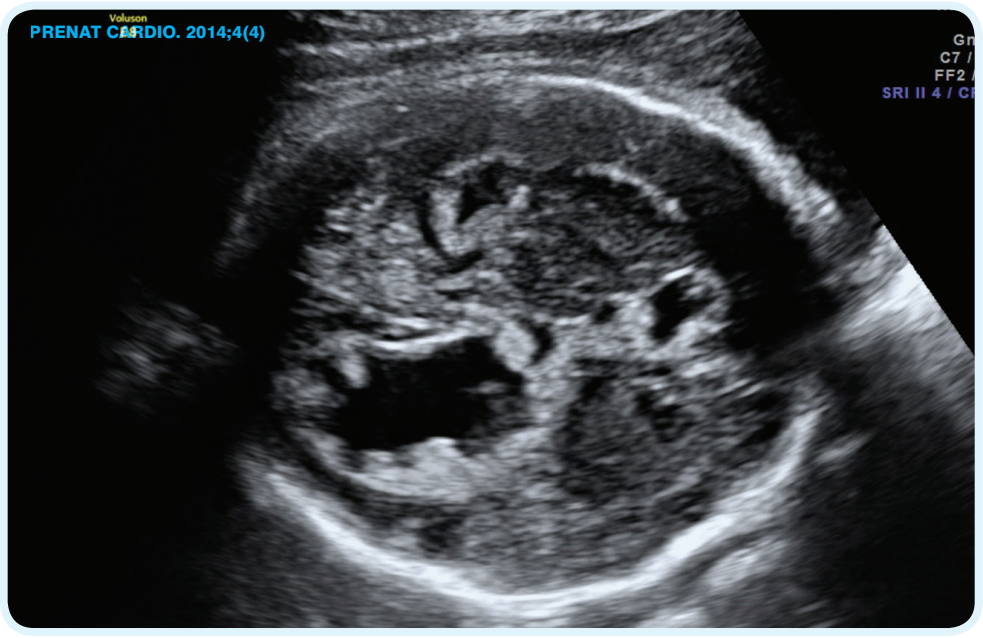

Figure 1. Fetal brain at 30th week of gestation suggestion previous bleeding and postbleeding ventricular dilatation of the lateral ventricle. Increased thickness of the ventricular walls of both ventricles suggested infection.

The histological workup showed a moderately cell dense, moderately pleomorphic tumor, morphologically of glial differentiation. The tumor cells were embedded in a fibrillary matrix and demonstrated a homogenous eosinophilic cytoplasm with irregularly configurated nuclei and moderately dense chromatin with brisk mitotic activity (12 mitoses in 10 HPF/40). We did not observe endothelial proliferation or necrotic areas. Occasionally, the tumor cells appeared in perivascular pseudorosettes.

By immunohistochemistry, the tumor cells showed strong and diffuse cytoplasmatic and fibrillary immunopositivity for glial fibrillary acidic protein (GFAP) and occasionally for epithelial membrane antigen (EMA) in "dots". Also patchy focal positivity of tumor cells for synaptophysin is seen. INI1 is regularily retained in nuclei, the tumor cells are negative for pan-cytokeratin (Lu-5) and heavy and light neurofilaments (200 & 70 kDa).

COMMENT ON THE NEUROPATHOLOGY

Our neuropathological work-up of this specimen showed a moderately cell dense, moderately pleomorphic tumor of mainly ependymal differentiation (i.e. occasional perivascular pseudorosettes best seen with GFAP, and "EMA dots"), as well as with focal positivity for synaptophysin suggesting focal neuronal differentiation, although immunoreactivity for synaptophysin may be seen also in non-neuronal tumors. However, these foci seem to have a more loose texture and slightly larger cells.

Hence this neoplasm is best described as congenital, highly malignant brain tumor with ependymal and focal neuronal differentation. We think that such congenital tumors do not have to necessarily fit into the usual WHO classification scheme.

DISCUSSION

Brain tumors diagnosed within 2 months after birth are considered as congenital; their incidence is estimated at 0,5 -1.9% tumors in childhood[1]. Only some of these cases are diagnosed prenatally, because brain tumors are less common in fetuses than in children[2] . The following series confirm how rare this pathology of fetuses and newborns is: Buetow at al.: 45 cases postnatal diagnoses of congenital tumor in the years 1964-1989[2]; a study by Nejat Feridek at al.[3]: seven cases of congenital brain tumors in newborns (recorded in 2000-2005), of which only 2 were diagnosed prenatally; and the Belgian – French study (Groupe de Recherche GRRIF en Radiopédiatrie et Imagerie fetale) where eleven centers

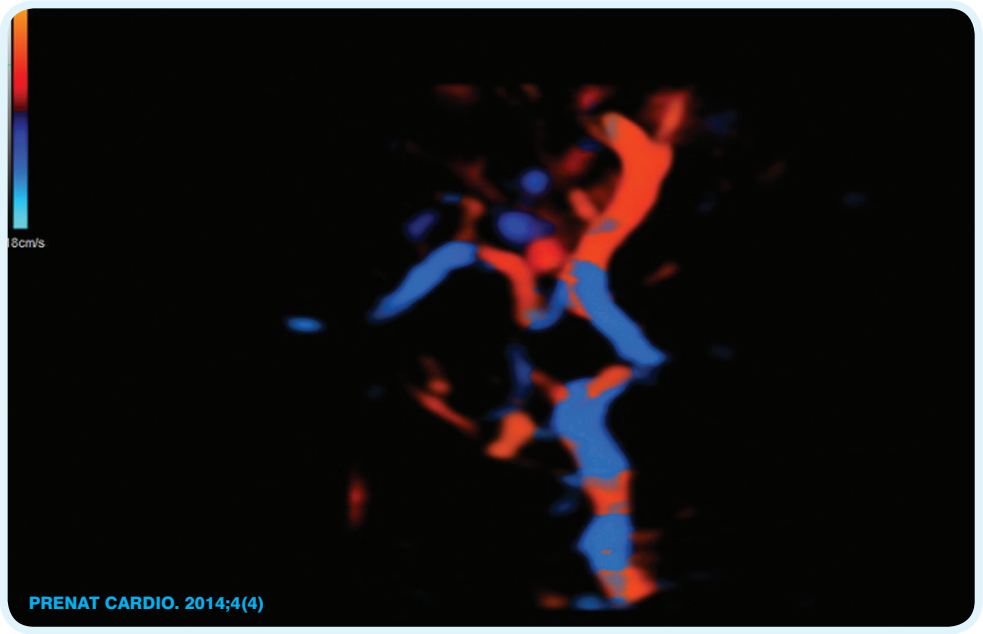

Figure 2. Asymmetrical vessels of the fetal brain at 30 wks of gestation

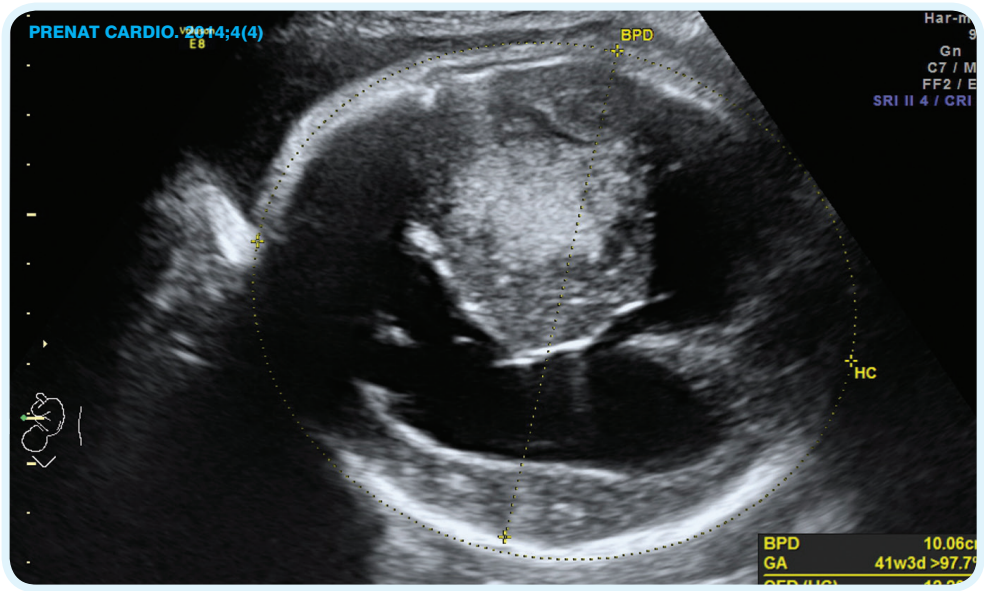

Figure 3. 6 weeks later , at 36 wks evident fetal brain tumor causing bilateral ventriculomegaly

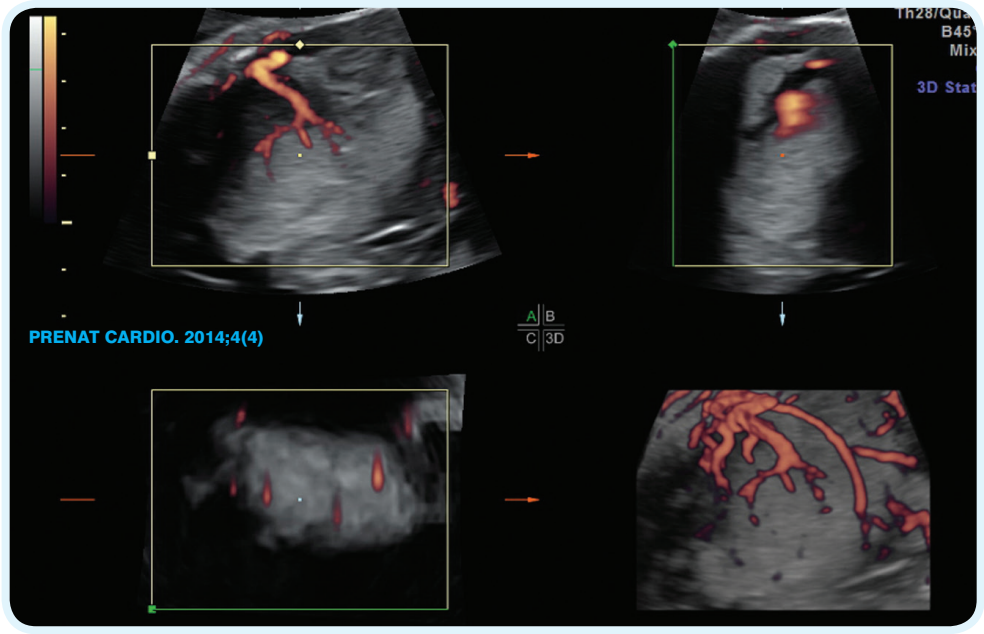

Figure 4. Increased vascularity of the fetal brain in power angio Doppler

for 14 years had included 27 cases, published in 2008[4]. The collection of a large group of cases was possible only through a meta-analysis of data from literature: Isaacs at al.[1] (2002) - their series consisted of 250 cases of brain tumors in fetuses or newborns, and M.Respondek-Liberska (2009)[5] who presented a meta-analysis of 92 cases of brain tumors in fetuses. The collected information in these series showed that the most common fetal tumors are teratomas and then gliomas[4,5].The most common symptoms of a prenatal brain tumor appears in the third trimester: ventriculomegaly especially asymmetric, heterogeneous lesion with cystic or solid component, sometimes with calcifications. Some types of tumors may show excessive vascularization (teratomas)[4,5] . Brain tumors may cause bleeding into the ventricles or tumor [3]. In such a case it can lead to fetal heart failure[5] .

The prognosis for a fetal brain malignant tumor is obviously serious. It depends on the tumor size, location, but primarily on the histologic type, which cannot be fully predicted based on imaging techniques. Final diagnosis as to the type of tumor is possible only postnatally after biopsy and neuropathological examination.

Neonatal survival in cases of congenital brain tumor by Isaac was approximately 28%[2], but according to Respondek-Liberska's[5] experience high survival applies only to sporadic cases of benign tumors (lipomas, tuberous sclerosis). According to the experience of neurosurgeons, children with choroid plexus papillomas, gangliogliomas and low grade astrocytomas have obviously the best prognosis, while teratomas and primitive neuroectodermal tumors have an extremely poor prognosis[2].

The prenatal ultrasound diagnosis of a brain tumor is difficult but the number of cases has been growing steadily. The tumor is usually noticeable if its diameter exceeds 10 mm[2] . The ultrasound pattern of a brain tumor can be heterogeneous and unnoticed by the less experienced ultrasonographer. Ventriculomegaly, particularly asymmetrical[6] is easy to spot and is often the first but late symptom, which is the basis for further investigation, as in the presented case. The differential diagnosis for a brain tumor should include: tuberous sclerosis, CNS bleeding, intrauterine infection, arachnoid cysts or vein of Galen aneurysm[7]. Further care and supervision of the fetus with a brain tumor is very important because of the lesion growth rate or possible prenatal fetal heart failure which may influence the newborn's prognosis. Delivery should take place in a referral center to avoid external transportation of a sick neonate, to provide optimal care and complete diagnosis. In case described here, the final neuropathological diagnosis was established outside of Poland: highly malignant brain tumor with focal ependymal and neuronal differentiation.

CONCLUSION

The presented case illustrates a rare type of fetal brain tumor associated with bleeding and secondary ventriculomegaly (observed from 28 weeks of gestation until the newborn's demise) that added expands the histopathology of the current brain tumors classification.

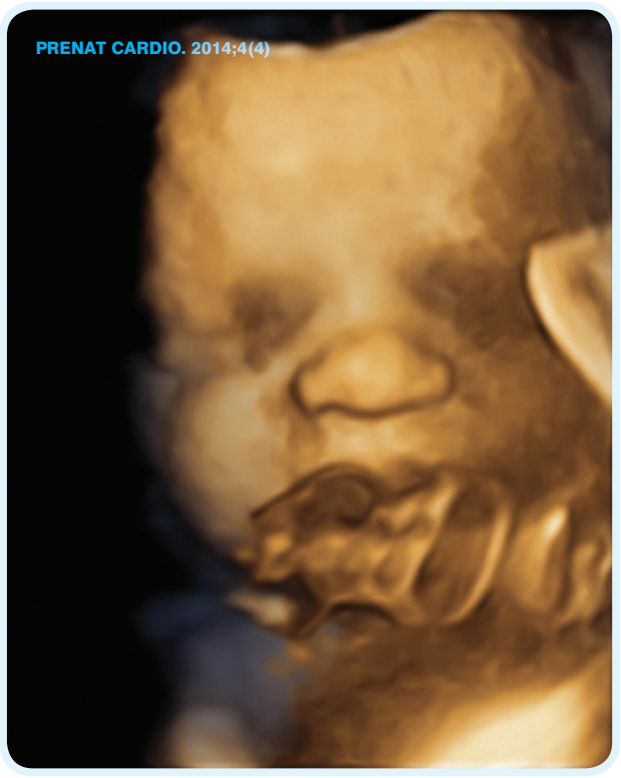

Figure 5. No signs of dysmorphia or forehead abnormality in 3D presentation of the fetal face.

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Authors and the division of work:

A. Nawara-Baran – initial diagnosis, literature search, first draft, submitting manuscript

K. Frontzek and H. Budka – histopathology evaluation and explanation, English corrections

P.P. Liberski – histopathology evaluation - English corrections, final version of the manuscript.

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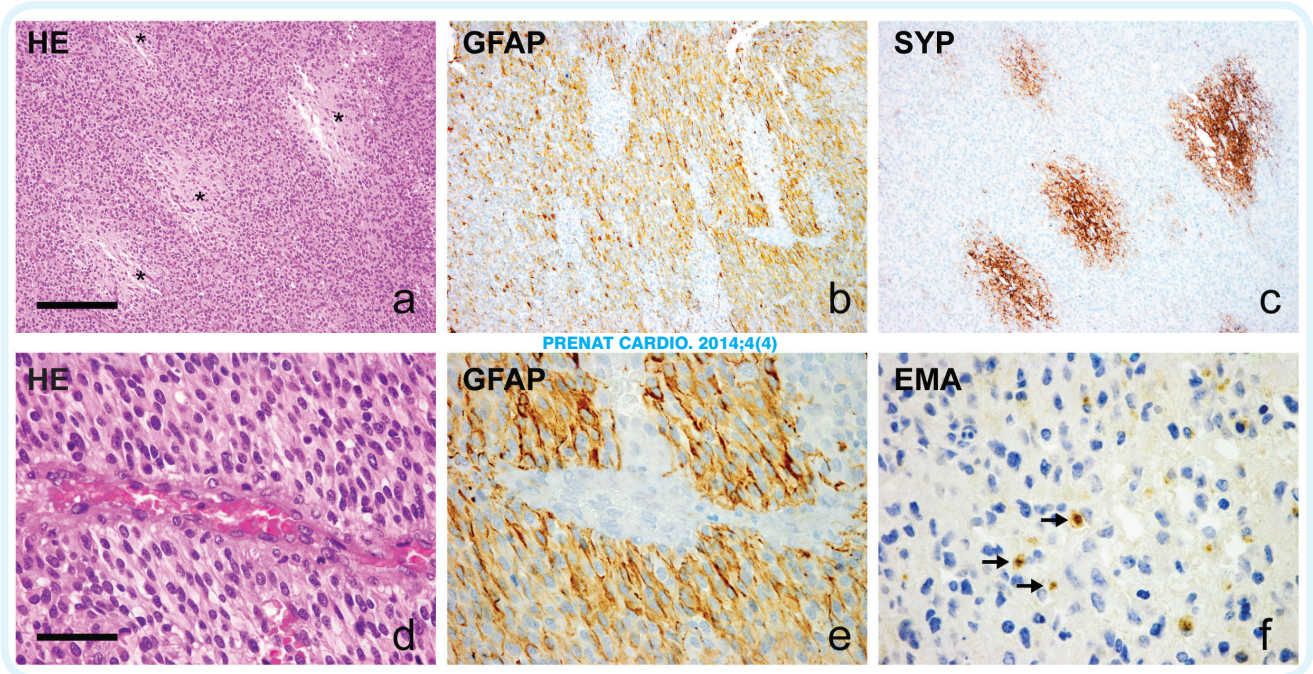

Figure 6. Neuropathological work-up showed a moderately pleomorphic tumor embedded in a fibrillary matrix. On occasion, pale areas were observed in H&E staining (a, asterisks) that were spared from immunopositivity for glial fibrillary acidic protein, GFAP (b) but exhibited strong and diffuse positivity for synaptophysin (c). Tumor cells further appeared to be organized in perivascular pseudorosettes (d) that showed diffuse perivascular positivity for GFAP (e). Rarely, immunohistochemical analysis for epithelial membrane antigen, EMA, demonstrated "EMA-dots" (f, arrows). a-c scale bar = 200 µm, d-f scale bar = 50 µm