




# Early Second-Trimester Spontaneous Miscarriage Due to Fourth Ventricle Choroid Plexus Papilloma

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**Abstract** Miscarriage due to fetal tumors is an extremely rare finding, with a varying incidence from 1.7 to 13.5 per 100,000 live births, with central nervous system tumors occupying a minority of these cases. Herein, we report the gross morphological and histological findings of a 17-gestational week spontaneous miscarriage in a 27 year old multi-gravida due to a fourth ventricle choroid plexus papilloma (CPP). The CPP was composed of a pronoun fibro-vascular stroma covered with a dense lining of tall cuboid sparsely ciliated single cell layer with rich in chromatin nuclei. The cytoplasm of the CPP covering cells was intensely colored when compared to the pale cytoplasm of the covering cells of the choroid plexus collected from the lateral ventricle, which also lacked in such pronoun fibrovascular stroma. The fourth ventricle was significantly dilated with parenchymal compression of nervous tissue towards the chondral fetal cranium.

**Keywords** Spontaneous miscarriage · Fetal tumor · Choroid plexus papilloma · Turner syndrome

## Introduction

Spontaneous miscarriages are the most severe complication in early pregnancy [1]. The reported figures (5% and 20% of all recognized pregnancies) vary from population to population, based on ethnicity, demographics, risk factors and prevention programs. In most cases, the underlining reason for miscarriage is chromosomal abnormalities, predominantly in the first trimester; advanced maternal age and exposure to environmental and habitual risk factors in the second and third trimester.

Miscarriage due to fetal tumors is an extremely rare finding, with the incidence varying from 1.7 to 13.5 per 100,000 live births, with central nervous system (CNS) tumors comprising a minority of these cases [2]. In most of these cases, however, the findings and diagnosis are ultrasound-based, with a following termination of pregnancy due to medical reasons and no follow up by histological verification. Although extremely valuable, ultrasound investigations do not allow a certain differential diagnosis between tumor and non-tumor growths, such as malformations.

## Report of Case

Herein, we report the gross morphological and histological findings of a 17 gestational week (GW) spontaneous miscarriage from a nulliparous 27-year-old multigravida, with a family history of a brother with an unspecified syndrome and a single previous spontaneous miscarriage. A

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trophoblast biopsy had been performed in the 15 GW of the current pregnancy and Turner syndrome (TS) had been documented. For that reason, a medical abortion was scheduled, however upon admission a spontaneous miscarriage had already commenced and was followed through without complications. Upon delivery, the fetus showed no signs of life, Apgar score was 0 and the fetus was determined to be stillborn.

No gross morphological changes were observed and the female gender was confirmed. The fetus was then frozen at  $-80^{\circ}\text{C}$ , approximately 10 min after birth. After a freezing period of 24 h, the fetus was dissected in conditions of maintaining continuous freezing.

### Pathological Findings

Upon opening of the cranial cavity, a diffuse subdural hematoma was observed. The cerebrum and parts of the cerebellum fractured upon extraction of the CNS and revealed a dilated lateral ventricular system, with a diffuse intraventricular hemorrhage and a thin cerebral parenchyma. The foramen magnum was enlarged, measuring 0.9 cm in diameter and was collected together with the CNS tissue adjacent to it. The remainder of the dissection revealed no abnormalities apart from an accessory left kidney.

The collected specimens were fixed in 10% buffered solution of formaldehyde and embedded in paraffin (FFPE) for staining with hematoxylin and eosin (H&E) and cresyl violet (CV). The histological evaluation of the FFPE under the H&E stain revealed a choroid plexus papilloma (CPP) in the fourth ventricle measuring 5 mm in size (Fig. 1a, b). The CPP was composed of a pronoun fibro-vascular stroma covered with a dense lining of tall cuboid sparsely ciliated single cell layer with rich in chromatin nuclei (Fig. 2a, b). No signs of atypia were observed in the CPP covering cells,

such as giant cells, varying cell and nuclear size, and composition. The cytoplasm of the CPP covering cells was however intensely colored, resembling early fetal choroid plexus cells prior to the 8 GW (Fig. 3a, b). The fourth ventricle was significantly dilated with parenchymal compression towards the chondral fetal cranium.

The telencephalon specimen revealed decreased cortical thickness with significantly dilated lateral ventricles. On the H&E stain, the choroid plexus of the lateral ventricles had normal cytoarchitectonics, no abundant fibro-vascular stroma and glycogen-rich cuboidal covering cell with clear cytoplasm (Fig. 3c, d). Under the CV stain, the cells of the CPP and the choroid plexus of the lateral ventricle revealed no difference in their staining characteristics (Fig. 3b, d).

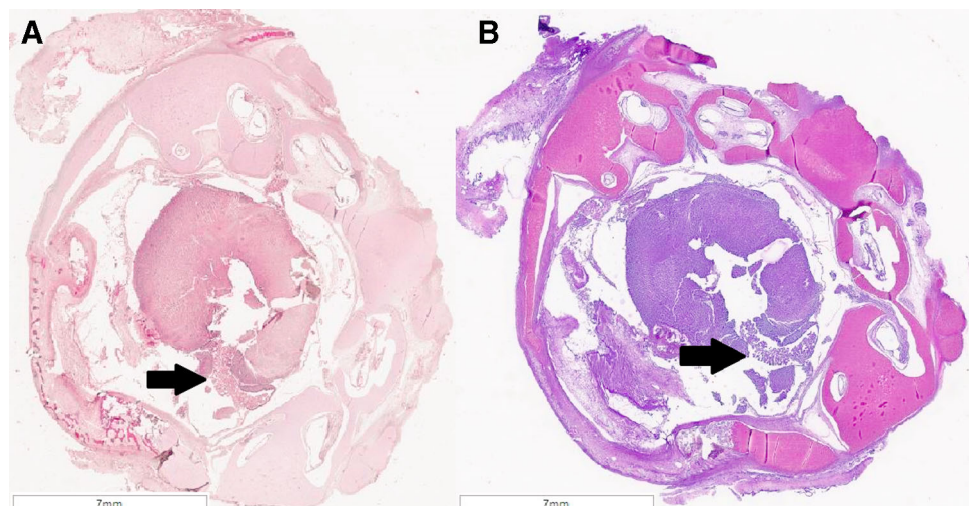
CPP is an extremely rare benign tumor entity, accounting for less than 1% of intracranial tumors (ICT) overall and around 5% of pediatric ICTs [3]. Fourth ventricle CPP is an extremely rare finding in fetal and neonatal pathology, as nearly all CPP in this group are of the lateral ventricles, whilst fourth ventricle CPP is usually observed in adults.

### Discussion

Although the presence of CPP, exclusively diagnosed via ultrasound, and other fetal CNS tumors is often associated with an underlying genetic syndrome, TS is very rarely associated with such a condition. Further on, the presence of CPP in the fetal, neonatal and childhood period is almost always exclusive to the lateral ventricles, whilst third and fourth ventricle CPP is more often associated with the adult population.

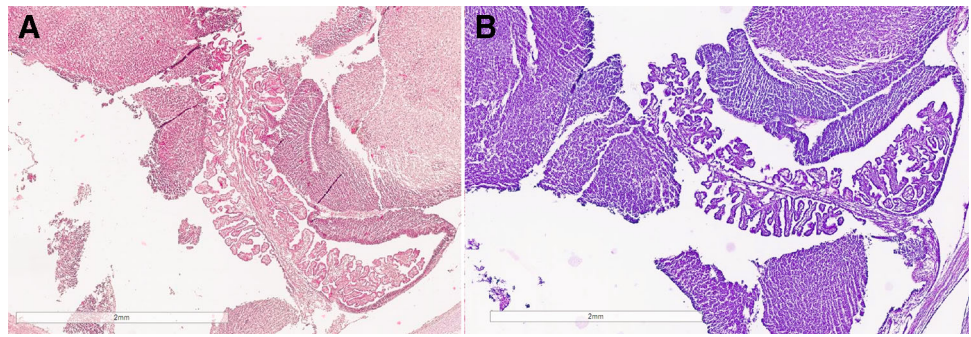
CPP whilst uncharacteristic of TS, is characteristic of another syndrome, which has been reported to coexist with TS in some cases and a prominent cause for miscarriage—Aicardi syndrome (AS) [4, 5]. AS is a rare X-linked genetic

**Fig. 1** Fourth ventricle with adjacent parts of cerebellum, medulla oblongata and the CPP (arrow) on H&E (a) and CV (b). Original magnification  $\times 2$

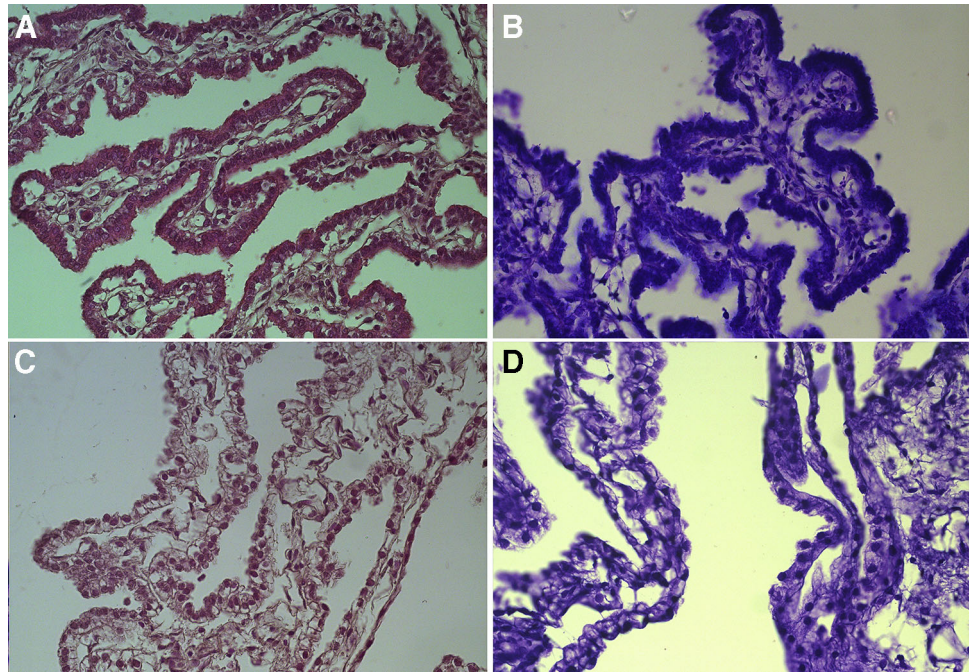




**Fig. 2** CPP—H&E (a) and CV (b). Original magnification  $\times 200$



**Fig. 3** Covering cells of the CPP—H&E (a) and CV (b) and internal control with covering cells of the choroid plexus of the lateral ventricle—H&E (c) and CV (d). Original magnification  $\times 400$



syndrome with a yet unidentified cause, resulting in a number of tumors in different locations in the fetal, neonatal and early childhood period, the most prominent of which is CPP. To our knowledge, this is the first reported case of an early first trimester spontaneous miscarriage with a histologically verified CPP of the fourth ventricle.

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#### Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Informed consent** Informed consent was obtained from all participants.

#### References

1. Regan L, Rai R. Epidemiology and the medical causes of miscarriage. *Best Pract Res Clin Obstet Gynaecol.* 2000;14(5):839–54.
2. Cho JY, Lee YH. Fetal tumors: prenatal ultrasonographic findings and clinical characteristics. *Ultrasonography.* 2014;33(4):240–51.
3. Prasad GL, Mahapatra AK. Case series of choroid plexus papilloma in children at uncommon locations and review of the literature. *Surg Neurol Int.* 2015;6(1):151.
4. Pianetti Filho G, Fonseca LF, da Silva MC. Choroid plexus papilloma and Aicardi syndrome: case report. *Arq Neuropsiquiatr.* 2002;60(4):1008–10.
5. Spennato P, La Porta A, Varone A, Ruggiero C, Buono S, Cinalli G. Aicardi and Turner syndrome in a 45,X0/46,XX female. *Clin Neurol Neurosurg.* 2013;115(6):820–2.