Clinical Case Report

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Hydrocephalus secondary to chemotherapy in a case of prenatally diagnosed giant immature grade 3 sacrococcygeal teratoma

A case report and literature review

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Abstract

Introduction: Sacrococcygeal teratoma (SCT) is a rare tumor in the general population, arising from multipotent stem cells. Whereas most of the cases diagnosed postnatally have good prognosis, the rate of mortality and morbidities associated with prenatally diagnosed SCT remain high, with a reported mortality rate of 30% to 50%. The outcome of fetal SCT can be unpredictable, with some cases with slow growth during fetal life, whereas others grow rapidly, causing multiple complications; also, some of these tumor will develop triggering fetal (preterm delivery, high-output cardiac failure, hydrops fetalis, intrauterine death) or maternal complications (distocia, placentomegaly, maternal mirror syndrome—preeclampsia). Even if prenatal criteria seem to define tumors at risk, it can not totally predict postnatal outcome as treatment-related complications can occur.

We present a case of giant prenatally detected SCT. The case was diagnosed at 24th week of gestation, and was closely monitored by serial ultrasound. The morphology of the lesion was defined by fetal MRI performed at 25th week of gestation. A baby girl with a huge sacrococcygeal tumor was born and surgery was performed 48 hours later. Pathological examination revealed a grade 3 immature teratoma. Because of the tumor size and pathological aspect, adjuvant chemotherapy was considered. The outcome was complicated by wound infection, sepsis, and subsequent hydrocephalus, induced by chemotherapy-induced immunosuppression.

Conclusion: Our case emphasizes not only the importance of prenatal monitoring of these cases but also the importance of individualized postnatal management, as unusual and unpredictable complications can occur and affect outcome.

Abbreviations: AFP = α-fetoprotein, BEP = protocol of chemotherapy (bleomicyn, etoposide, and cisplatin), CT = computed tomography, MRI = magnetic resonance imaging, SCT = sacrococcygeal teratoma.

Keywords: chemotherapy, fetal MRI, hydrocephalus, immature teratoma, prenatal diagnosis, sacrococcygeal teratoma

1. Introduction

Sacrococcygeal teratoma (SCT) represents the most common tumor of the neonatal period, and accounts for 35% to 60% of all teratomas,[1] but they are rare lesions, with an incidence of 1 to 35,000 to 40,000 births.[2] In recent decades, an increasing number of SCT have been detected by prenatal ultrasound examination of the fetus. Antenatal diagnosis of these tumors helps to establish the extension of the tumor, its effect on fetal development (fetal hydrops, polihydramnios), the presence or absence of tumor hemorrhage, and the rate of fetal growth. Fetal magnetic resonance imaging (MRI) is an adjuvant tool used for better definition of this condition. Correct prenatal evaluation of fetuses with SCT is important for establishing prenatal (fetal therapy in selected cases) and postnatal management of these cases.

2. Case report

We present a case of a female fetus, diagnosed by prenatal ultrasound with a sacrococcygeal tumor at 24th week of gestation. The pregnancy had been followed up regularly until the moment of the morphology scan, when the tumor was for the first time identified. At that moment, the lesion measured 36 × 26 mm, with a nonhomogenous appearance on the ultrasound sections, with no signs of fetal hydrops or placentomegaly. One week later, the fetal MRI investigation revealed a sacrococcygeal lesion with a mixed structure, with solid and cystic elements, measuring 38 × 35 × 30 mm (Fig. 1). The scan had also revealed some degree of placentomegaly, and no other morphological

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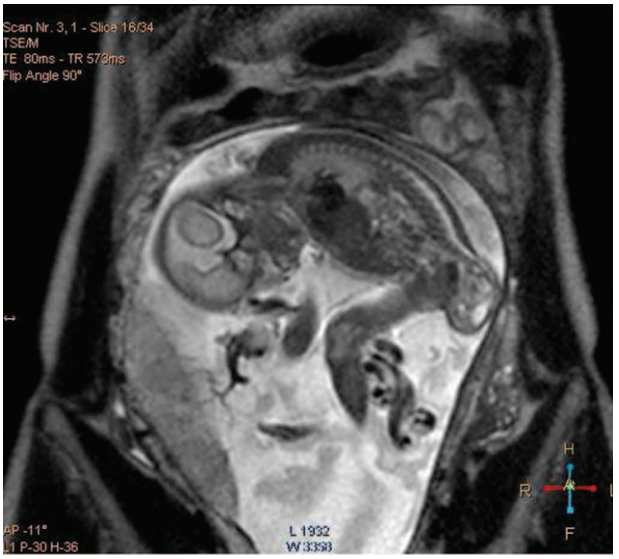

Figure 1. Fetal MRI. Note the sacrococcygeal lesion. MRI = magnetic resonance imaging.

abnormalities. This appearance was suggestive at the moment of an Altman type I SCT.

Considering the supposed diagnosis, the fetal age, and the dimension of the lesion, a close outpatient ultrasound and external fetal and mother monitoring was decided to be appropriate in this case. Seriate ultrasounds were done to appreciate the fetal and tumor growth (Table 1), signs of fetal hydrops, or placentomegaly.

Table 1

Tumor growth according to age of pregnancy.

Fetal age (wks)	Dimension of the tumor, mm
25	32/34
28	53/37
30	69/50
32	96/79
34	108/94
39	130/90

There was no aggravation of the fetal or mother status, so a female infant was born at 39 weeks of gestation by a scheduled caesarean section. The child weighted 3850 g and had an Apgar score of 9 at 5 minutes. A large sacrococcygeal lesion was confirmed at postpartum examination, with a diameter of 22 cm (Fig. 2). Thirteen hours later, with good vital parameters, she was transferred to the Neonatal Intensive Care Unit of the Pediatric Surgery Department for proper management and cure. Biological and imagistic (abdominal, transfontanelar, and cardiac ultrasounds) examinations were done in the first 48 hours of life, which revealed no significant associated abnormalities. A type I Altman tumor was confirmed. The serum markers showed an elevated level of α-fetoprotein (AFP) (>4425.29 UI).

On the second day of life, the child underwent surgical excision of the sacrococcygeal tumor, with early ligation of the medium sacral artery, coccyx excision, and no associated complication (Fig. 3). The excised lesion weighed 800 g. The pathological examination revealed an immature teratoma, with a large quantity of nervous mature and immature tissue with calcifications (Fig. 4).

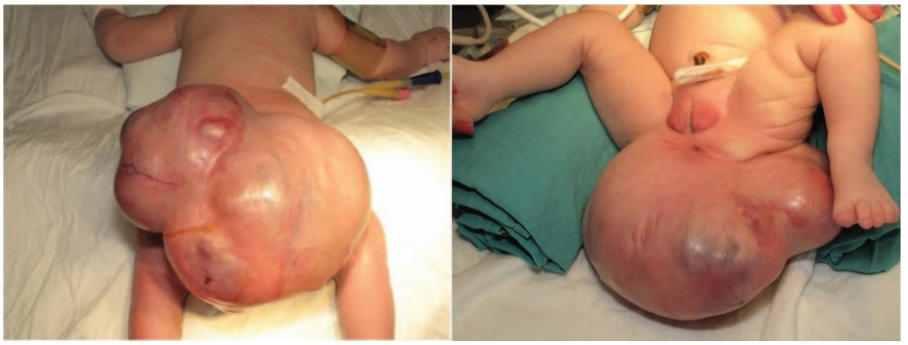

Figure 2. Sacroccocygeal tumor, postnatal appearance.

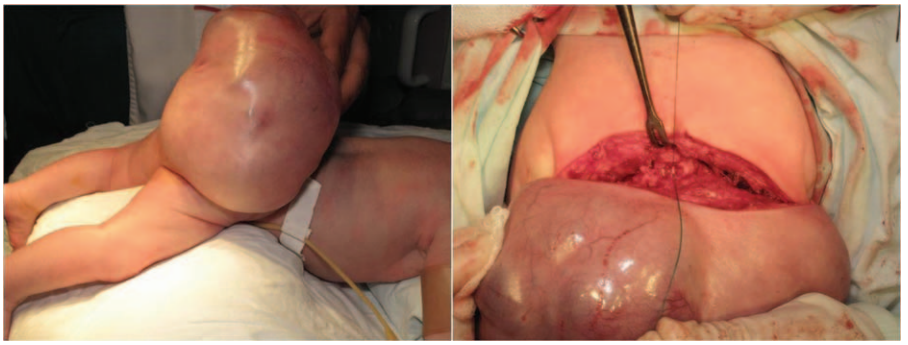

Figure 3. Intraoperative appearance.

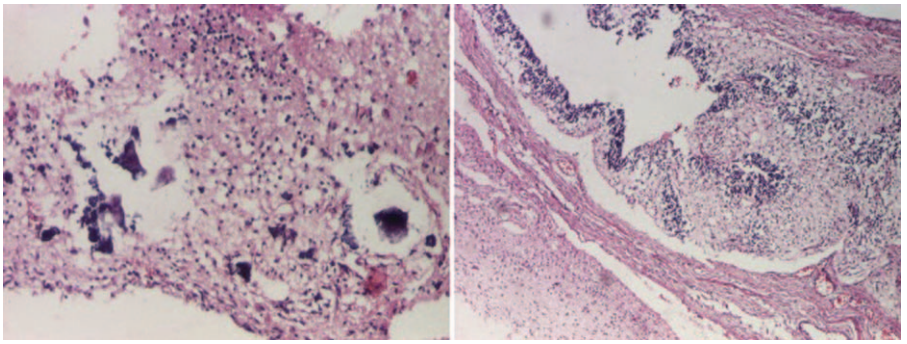

Figure 4. Optical microscopy, hematoxylin and eosin; (magnification 100×) showing calcifications in the mature nervous tissue (A) and associated immature and mature nervous structures (B).

Because of the histological appearance, the child underwent a bleomicyn, etoposide, and cisplatin (BEP) protocol of chemotherapy. The postoperative course was complicated by surgical wound dehiscence, infection, and sepsis, with blood culture positive for *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, treated by local wound care and prolonged intravenous (IV) antibiotics. Subsequently, the child developed subarachnoid hemorrhage and secondary progressive active hydrocephaly [diagnosed by ultrasound and computed tomography (CT) scan at the age of 6 weeks] (Fig. 5), that required a ventriculoperitoneal shunt at the age of 3 months.

The child's outcome was positive after 8 cycles of chemotherapy, with good clinical development, no impairment in micturition or defecation, functional ventriculoperitoneal shunt, normal neurological function, normal values of AFP (4.71 UI/mL), clear pelvic CT scan, with no signs of local recurrence at the age of 18 months.

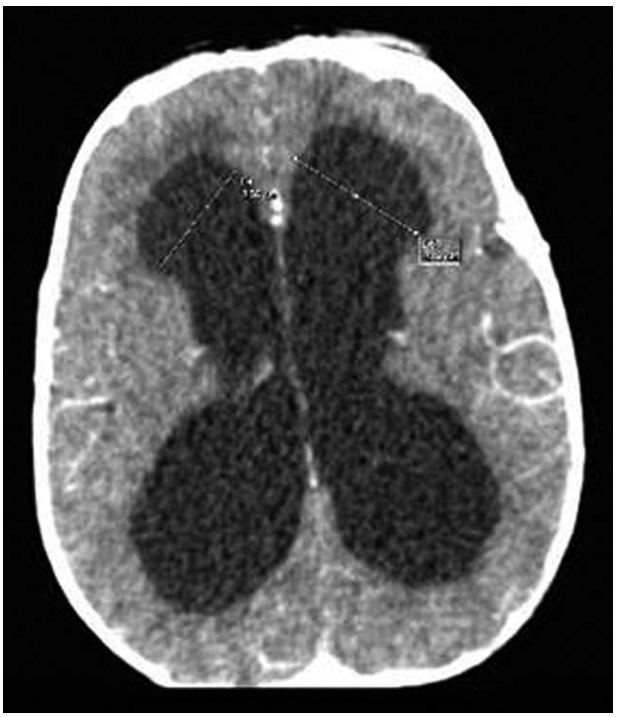

Figure 5. Computed tomography scan showing hydrocephalus (age 3 months).

3. Discussion

Overall survival rate of prenatally diagnosed SCT ranges between 47% and 83%, but is nearly 0% for those who will develop fetal hydrops.[3] There is no general consent regarding the prognostic factors for the postnatal outcome of prenatal diagnoses of SCT. The Altman classification of the tumor into 4 types, according to the prevalence of its extrapelvic or intrapelvic component, showed no correlation with the outcome. The relation type between the solid and cystic component of the tumor seems to be, in contrast, predictive for the outcome, as the solid part of the lesion is usually very vascularized, with high growth potential, and increased risk for cardiac failure and hemorrhage.[4,5] Westerburg et al[6] suggested that the tumor's maximum diameter seemed not to be an independent factor for poor outcome, although no fetuses with tumors less than 10 cm in diameter died. In a study published on 28 cases, Coleman et al[7] reported that faster SCT growth during fetal life is associated with higher mortality, whereas patients with pour outcome and adverse events had an average growth rate 3 to 4 times higher than the ones with positive outcome. The study used the tumoral volume as growth parameter, but could not define a cut-off value for good or bad outcome.[7]

A recent study tried to make a classification of these lesions according to their dimensions and their growing rate. There were 3 groups defined, as follows:

(1) Group A—with tumor diameter less than 10 cm, absent or mild vascularization, slow growth; this group seemed to be associated with no mortality. The mother morbidities lead to caesarean section if the tumor dimensions exceeded 7 cm.
(2) Group B—with tumor diameter more than 10 cm, high vascularization or cardiac failure, and rapid growth; this group is associated with high fetal mortality and high rates of mother and child morbidities.
(3) Group C—with tumor diameter more than 10 cm, but mild vascularization, predominant cystic structure, and slow growth.[8]

In the same study, a growth rate higher than 8 mm/wk was considered as a "fast growth rate" with poor prognosis. A tumor diameter greater than 4 cm at 20 weeks of gestation was also proven to be a sign for a complicated outcome.[9]

In our case, the prenatal diagnosis allowed for a close monitoring of tumor development. The fetal MRI was useful in identifying the tumor structure and vascularization. The closed ultrasound follow-up assessed the tumor rate growth and the absence of any complications as placentomegaly, hydrops fetalis,

or cardiac failure. The tumor growth rate, of a medium of 8 mm/wk, was associated with a good fetal outcome, which allowed a scheduled c-section at 39th week of gestation.

The pathological appearance of the lesion was also defined as a predictor factor for the postnatal patients' need for adjuvant chemotherapy, long-time outcome, and recurrence risk. According to Dehner,[10] teratoma can be classified as mature, immature (characterized by the presence of immature nervous tissue), and malignant (teratoma plus one or more malignant elements). The immature teratoma was also classified by O'Connor and Norris[11] into 3 grades: immature tissue less than 1 low power field/examined slide; immature tissue on 1 to 3 low power fields/examined slides; and immature tissue on more than 3 low power fields on examined slides. Malignancy in the neonatal period is rare (up to 22%)[12]; Altman et al reported an incidence of malignancy of only 5% when the tumor is treated in the first month of life. Most of the neonatal SCTs are benign, mature, or immature, and surgery (with wide and complete resection of the tumor, without rupture or splitting, and coccygectomy) is the main therapy. Associated chemotherapy is the choice for malignant lesions, and also for some immature tumors. The recurrence rate of SCT varies from 2% to 23%.[13,14] The high-grade immature teratoma are known to have a high risk of recurrence comparing with matures' one or low-grade immature. The recurrence rate was previously reported as being low for mature teratoma (0%–26% of the cases) and malignant ones (0%–36%), whereas 12% to 55% of immature teratomas will reoccur after correct surgical resection.[15] Most of the recurrences will appear in the first 3 years after the primary surgery, so serum markers (AFP) and rectal digital examination every 3 months are mandatory. In our case, the pathological examination revealed a type 3 immature teratoma, so adjuvant chemotherapy was considered, with no clinical, imagistic, or biological signs of reoccurence at the age of 3.

Although, according to the UK Children's Cancer Study Group (GC3), and also the American National Cancer Institute, immature teratomas are treated only with surgical resection, we decide to associate the chemotherapy cycles, considering the case at high risk because of dimensions and pathologic aspect. There are several reports in the literature that sustain the idea that large tumors, over 10 cm diameter, may possibly have imperceptible tiny foci of malignant tissue that can mistakenly be reported on pathological examination as mature or immature. Those malignant foci of tissue can lead to tumor malignant recurrence,[16] so chemotherapy can play a role in lowering the rate of malignant recurrence.

The role of postoperative chemotherapy in the management of neonatal immature SCT is still controversial. There are some authors reporting a decrease in the malignant relapses in those cases,[17] whereas others recommended adjuvant therapy alone for incomplete resection.[18,19]

In a study published by the UK Children's Cancer Study Group on extracranial teratomas in children, despite given protocols, from 98 cases of SCT, the chemotherapy was used in 6 cases of immature tumor, but no proven benefit was found, whether given preoperatively, as adjuvant therapy or for benign relapse, so the efficacy of chemotherapy in those benign tumors was difficult to asses.[20] There are many authors who raise concerns regarding the chemotherapy-related adverse effects that weighed against its doubtful efficiency in case of neonatal immature SCT, so they do not recommend it.

The most frequently reported postsurgical complications of SCT are bleeding, wound dehiscence, neuropathic bladder, bowel incontinence, and constipation. Large wound dehiscence associated with wound infection, sepsis, and subsequent subarachnoid hemorrhage is a rare complication of the tumor treatment.

The child in the presented case was treated with 8 cycles of BEP, as the authors considered it a high-risk tumor (huge grade 3 immature teratoma). As a consequence of the immunosuppression associated with chemotherapy cycles, the child developed sepsis and secondary hydrocephalus. We consider the hydrocephalus as an acquired lesion, a side effect associated with chemotherapy cycles, as the aspect of fetal cerebral ventricles was normal during prenatal scans, the immediate postnatal appearance of the transfontanelar ultrasound was normal, and clinical and imagistic signs of subarachnoid hemorrhage and hydrocephalus developed after wound infection associated with generalized sepsis. Thus, this case report may underscore the need for hesitancy concerning chemotherapy in immature teratoma and show a case of possible severe consequences.

4. Conclusions

Sacrococcygeal teratomas are unusual tumors arising from the coccyx. Our case highlights the importance of prenatal diagnosis of giant SCT, associated with close ultrasound monitoring of its growth rate and of its fetal or maternal hemodynamic consequences, as prognostic factors for intra and postnatal outcome. Also, prenatal diagnosis will allow a clear definition of tumor structure and anatomy, provided by fetal MRI. Our case also emphasizes the importance of complete tumor resection and good pathological examination to minimize the reoccurrence risk, but, on the other hand, prenatal diagnosis cannot completely predict the postnatal outcome, because an individualized therapeutic approach must be considered in each case of SCT, as possible unusual complications can be associated with their outcome. We consider that this case report also stresses out the importance of clear treatment guidelines to avoid possible complications of aggressive treatment regimes. We consider in this particular case that the hydrocephalus was a rare and unpredictable complication associated with large surgical wound dehiscence, infection, sepsis, and immunosuppression induced by chemotherapy in a immature grade 3 teratoma.

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