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Rare fetal tumors

Nadir fetal tümörler

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ABSTRACT

Aim: Congenital tumors in fetuses are exceedingly uncommon. The majority of these tumors will be primarily addressed through intrauterine surveillance. They may occur without any clinical symptoms or could lead to serious complications, such as hydrops. Recent progress in prenatal genetic diagnostics and imaging techniques has significantly enhanced the ability to detect fetal tumors and congenital anomalies.

Materials and Methods: A retrospective case series was conducted at a tertiary referral center over a ten-year period, from January 1, 2014, to January 1, 2024, on confirmed cases of fetal tumors identified within our perinatology center. Patients suspected of having fetal tumors underwent biweekly ultrasonographic assessments to monitor critical parameters. Relatively more common cases of fetal tumors (lymphangioma and sacrococcygeal teratoma) were not included in the study.

Results: A total of 16 cases of various type of fetal tumors from different origins were identified. Associated anomalies were identified in three cases, including two cases of epignathus and the case of glioblastoma multiforme. Fetal growth restriction, fetal anemia and amniotic fluid abnormalities were not detected in any of the cases during prenatal monitoring. Hydrops occurred only in one case involving an intrapericardial teratoma. Eleven cases managed to reached delivery and four of them required surgery. Malignancy was detected in 2 cases after surgical intervention

Conclusion: Ultrasonography is the first step imaging method for evaluation of the fetal tumors. However, it is not always easy to determine the location and histology diagnosis of the mass by ultrasonography.

Keywords: Fetal tumor,rare tumor, prenatal diagnosis, ultrasonography

ÖZ

Amaç: Fetüslerde konjenital tümörler son derece nadirdir. Bu tümörlerin büyük çoğunluğuna prenatal dönemde tanı koyulabilmektedir. Bazen herhangi bir klinik bulgu oluşturmazken, bazen de hidrops gibi ciddi komplikasyonlara yol açabilirler. Prenatal genetik tanı ve görüntüleme tekniklerindeki son gelişmeler, fetal tümörleri ve konjenital anomalileri tespit etme becerisini önemli ölçüde artırmıştır.

Gereç ve Yöntemler: Bu retrospektif çalışmada 1 Ocak 2014 ve 1 Ocak 2024 tarihleri arasında üçüncü basamak bir hastanede tanısı doğrulanmış fetal tümör vakaları değerlendirilmiştir. Fetal tümör olduğundan şüphelenilen hastalar kritik parametreleri değerlendirmek için iki haftada bir ultrasonografik değerlendirmeye tabi tutulmuştur. Nispeten daha sık görülen fetal tümör vakaları (lenfanjiom ve sakrokoksigeal teratom) çalışmaya dahil edilmemiştir.

Bulgular: Farklı kökenlerden gelen çeşitli tiplerde toplam 16 fetal tümör vakası tespit edilmiştir. İki epignathus ve bir glioblastoma multiforme vakası olmak üzere üç vakada ek anomaliler gözlenmiştir. Prenatal takip sırasında hiçbir vakada fetal büyüme kısıtlılığı, fetal anemi ve amniyotik sıvı anormallikleri tespit edilmemiştir. Sadece intraperikardiyal teratom içeren bir olguda hidrops meydana gelmiştir. On bir olgu doğuma ulaşmayı başarırken, dördüne cerrahi müdahale uygulandı. Cerrahi müdahale sonrasında 2 olguda malignite tespit edildi

Sonuç: Ultrasonografi fetal tümörlerin değerlendirilmesinde ilk basamak görüntüleme yöntemidir. Ancak ultrasonografi ile kitlenin yerini ve histolojik tanısını belirlemek her zaman mümkün değildir.

Anahtar Kelimeler: Fetal tümör, nadir tümör, prenatal tanı, ultrasonografi

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INTRODUCTION

Congenital tumors in fetuses are exceedingly uncommon. These tumors typically consist of embryonal or fetal tissues that arise due to inadequate cytodifferentiation or maturation during the stages of embryonic or fetal development. Malignant tumors are rarely observed in neonates and are infrequently associated with neonatal mortality or morbidity (1).

Most of these tumors will be managed primarily through intrauterine monitoring; however, if fetal hydrops occurs as a result of particular tumors or their specific locations, in-utero therapy or specialized delivery methods may be necessary to improve neonatal care (2).

Recent advancements in prenatal genetic diagnosis, along with improvements in prenatal imaging and the assessment of fetal anomalies, have significantly enhanced the ability to prepare families for counseling. These developments have also revealed new horizons for considering prenatal interventions for congenital defects that could lead to fatal outcomes, including fetal tumors (3). Developments in fetal therapy and surgical techniques, particularly those involving minimally invasive methods, have not only facilitated the survival of uncommon tumor cases but have also enhanced long-term prognoses.

Due to the rarity of fetal tumors, most literature reports are based on experiences involving only a limited number of cases.The aim of current study to evaluate clinical characteristics and outcomes of the rare fetal tumors.

MATERIALS AND METHODS

A retrospective case series was conducted at a tertiary referral center over a ten-year period, from January 1, 2014, to January 1, 2024, focusing on confirmed cases of fetal tumors identified within our perinatology center. We systematically examined the ultrasound database alongside prenatal genetic counseling records for cases that were diagnosed with fetal tumors. Relatively more common cases of fetal tumors (lymphangioma and sacrococcygeal teratoma) were not included in the study.

Patients suspected of having fetal tumors underwent biweekly ultrasonographic assessments to monitor critical parameters including amniotic fluid index, fetal growth restriction, fetal anemia, ascites, and any associated anomalies. The volume of amniotic fluid was assessed using the amniotic fluid index, with values <50 mm indicating oligohydramnios and values > 250 mm indicating polyhydramnios. Fetal growth restriction (FGR) was identified when the abdominal circumference is below the 3rd percentile in biometric assessments. The diagnosis of fetal anemia was established when the peak systolic velocity in the middle cerebral artery is ≥1.5 multiples of the median (MoM).

All cases were followed-up in an outpatient setting. There was no established maximum gestational age regarding the timing of delivery. In cases which the fetal prognosis is unfavorable, it is advised to consider termination following a thorough discussion with the family. The method of delivery was decided by the clinicians according to the labor's progression.

All cases received genetic counseling, and fetal karyotyping was suggested. For those patients who did not will to have genetic diagnostic tests, chromosome analysis was performed in the postnatal period, in conjunction with the routine heel prick blood test. In all cases, the definitive diagnosis of fetal tumors was validated through the pediatric surgery team (in cases that require surgery), autopsy (in terminated cases), or further imaging methods (Ultrasonography, CT, and MRI). The most recent data concerning the cases was gathered through evaluations conducted by pediatricians and pediatric surgeons, along with direct conversations with the parents involved.

All examinations were performed by expert specialists in maternal-fetal medicine utilizing a 5 MHz convex transducer and a 9 MHz transvaginal transducer (VOLUSON E6, GE). Descriptive data are presented as median/range, mean±SD or numbers and %. Statistical analyses were carried out using the Statistical Package for the Social Sciences Version 26.0 (SPSS, IBM, Chicago, IL, USA). The study protocol received approval from the local ethics committee (Date 09/10/2024 No:69).

RESULTS

From 2014 to 2024, a total of 16 cases of various type of fetal tumors from different origins were followed-up in our maternal-fetal medicine center, all of which were confirmed through postnatal period by surgery or further imaging methods in living cases and by autopsy in terminated cases. The median age of the cohort was 28 (range 20-41) years old and the median gestational age for the first admission was 24.5 (range 13-39) weeks. Demographic, clinical characteristics and perinatal outcomes of the study group were summarized in Table 1. The most common reason for referral to our center was abdominal mass with six cases (37.5 %).

Associated anomalies were identified in three cases, including two cases of epignathus and the case of glioblastoma multiforme (GBM). One case of epignathus was associated with bilateral cleft lip-palate and micrognatia, while the other was associated with hydrocephalus, hypertelorism and diaphragmatic hernia. A double aortic arch was identified in the case of GBM. Fetal

growth restriction, fetal anemia and amniotic fluid abnormalities (polyhydramnios or oligohydramnios) were not detected in any of the cases during prenatal monitoring. Hydrops occurred only in one case involving an intrapericardial teratoma.

Table 1. Demographic, clinical characteristics and perinatal outcomes of the study group

Age, years (median/range)	28 (20-41)
Parity (median/range)	1.5 (1-5)
Consanguineous marriage (n,%)	1 (6.3)
GA at prenatal diagnosis, weeks (median/range)	27 (17-39)
Reason for referral	
Abdominal mass	6 (37.5)
Hydrocephaly	3 (18.8)
Cranial mass	2 (12.5)
Cardiac anomaly	2 (12.5)
Neck mass	1 (6.3)
Vertebral mass	1 (6.3)
Multiple anomaly	1 (6.3)
Associated anomalies (n,%)	3 (18.8)
Karyotype result	
Normal (n,%)	13 (81.3)
Unknown (n,%)	3 (18.8)
Perinatal outcomes	
Termination	5 (31.3)
Delivery	11 (68.7)
Mode of delivery	
Vaginal (n,%)	6 (37.5)
Cesarean (n,%)	5 (31.3)
GA at delivery, weeks (median/range)	38 (33-40)
Birthweight, gram (mean±SD)	3012 ±644
Postnatal surgery (n,%)	4 (25)

GA: gestational age

All cases underwent genetic counseling and were presented with the opportunity for genetic diagnostic testing; nonetheless, prenatal genetic analysis was performed in only two cases via amniocentesis. In three cases that resulted in termination, genetic analysis was not carried out, while postnatal karyotype analysis in the remaining cases indicated normal findings (Table 1).

Types of tumors and locations, prenatal diagnosis and prenatal-postnatal outcomes were summarized in Table 2. Postnatal diagnoses and number of cases are as follows: 2 choroid plexus papilloma, 1 GBM, 1 immature teratoma, 2 epignathus, 1 neck hemangioma, 1 abdominal hemangioma, 3 unidentified adrenal mass, 2 liver hemangioma, 2 intrapericardial teratoma and 1 soft tissue infantile fibrosarcoma. Eleven cases managed to reached delivery and four of them required surgery. Malignancy was detected in 2 cases after surgical intervention, leading these patients to receive advanced treatment options. In 3 out of 5 cases where neuroblastoma was suspected prenatally, adrenal masses were detected during the postnatal assessment. Nevertheless, a definitive diagnosis was still difficult to achieve, despite the use of advanced imaging methods (Ulrasonography, CT, MRI) and the analysis of particular tumor markers. A retroperitoneal hemangioma and liver hemangioma were other definitive diagnoses in remaining two cases. GBM and choroid plexus papilloma were found postnatally in 2 cases who were followed up with a prenatal prediagnosis of cranial hemorrhage. In remaining cases although a definitive diagnosis could not be made in the prenatal period, the fetal tumor and its characteristics were correctly identified.

Table 2. Types of tumors and locations, prenatal diagnosis and prenatal-postnatal outcomes

Location and tumor types	No (%)	Prenatal diagnosis (n)	Termination (weeks)	Operation	Current status
Kranium					
CPP	2 (12.5)	Hemorrhage (1) CPP (1)	+ (34) -	- +	- Intraoperative exitus at 3 months
GBM	1 (6.3)	Hemorrhage	-	+	Living after CT and RT
Immature teratoma	1 (6.3)	Solid tm	+ (26)	-	
Epignatus	2 (12.5)	Epignatus Epignatus	+ (18) -	- -	- Exitus at 11 days
Neck					
Hemangioma	1 (6.3)	Hemangioma	+ (25)	-	-
Abdomen					
Hemangioma	1 (6.3)	Neuroblastoma	-	+	Living
Adrenal mass (unidentified)	3 (18.8)	Neuroblastoma (3)	-	-	Living
Liver hemangioma	2 (12.5)	Neuroblastoma (1) Liver hemangioma (1)	- -	- -	Living Living
Heart					
Teratoma	2 (12.5)	Mesenchymal tm (1) Teratoma (1)	+ (27) -	- -	- Living
Soft tissue					
Infantile fibrosarcoma	1 (6.3)	Soft tissue tm	-	+	Living after KT

CPP: choroid plexus papilloma; CT: chemotherapy; GBM: glioblastome multiforme; RT: radiotherapy; tm: tumor

DISCUSSION

Fetal tumors are uncommon (4). However, the extensive application of contemporary ultrasound methods has led to a greater identification of these tumors during prenatal examinations. Although certain neoplasms can emerge in the early stages of pregnancy, most typically manifest later in the gestational period.

Fetal tumors frequently occur in the abdominal region, making it one of the most prevalent locations (5). In our study it was the most common site with 6 cases (37.5 %). Of these cases, it becomes evident that they are predominantly located in and around the adrenal gland, leading us to suspect the presence of an adrenal mass. One of the masses initially presumed to be located in the adrenal gland was actually identified in the retroperitoneal space, while another was discovered in the liver (Figure 1). Our primary challenge in abdominal tumors was in pinpointing the mass's location rather than diagnosing it. The findings indicate that rare tumors originating from uncommon sources were often misdiagnosed (5). Therefore it suggests that, alongside ultrasound, more sophisticated diagnostic techniques may be required for accurate diagnose of intraabdominal tumors. Despite the diagnostic difficulties, it should be noted that cases with adrenal masses and hemangiomas of the liver are followed up in the postnatal period without any intervention. It is important to acknowledge that, based on the diagnosis and results concerning, the abdominal tumors observed in the study group had benign nature, and had favorable prognosis for all cases.

Choroid plexus tumors are papillary neoplasms originate from neuroectodermal tissue, specifically developing from the choroid plexus epithelium located within the cerebral ventricles (6). The rarity of these tumors, along with their similarity to more common intracranial diseases such as hemorrhage, infection,

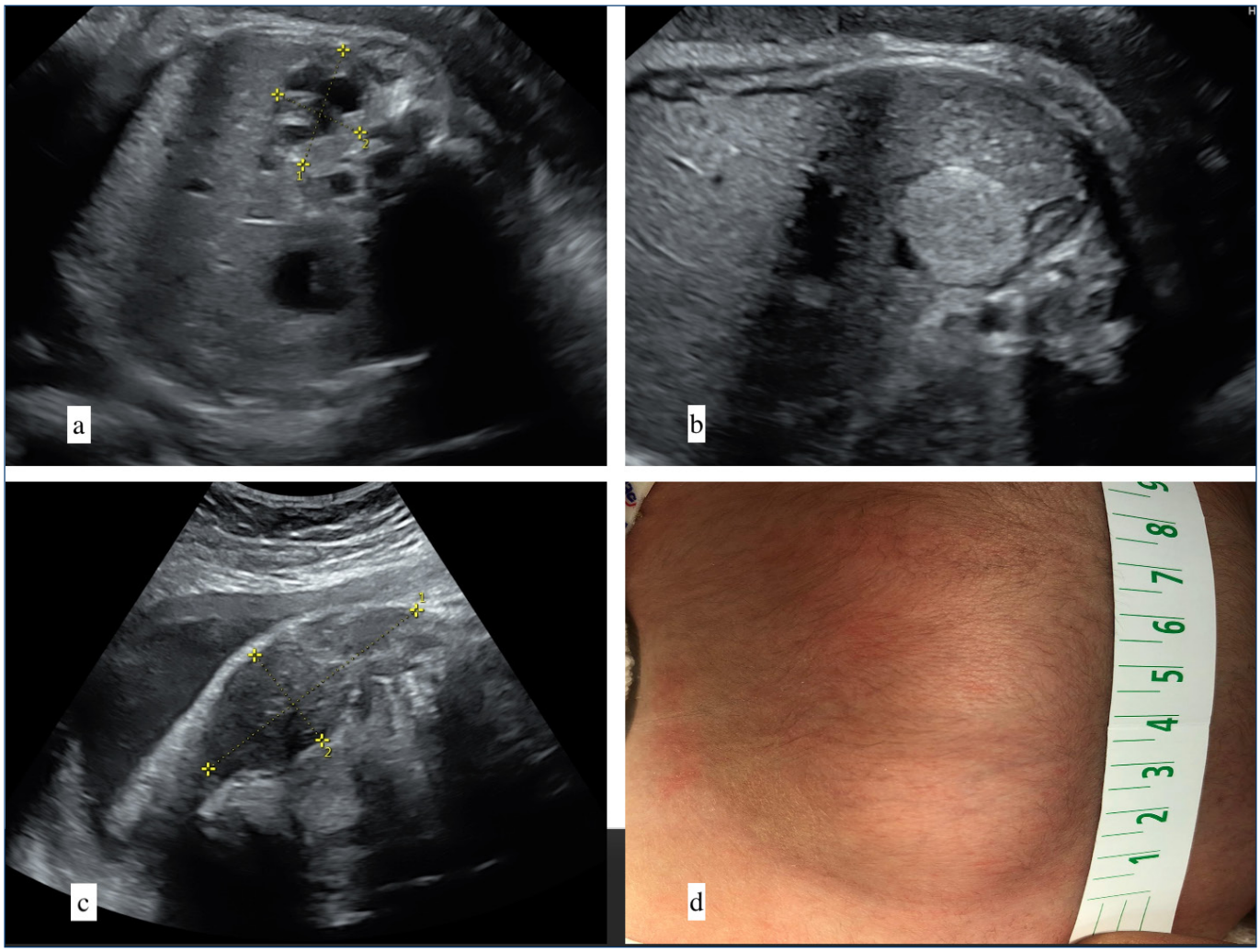

Figure 1. a) Heterogenous mass with solid and cystic areas in right upper quadrant at 38 weeks of gestation. The mass was confirmed to be located in the adrenal gland postnatally, but the diagnosis is unclear, **b)** Solid homogenous mass in right upper quadrant at 35 weeks. Prenatal diagnosis was neuroblastoma. A liver hemangioma was diagnosed postnatally, **c)** Soft tissue mass in right lower back at 33 weeks, **d)** Postnatal appearance of the mass. Surgery confirmed malign infantil fibrosarcoma.

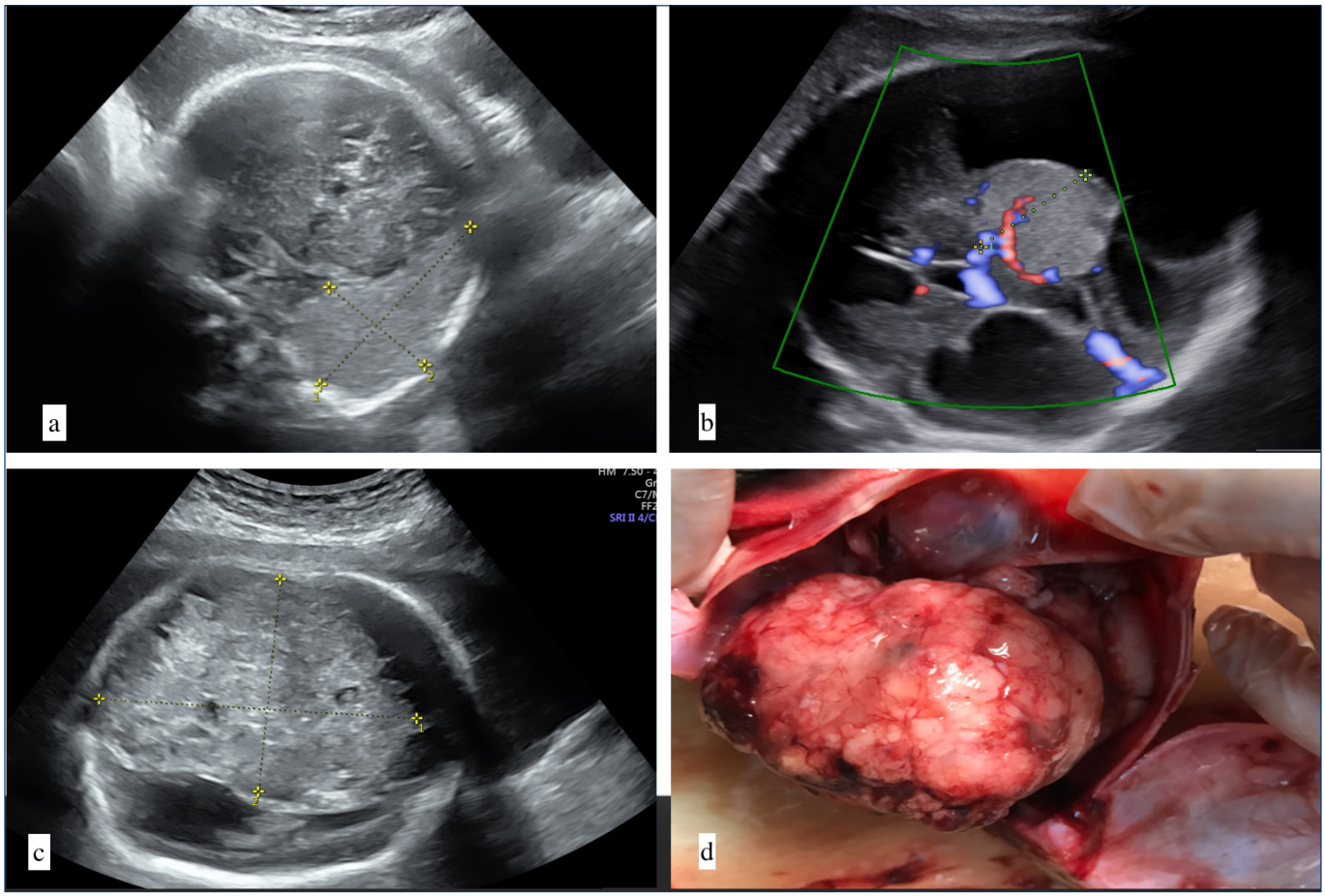

Figure 2. a) Coronal section of cranium at 36 weeks of gestation. Homogeneous mass mimicking haemorrhage. Postnatal surgery confirmed the diagnosis of glioblastoma multiforme, **b)** Choroid plexus papilloma at 32 weeks. Homogeneous hyperechogenic mass with significant blood supply, **c)** Transverse section of cranium at 25 weeks. Heterogenous solid mass occupying almost whole cranium with echogenic areas within, **d)** Macroscopic appearance of immature teratoma in the same case during fetal autopsy.

and hydrocephalus due to congenital anomalies, may result being misdiagnosed (7). In the study group, two cases of choroid plexus papilloma were identified (Figure 2); however, a prenatal diagnosis was successfully established in one case. The other case was initially diagnosed as intracranial hemorrhage.

As choroid plexus tumors, various other solid intracranial masses, can be misinterpreted as intracranial hemorrhage (8). Necrotic and hemorrhagic areas within the tumor may create a heterogeneous appearance similar to hemorrhage. One case in our study with postnatal diagnosis of GBM, was misinterpreted as intracranial hemorrhage due to morphological changes seen in the growing tumor during pregnancy (Figure 2). Intracranial teratomas are more clearly delineated via ultrasound imaging due to their solid tumor characteristics and echogenic structure (9). The case of intracranial teratoma in our study had an echogenic solid mass that almost completely filled the cranium and the pregnancy was terminated due to poor prognosis (Figure 2). Epignathus in two cases was identified as a part of multiple anomalies. Prenatal ultrasonography revealed protruding echogenic oral mass that is very spesific to an epignathus case like previously reported (10).

Fetal intrapericardial teratomas are very rare and in benign nature. However, due to their specific location, they can be fatal for the fetus, causing severe pleural effusion, cardiac tamponade and eventually fetal hydrops (11) . A case within the study group was terminated at 27 weeks of gestation as a result of significant compression of the left ventricular outflow tract, which led to the development of fetal hydrops. In the other case, a cystic mass that exerted slight pressure on the right ventricular outlet, which progressively diminished during the postnatal follow-up. Nevertheless, given that there have been no reported cases of regressing intrapericardial teratoma in the existing literature, and considering that our postnatal diagnosis relies on imaging techniques, the identification of teratoma in this particular case is suspicious (12-14)

The most unusual case in current study was identified at 30 weeks of gestation with a mass located at the back of the fetus, distorting the vertebral column extending from left thoracal

region to lower lomber region. The mass, which did not lead to any complications (15) during the prenatal period, was surgically removed after delivery and diagnosed as infantile fibrosarcoma (Figure 1). As another case, a huge hemangioma at the neck that have a large feeding artery arising from carotis had steal effect. In doppler examinations, reverse flow in aortic arch was detected and significant portion of carotis flow was diverted to the mass. The pregnancy was terminated due to a poor fetal prognosis, and similar cases have been reported in the current literature (16).

The overall survival rate was in our study group was 56.3 % and lower than previously reported (3, 17). This may be explained by the poorer prognosis of intracranial tumors and the presence of cases with multiple anomalies.

Ultrasonography is the first step imaging method for evaluation of the fetal tumors. However, it is not always easy to determine the location and histology diagnosis of the mass by ultrasonography. Advanced imaging methods like MRI may be utilized to confirm the diagnosis (9, 18). Although a definitive diagnosis may be established during the prenatal period, there exists a paucity of evidence-based information for management strategies of fetal tumors.

CONCLUSION

In conclusion, as fetal tumors are rare, they may have serious effect on the mother and fetus. Prenatal ultrasound is first step method to diagnose the location and type of the tumor and for prenatal surveillances. Prenatal diagnosis facilitates a multidisciplinary approach, enabling the prediction of potential complications and the consideration of proper management strategies, thereby enhancing perinatal outcomes.

Author Contributions

TU, EOM, DO; CA: conceptualization, methodology, supervision; TU, EOG, GM: data curation; TU, EOG, DO, CA: formal analysis; TU: writing- original draft

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Conflict of Interests

Authors declare no conflict of interest for this article.

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