

## Prenatal ultrasound diagnosis of congenital infantile fibrosarcoma and congenital hemangioma: Three case reports

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### Abstract

#### BACKGROUND

Congenital infantile fibrosarcoma (CIF) and congenital hemangioma (CH) have similarities on prenatal ultrasound and are rare.

#### CASE SUMMARY

We report 3 cases of fetuses with superficial hypervascular tumors, confirmed by postnatal pathology as CIF (1 case) and CH (2 cases, including 1 in a twin fetus). In Case 1, a mass with a rich blood supply in the fetal axilla was discovered by prenatal ultrasound at 28+0 wk of gestation. The postpartum pathological diagnosis was CIF, the mass was surgically removed, and the prognosis of the

child was good. In Case 2, at 23+1 wk of gestation, a mass was discovered at the base of the fetus's thigh on prenatal ultrasound. The postpartum pathological diagnosis was CH. After conservative treatment, the mass shrank significantly. Case 3 occurred in a twin fetus. At 30+0 wk of gestation, prenatal ultrasound revealed a bulging mass with a rich blood supply on the abdominal wall of one of the fetuses. Three weeks later, the affected fetus died, and the unaffected baby was successfully delivered by emergency cesarean section. The affected fetus was pathologically diagnosed with CH.

### CONCLUSION

Prenatal ultrasound can provide accurate information, such as the location, size and blood supply of a surface mass in a fetus. We found similarities between CIF and CH in prenatal ultrasound findings. Although it is difficult to distinguish these conditions by prenatal ultrasound alone, for superficial hypervascular tumors that rapidly increase in size in a short period, close ultrasound monitoring of the fetus is required to quickly address possible adverse outcomes.

**Key Words:** Congenital infantile fibrosarcoma; Congenital hemangiomas; Prenatal ultrasound; Fetal tumor; Case report

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**Core Tip:** Congenital infantile fibrosarcoma (CIF) and congenital hemangioma (CH) found prenatally are very rare. We report one case of CIF and two cases of CH, one of which involved a twin fetus. The imaging, pathological, treatment and follow-up data in our manuscript are very detailed. These data can provide useful clinical experience for prenatal diagnosis and consultation for such tumors.

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## INTRODUCTION

Congenital infantile fibrosarcoma (CIF) and congenital hemangioma (CH) are two types of hypervascular tumor in newborns and infants that may involve the body surface. The incidence rate of soft tissue sarcomas in the first year of life was reported to be 16.0 per million[1], and one prospective study reported CH in 2/594 newborns (0.3%)[2]. Most current research focuses on infants and children[3,4]. Fetal CH is relatively common in existing related reports, while there are few reports on CIF, another extremely rare fetal tumor. Following a literature review, only 6 cases with both prenatal ultrasonography and confirmation by immunochemistry and specific fusion genes after delivery were reported. Both CIF and CH can manifest as body surface masses with rich blood supplies on prenatal ultrasound, which brings challenges in prenatal diagnosis. Given the rarity of cases detected prenatally and confirmed as CIF or CH postnatally, this report summarizes the cases of fetal CIF and CH discovered by prenatal ultrasound in our hospital. One case of CIF and two cases of CH, including one case in a twin fetus, provide experience in prenatal counseling and perinatal management for such tumors discovered prenatally.

## CASE PRESENTATION

### Chief complaints

**Case 1:** A 31-year-old Chinese singleton primigravida (gravida 1 para 0) at 34+5 wk of gestation was admitted to our hospital due to abnormalities shown on fetal imaging examination 6 wk previously.

**Case 2:** A 29-year-old Chinese singleton primigravida (gravida 1 para 0) at 23+1 wk of gestation presented to our hospital for routine follow-up.

**Case 3:** A 32-year-old Chinese twin pregnant woman (gravida 2 para 1) at 30+0 wk of gestation was admitted to our hospital due to abnormalities shown on fetal imaging examination 2 wk previously.

### History of present illness

**Case 1:** The patient was admitted to Xijing Hospital for routine follow-up at 28+0 wk of gestation. Fetal imaging examinations revealed a mass in the left axilla and the left chest wall of the fetus. The pregnant woman had been followed up by

ultrasound and had not received any treatment.

**Case 2:** The patient had no history of disease.

**Case 3:** The patient was admitted to Xijing Hospital for routine follow-up at 28+3 wk of gestation. Fetal imaging examination showed a mass protruding from the abdominal wall of one of the twins. The affected fetus was alive without pleural or peritoneal effusions. No abnormalities were found in the other twin fetus. The pregnant woman had been followed up by ultrasound and had not received any treatment.

### **History of past illness**

**Case 1:** The woman had no history of past disease.

**Case 2:** The woman had no history of past disease.

**Case 3:** The woman delivered her first child vaginally 5 years ago.

### **Personal and family history**

**Cases 1-3:** The personal and family histories of all patients were unremarkable.

### **Physical examination**

**Case 1:** The pregnant woman's physical examination was normal. Physical examination of the newborn revealed a mass of approximately 7.0 cm × 5.0 cm from the left axilla to the left chest wall. The surface of the mass was purplish red and hyperemic, without ulceration or hemorrhage. The mass was tough and unsmooth, and the fetus had poor mobility and tenderness.

**Cases 2:** The pregnant woman's physical examination was normal. Physical examination of the newborn revealed a purplish red mass of approximately 7.0 cm × 6.0 cm at the root of the right thigh, with unclear borders, tough quality, and no rupture on the surface. The mobility of the right lower limb was poor.

**Case 3:** The pregnant woman's physical examination was normal. The affected fetus was stillborn with an enormous mass in the thoracic and abdominal wall. The vital signs of the other fetus were stable.

### **Laboratory examinations**

**Case 1:** Laboratory examinations of the pregnant woman showed no abnormalities. The newborn's postpartum laboratory examination results for platelet count, D-dimer level, prothrombin time and fibrinogen level, which were  $52 \times 10^9/L$ , 20360.00 ng/mL, 15.1 s and 0.33 g/L, respectively, were abnormal.

**Case 2:** The pregnant woman's laboratory examinations showed no abnormalities. The newborn's postpartum laboratory examination results for hemoglobin concentration, platelet count and D-dimer and fibrinogen level, which were 85 g/L,  $25 \times 10^9/L$ , 78930.00 ng/mL and 0.84 g/L, respectively, were abnormal.

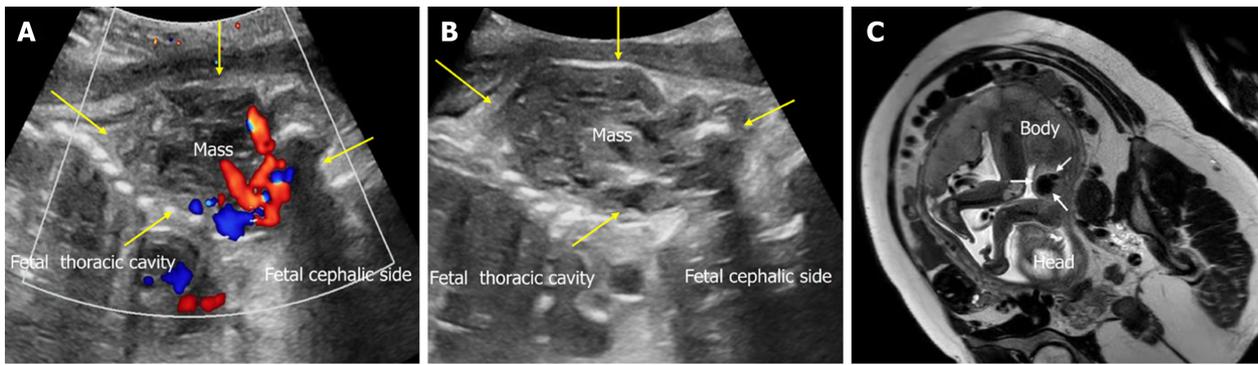
**Case 3:** The pregnant woman's laboratory examinations showed no abnormalities.

### **Imaging examinations**

**Case 1:** The prenatal ultrasound images at 34+5 wk of gestation showed a well-defined, heterogeneous soft tissue mass, 5.5 cm × 4.5 cm in size, from the left axilla to the left chest wall of the fetus. The mass mainly comprised isoechoic solid components. Color Doppler flow imaging (CDFI) revealed abundant blood flow within the mass, with a dendritic distribution (Figures 1A and B). Prenatal magnetic resonance imaging revealed an irregular soft tissue mass in the fetal axilla on the T2 weighted image (Figure 1C). The size of the lesion was more extensive on postnatal ultrasound than on prenatal ultrasound, and the lesion had increased arterial blood flow. Pulse Doppler flow imaging showed low-resistance blood flow within the mass (resistance index, RI was 0.19) (Figure 2A and B). X-ray showed a vast basal arc-shaped soft tissue density shadow in the left axilla and lateral chest wall. The boundary with the chest wall tissue was unclear, and the adjacent ribs were compressed, deformed, and displaced inward (Figure 2C).

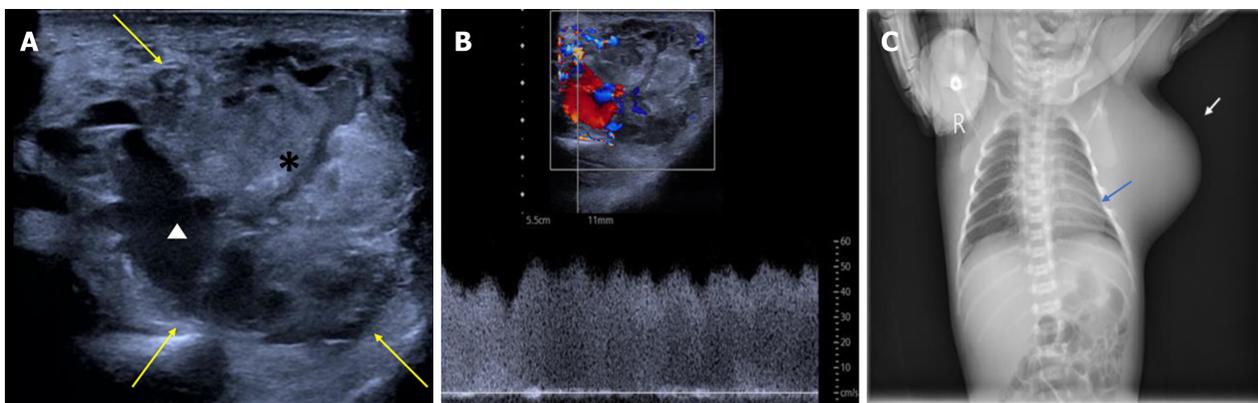
**Case 2:** A well-defined, heterogeneous mass (2.6 cm × 1.4 cm) was found at the root of the right thigh of the fetus on ultrasonography at 23+1 wk of gestation. CDFI showed sparse punctate blood flow around the mass (Figure 3).

**Case 3:** Prenatal ultrasound at 30+0 wk of gestation showed that in one of the twins, a heterogeneous mass (7.1 cm × 4.9 cm) protruded from the subcutaneous layer of the thoracic and abdominal wall to the body surface with a clear boundary, complete capsule, smooth surface, and regular shape. The boundary between the mass and the abdominal wall was unclear. CDFI showed abundant blood flow within the mass, with a dendritic distribution (Figure 4). Prenatal ultrasound at 33+0 wk of gestation showed that the affected fetus had no heartbeat, and the volume of the mass in the thoracic and abdominal wall had increased significantly, to 9.6 cm × 5.5 cm. Compared to the previous examination, the internal echoes of the mass were more chaotic. The mass had a clear boundary and regular shape, and no apparent defect was found in the abdominal wall. CDFI showed no blood flow in the mass. At the same time, the whole body of the fetus showed edema, and the thickness of the scalp was approximately 6 mm. Effusion was found in the pleural cavity and pericardial cavity of the affected fetus, accompanied by unclear amniotic fluid (Figure 5).



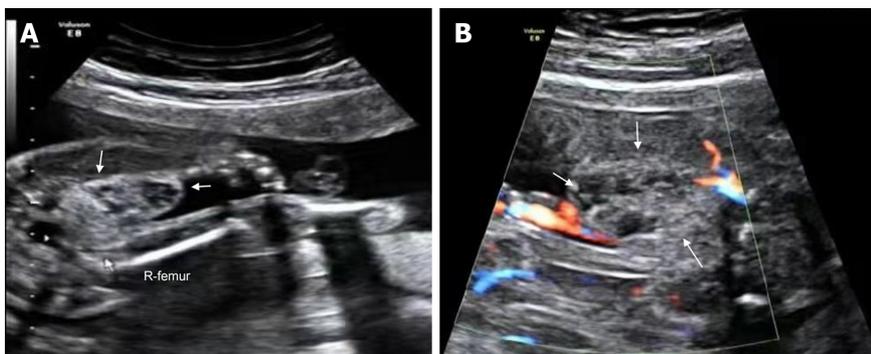
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**Figure 1 Prenatal imaging of congenital infantile fibrosarcoma in Case 1.** A: Color Doppler flow imaging of the axillary mass in the fetus at 34+5 wk of gestation, showing abundant blood flow within the mass. Yellow arrow, the mass; B: Two-dimensional ultrasound showing the longitudinal section of the fetus at 34+5 wk of gestation, revealing a heterogeneous mass in the left axilla. Yellow arrow, the mass; C: Magnetic resonance imaging (MRI) at 28+6 wk of gestation documenting a solid mass in the left axilla. White arrow, the fetal mass on MRI.



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**Figure 2 Postnatal imaging of the congenital infantile fibrosarcoma in Case 1.** A: One-day postnatal two-dimensional ultrasound using a linear array transducer with a frequency of 5-12 MHz, revealing a well-defined mass in the left axilla consisting mainly of isoechoic parenchymal components (\*) with a few anechoic areas (white triangle) within the mass. Yellow arrow, the boundary of the mass; B: One-day postnatal pulse Doppler ultrasound revealing a rich blood flow and low resistance blood flow spectrum in the mass; C: Postnatal X-ray of the newborn showed a soft tissue density shadow protruding from the left axilla and lateral chest wall, resulting in compression of the adjacent ribs (blue arrow). White arrow, the mass on X-ray.



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**Figure 3 Prenatal ultrasonic imaging of the congenital hemangioma in Case 2.** A: Prenatal two-dimensional ultrasound image revealing a well-defined, heterogeneous mass at the root of the right thigh of the fetus at 23+1 wk of gestation. White arrow, the mass; R-femur, the right femur of the fetus; B: CDFI of the mass at the root of the right thigh of the fetus at 23+1 wk of gestation showing sparse punctate blood flow around the mass. White arrow, the mass.

**Further diagnostic work-up**

**Case 1:** The postoperative pathological findings in Case 1 were as follows: The tumor cells showed eosinophilic, diffuse sheets of monotonous round cells with fine chromatin and indistinct nucleoli. Immunohistochemistry demonstrated the expression of smooth muscle actin (SMA), CD34, and CD31 in tumor cells, and the Ki-67 proliferation index was approximately 20%. Using fluorescence in situ hybridization (FISH), the tumor cells showed NTRK3 gene rearrangement, with break-apart green (telomeric) and red (centromeric) signals, which confirmed the diagnosis of CIF (Figure 6).

**Case 2:** Case 2 underwent ultrasound guided biopsy of the lesion.

**Case 3:** Pathological examination of the lesion from the stillborn fetus was conducted.

**FINAL DIAGNOSIS**

**Case 1:** CIF.

**Case 2 and Case 3:** CH.

**TREATMENT**

**Case 1:** The patient delivered a baby boy by cesarean section at 37+0 wk of gestation. Owing to the detection of thrombocytopenia and abnormal coagulation function, platelets, human fibrinogen and plasma were administered. After correcting coagulation dysfunction, surgical resection of the tumor was performed on Day 50.

**Case 2:** The patient delivered a baby boy at 40+0 wk of gestation. Owing to the detection of anemia, thrombocytopenia and abnormal coagulation function, cell suspensions and platelets were administered. Oral prednisone and propranolol were administered and were adjusted based on the changes in the CH. In addition, the tumor was closely monitored.

**Case 3:** After urgently promoting fetal lung maturity, the pregnant woman delivered two fetuses by cesarean section, one of which was stillborn and had a considerable mass in the thoracic and abdominal wall. The vital signs of the other fetus were stable.

**OUTCOME AND FOLLOW-UP**

**Case 1:** After the operation, the child recovered well, and the tumor had not recurred at 12 mo of follow-up.

**Case 2:** The mass on the right thigh became softer and smaller in size. At present, the child is two years old. The lesion on the right thigh has no noticeable bulge, and movement of the right leg is unrestricted.

**Case 3:** The newborn was discharged after a period of observation. A summary of the characteristics of the above three cases is shown in Table 1.

**DISCUSSION**

CIF is rare, accounting for less than 1% of all childhood cancers; these tumors are mainly detected at birth (30%) or in the first year of life and are rarely detected prenatally[5]. Prenatal imaging is very useful for detecting abnormal fetal masses, but the final diagnosis relies on postpartum pathology confirmation. CIFs are usually located in subcutaneous tissues and develop in different parts of the body, most commonly in the extremities. Complete surgical resection is usually curative and sufficient in most cases[6]. Our findings were consistent with data in previous literature[7-11]. Fibrosarcoma is a highly vascular tumor, which leads to difficulties in interpretation on prenatal ultrasound and can show rapid growth. We have summarized these studies (Table 2) and compared their results to the present study. Prenatal imaging features of CIF are nonspecific, and the diagnosis of CIF is challenging. On prenatal sonography, CIF appears as a large, expansive, solid soft tissue mass. It usually presents as a heterogeneous lesion with high growth potential that tends to compress adjacent structures, and cystic echogenicity may be present within the mass. Central necrosis or hemorrhagic areas might be present depending on the rate of increase in the dimensions of the mass[12,13]. The blood supply arteries of CIFs are similar to typical tumor vessels, with irregular calibers and unorganized branching patterns[14]. The immunophenotype for CIF is nonspecific, with variable expression of desmin, muscle-specific actin, CD34, and S100 protein. ETV6/NTRK3 gene fusion is vital in making the correct diagnosis. Complete surgical resection is still the primary treatment for CIF. CIF can ulcerate within the uterus and cause many complications, such as polyhydramnios, torsion, anemia, hemorrhagic shock, hemolysis, oppression of adjacent organs, and cardiac insufficiency, all of which may threaten the life of the fetus[9]. In view of the imaging features, location and rapid growth of CIFs, we believe that prenatal diagnosis of soft tissue tumors and suspected fibrosarcoma is possible. It is essential to continuously monitor

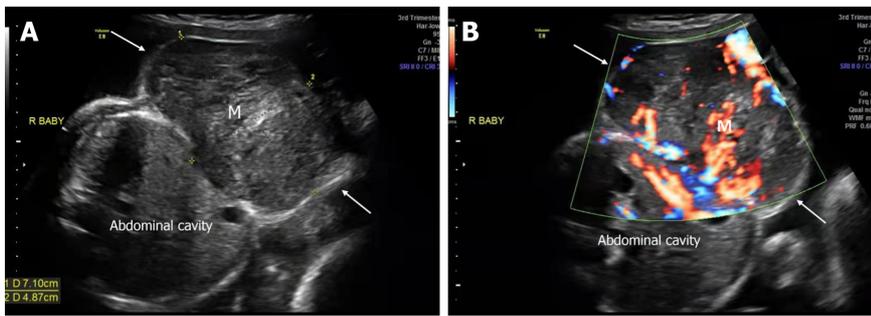
**Table 1 Summary of the three cases**

	<b>Case 1</b>	<b>Case 2</b>	<b>Case 3</b>
Age (yr)	31	29	32
History of gravida and para	G 1 P 0	G 1 P 0	G 2 P 1
Singleton/Twin	Singleton	Singleton	Twin
GA at diagnosis (wk + d)	28 + 0	23 + 1	28 + 3
Location	The left axilla to the left chest wall	The root of the right thigh	Thoracic and abdominal wall
Prenatal fetal ultrasound findings at diagnosis	Size (cm)	3.2 × 3.0	2.6 × 1.4
	Echoes	Heterogeneous	Heterogeneous
	Boundary	Clear	Clear
	Shape	Irregular	Irregular
	Blood flow (Adler)	Grade III	Grade I
Prenatal management	None	None	At 33 + 0 wk, due to intrauterine fetal death on the affected side, dexamethasone was given to promote lung maturation of the contralateral fetus
GA at delivery (wk + d)	37 + 0	40 + 0	33 + 3
Mode of delivery	Caesarean section	Normal spontaneous vaginal delivery	Caesarean section
Apgar score			/
1 min	9	9	
5 min	10	10	
10 min	10	10	
Postnatal physical examination: Restricted movement of affected limbs	Yes	Yes	/
Postnatal fetal ultrasound findings			/
Size (Compared to the last prenatal ultrasound)	Increase	Unchanged	
Repeat ultrasound (growth trend in size in the short-term)	Yes	Yes	
Blood flow (Adler)	Grade III	Grade III	
Postnatal ultrasound-guided biopsy	Yes	Yes	
Other postnatal imaging examinations	X-ray	MRI	/
Postnatal laboratory examination: Coagulation dysfunction	Yes	Yes	/
Postnatal management	Surgery + chemotherapy	Chemotherapy	/
Pathological results	CIF	CH	CH
Follow-up outcome (duration)	No recurrence (12 mo)	No recurrence (24 mo)	Death

GA: Gestational age; G: Gravida; P: Para; MRI: Magnetic resonance imaging; CIF: Congenital infantile fibrosarcoma; CH: Congenital hemangioma.

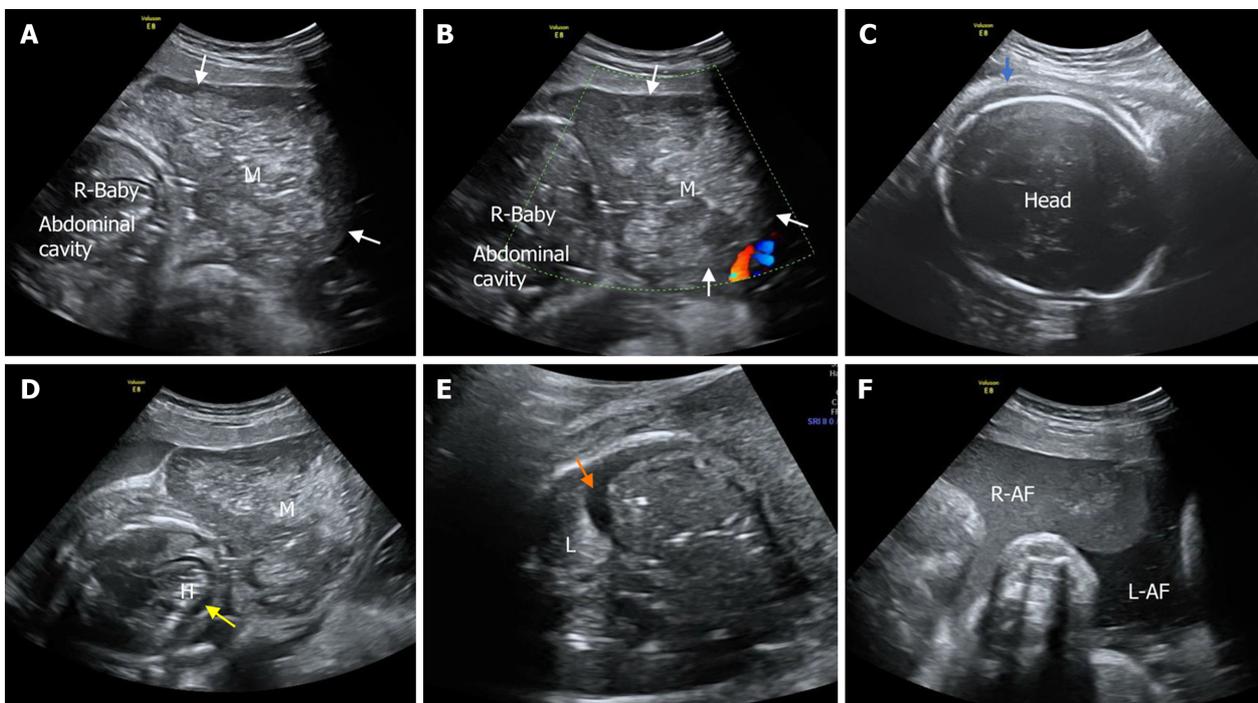
fetal vital signs and tumor development by ultrasound. For children with concomitant coagulation dysfunction, surgical resection after the correction of coagulation dysfunction can achieve good results. Long-term follow-up is necessary before it can be safely assumed that the child has been cured.

CH is the most common hypervascular benign tumor in fetuses. The prenatal imaging features of our patients were consistent with previous literature[3]. Ultrasonic features of CH included a high-vessel density, a high peak systolic velocity, and visible blood vessels. Brix performed Doppler ultrasound imaging of 3 fetuses with prenatally discovered CH, all of which showed abundant and rapid blood flow[15]. In Case 2 of our study, the lesion was small and did not have a rich blood supply at the time of prenatal ultrasound, but it grew rapidly during the monitoring process. Postnatal



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**Figure 4** Prenatal ultrasonic imaging of the congenital hemangioma of the affected twin fetus in Case 3 at 30+0 wk of gestation. A: Two-dimensional ultrasound of the abdominal horizontal cross-section of the mass of the affected fetus revealing a heterogeneous hypoechoic mass with a clear boundary, protruding outward from the abdominal wall; B: CDFI in the horizontal cross-section of the fetal abdomen revealed abundant blood flow within the mass. R: Right; M: Mass; white arrow, the mass.



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**Figure 5** Prenatal ultrasonic imaging of the congenital hemangioma of the affected twin fetus in Case 3 at 33+0 wk of gestation. A: Two-dimensional ultrasound of the abdominal horizontal cross-section of the mass of the affected fetus revealing that the mass was enlarged and heterogeneous; B: CDFI of an abdominal horizontal cross-section of the mass showing no blood flow signal within the mass. M: Mass; R: Right; white arrow, the mass; C: A two-dimensional ultrasound image of the fetal head showing subcutaneous edema (blue arrow); D: A two-dimensional transverse section of the fetal chest showing intrapericardial fluid collection (yellow arrow). H, heart; M, mass; E: A two-dimensional thoracic horizontal cross-section of the affected fetus showing fetal pleural effusion (orange arrow). L: Lung; M: Mass; R: Right; white arrow, the mass; F: Two amniotic cavities on two-dimensional ultrasound showing that the amniotic fluid of the affected fetus (R-AF) was not clear. R-AF: Right amniotic fluid. LAF left amniotic fluid.

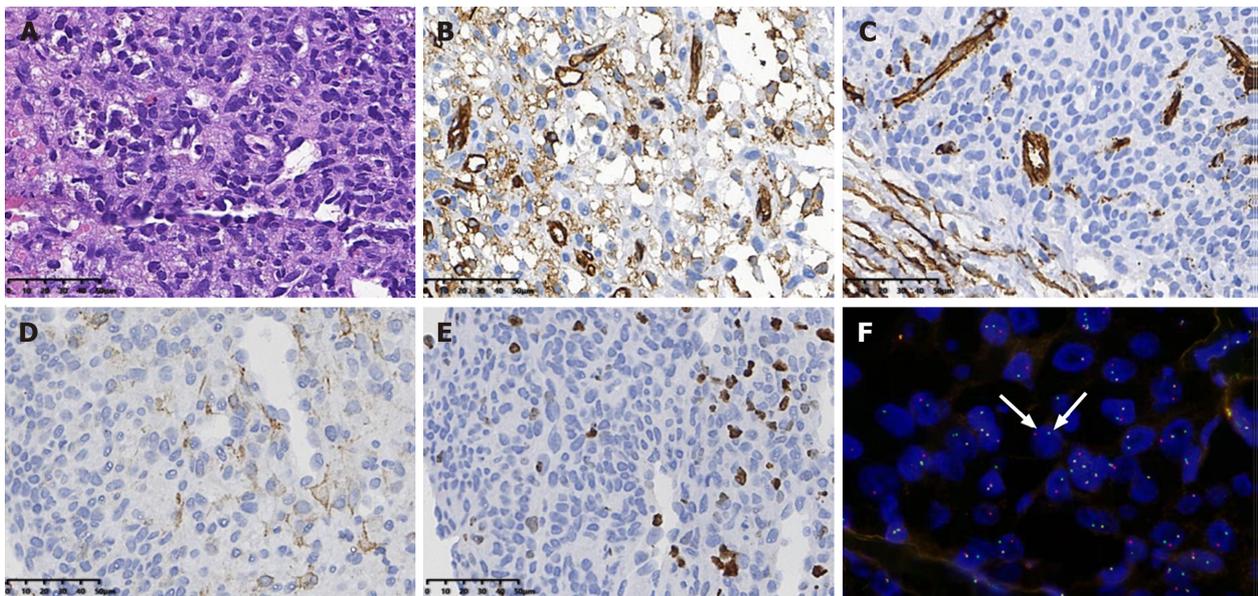
ultrasonography revealed a highly vascular soft tissue mass with smooth contours. In large lesions, complications such as thrombocytopenia, coagulation disorders (an increased prothrombin time, a decreased fibrinogen level, increased D-dimer levels, *etc.*), high cardiac output, or bleeding are usually present[3]. In Case 2, coagulation dysfunction also occurred after birth, and good results were achieved after the correction of coagulation function and conservative medical treatment. Unlike previous reports, Case 3 involved a twin fetus. Monitoring of the affected fetus and protection of the healthy fetus are key issues. In Case 3, after the prenatal discovery of a hypervascular mass on the surface of one of the twins, 5 wk later, the volume of the mass had increased significantly, and intrauterine stillbirth and fetal edema occurred. We speculated that this might be due to the large size of the lesion and high flow in tumor vessels leading to heart failure, resulting in fetal death. A previous study also showed that CH is a high-flow vascular tumor that can cause high-output heart failure[16]. This might also be one of the causes of fetal death in utero. Although CHs are benign tumors, in Case 3, the CH progressed rapidly and led to an adverse outcome. Close ultrasonography follow-up was necessary, especially when the volume of the tumor increased rapidly and when CDFI demonstrated hypervascularization. In Case 3, after the

**Table 2 Literature review of cases with both ultrasound findings and NTRK3 gene diagnosis of congenital infantile fibrosarcoma**

Ref.	GA at diagnosis (wk)	Sex	Site	Size (cm)	Coagulopathy	Treatment	Outcome	GA at delivery (wk)	Modality of delivery	Birth weight (kg)	Prenatal ultrasound findings	Immunocytochemistry	ETV6/NTRK3 gene fusion detected	Affected organs or metastasis
Nonaka <i>et al</i> [7], 2004	19	Male	Back	6.1×2.2	-	-	-	29	Pregnancy terminated at 29 wk	1.4	Solid mass involving the soft tissue at the rightparaspinal area	Vim(+)	Yes	Liver and left adrenal gland
Al-Salem <i>et al</i> [4], 2011	-	Male	Sacrococcygeal	12.0×10.0	-	S	No recurrence during follow-up	40	Cesarean section	4.1	Not described in detail	Vim(+), Ki67(+)> 5%	Yes	Bone margin and skeletal muscle
Dumont <i>et al</i> [8], 2011	36	Male	Right leg	9.0×8.0	Hemorrhagic shock	S*	Died at day 8 of life	38	Cesarean section	3.3	Poorly vascularized	Vim(+)	Yes	-
Tsang <i>et al</i> [9], 2013	37	-	Right frontal	9.0×7.0	-	S	No recurrence during follow-up	37	Cesarean section	-	Not described in detail	Vim(+)	Yes	Skull
Kraneburg <i>et al</i> [10], 2013	36	Male	Left leg	11.8×9.3	Bleeding, anemia, hypovolemia	S*	No recurrence during follow-up	36	Vaginal delivery	2.1	Well-circumscribed, intracavitary, homogenous solid mass	-	Yes	-
Sivrikoz <i>et al</i> [11], 2020	24	Male	Anterior fetal neck and oropharyngeal	5.5×5.4	-	S+C	No recurrence during follow-up	36	Cesarean section	2.9	Hypervascular with irregular borders	Ki-67(+) 1%	Yes	Masseter muscle, parotid gland, thyroid gland
The present study, 2022	28	Male	Left axilla to the left chest wall	3.2×3.0	Consumptive coagulation dysfunction	S+C	No recurrence during follow-up	37	Cesarean section	2.6	Well-defined, heterogeneous with abundant blood flow	Ki-67 (+) 20%, SMA (+), CD34 (+) and CD31 (+)	Yes	Pectoralis and adjacent ribs

GA: Gestational age; S: Surgery; C: Chemotherapy; \*: Amputation; vim: Vimentin; -: Not mentioned; SMA: Smooth muscle actin.

affected fetus died in utero, treatment to promote fetal lung maturation and emergency cesarean section were performed immediately, which ensured stability of the vital signs of the normal fetus and achieved good results. Based on our experience and previous studies, in the case of prenatal detection of a suspected fetal tumor, biweekly ultrasonography is recommended for the first four weeks after diagnosis to dynamically assess the likelihood of delivery and fetal cardiac status[15].



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**Figure 6 Pathological findings of the congenital infantile fibrosarcoma in Case 1.** A: H&E staining image. The tumor cells showing eosinophilic, diffuse sheets of monotonous round cells with fine chromatin, and indistinct nucleoli; B-D: Immunohistochemistry demonstrated the expression of smooth muscle actin, CD34, and CD31 in the tumor cells; E: The immunochemical study showed that the Ki-67 proliferation index was approximately 20%; F: Using fluorescence in situ hybridization, the tumor cells showed NTRK3 gene rearrangement, with break-apart green (telomeric) and red (centromeric) signals (white arrows).

## CONCLUSION

In summary, both CIF and CH may present as soft tissue masses with rich blood supplies on the fetal body surface prenatally. Once discovered, close dynamic ultrasonography is very important, especially for large lesions that grow rapidly. Prenatal ultrasound can provide accurate information such as the location, size, growth direction and blood supply of the tumor, which can provide useful information for perinatal management strategies. Although it is difficult to differentiate between CH and CIF with prenatal ultrasound, it can provide useful imaging information and is a convenient means of monitoring. Especially for lesions that occur prenatally in one twin, close ultrasonographic monitoring may allow early prediction of adverse outcomes in the affected fetus. Once adverse outcomes occur, prompt obstetric intervention can ensure successful delivery of the healthy fetus.

## FOOTNOTES

**Author contributions:** Liang RN drafted the manuscript; Jiang J submitted the manuscript; Zhang J was responsible for following up the cases; Liu X provided pathological examination; Ma MY collected images; Liu QL provided postnatal hospitalization treatment; Ma L provided pathological diagnosis; Zhou L provided prenatal ultrasound examination of one of the fetuses; Wang Y provided prenatal MRI examination of one of the fetuses; Wang J searched for the references and generated the figures; Zhou Q revised the manuscript; Yu SS designed the manuscript.

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