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ORIGINAL RESEARCH

The Clinical Value of Prenatal Ultrasonography in the Differential Diagnosis of Fetal Suprarenal Space-Occupying Lesions

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Objective: This study aimed to investigate the value of prenatal ultrasonography in the differential diagnosis of fetal space-occupying lesions in the adrenal gland.

Methods: Thirty-six fetuses with adrenal gland space-occupying lesions diagnosed by prenatal ultrasonography between January 2019 and July 2021 were included in this retrospective study. The clinical data, ultrasonographic features, treatments, and prognoses of the fetuses were analyzed. Postnatal diagnoses were made using computed tomography (CT), magnetic resonance imaging, and surgical resection.

Results: Of the 36 fetuses, 10 were diagnosed with adrenal hematomas, eight with adrenal neuroblastomas, seven with adrenal cysts, seven with subphrenic pulmonary sequestration, and four with adrenal teratomas. The accuracy of prenatal diagnosis was highest in those with adrenal cysts and subphrenic pulmonary sequestration, with the accuracy being 85.7% for both conditions. The mean gestational age at first detection of subphrenic pulmonary sequestration was 22.5 ± 3.1 weeks, which was significantly lower than that of other diagnoses ($P < 0.05$), and the mean diameter of adrenal cysts was 15.1 ± 4.2 mm, which was significantly smaller than that of other lesions ($P < 0.05$). All newborns with adrenal teratomas and neuroblastomas were treated surgically. Five of the seven patients with subphrenic pulmonary sequestration and three of the seven patients with cysts were also treated surgically. Follow-ups of the remaining cases were carried out by enhanced CT examination, and the prognoses were good.

Conclusion: Prenatal ultrasonography can help differentiate between different types of fetal adrenal space-occupying lesions, and there is a high coincidence rate between the diagnosis of adrenal cysts and subphrenic pulmonary sequestration.

Keywords: ultrasonography, prenatal diagnosis, suprarenal space-occupying lesion, fetus mass

Introduction

Fetal suprarenal space-occupying lesions are clinically rare, and their accurate diagnosis remains a challenge for clinicians.[1] With the popularization of ultrasonography and improvements in imaging techniques over the past two decades, most space-occupying lesions in the suprarenal region can be detected prenatally.[2,3] However, the treatment methods and prognoses are varied due to differences in characteristics of diverse types of lesions.[4] Besides, most studies have been case reports or small sample case series.[1–3] Thus, early diagnosis is also particularly important for developing successful intervention programs and improving the prognosis of newborns.[5,6]

The present study aimed to investigate the clinical value of prenatal ultrasonography in the differential diagnosis of fetal suprarenal space-occupying lesions by analyzing the features, treatments, and prognoses of fetuses with such lesions who underwent prenatal ultrasonography.

Patients and Methods

Study Subjects

All fetuses diagnosed with space-occupying lesions in suprarenal region who underwent prenatal ultrasonography in the Jiangxi Maternal and Child Health Hospital from January 2019 to July 2021 were included in this retrospective study.

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Patients with suprarenal lesions on ultrasound graph were included. Patients who died after birth and those whose parents refused to participate were excluded. All lesions were confirmed by postpartum ultrasound, enhanced computed tomography (CT), magnetic resonance imaging (MRI), or surgery following the induction of labor.[7] The study was approved by the hospital's ethics committee, and all families gave their written informed consent before participating in the research.

Instruments and Methods

Color Doppler ultrasound was carried out using Voluson E8 (GE, USA) apparatus. When suprarenal space-occupying lesion was found, its size, shape, internal echoes, calcification, and position were recorded. After delivery, some newborns underwent pathological biopsy during surgery, with the others undergoing ultrasound, enhanced CT, or MRI every two to four weeks in the outpatient clinic to monitor changes in the adrenal mass. Malignant transformation on imaging often showed an increased lesion diameter, solid components, or blood flow, and irregular margins.

Statistical Analysis

SPSS version 22.0 was used for data analysis. Normally distributed measurement data were expressed as mean ± standard deviation (SD), and comparisons were examined using Student's *t*-test. The categorical data were expressed as n (%), and differences between two groups were examined using χ^2 analysis or Fisher's exact test. The test level was $\alpha = 0.05$, and $P < 0.05$ was considered statistically significant.

Results

General Conditions

A total of 36 cases (20 males and 16 females) were included (Figure 1). The median follow-up time was 9 months and ranged from 6 to 12 months. All patients were singleton pregnancies, and the age of the pregnant women ranged from 21 to 41 years, with a mean age of 27.3 ± 4.1 years. The gestational ages of the fetuses ranged from 24 to 39 weeks, with a mean age of 31.6 ± 2.5 weeks.

Of the 36 fetuses in the study, space-occupying lesions were located in the left suprarenal region in 20 cases and in the right in 16 cases. According to the results obtained from autopsy, surgical pathology, and radiographic follow-up, 10 cases of adrenal hematoma, 7 cases of adrenal cyst, 7 cases of subphrenic pulmonary sequestration, 8 cases of adrenal neuroblastoma, and 4 cases of adrenal teratoma were diagnosed. The accuracy of prenatal diagnosis was the highest in the case of adrenal cysts and subphrenic pulmonary sequestration (both 85.7%), followed by adrenal hematoma (80%), and adrenal neuroblastoma (62.5%). The accuracy of prenatal diagnosis was lowest in the case of adrenal teratomas (50%). The coincidence rate between prenatal and postpartum diagnosis is shown in Table 1.

Ultrasonographic Characteristics

Diagnoses were made based on the following ultrasonographic characteristics. 1) Adrenal neuroblastomas presenting as a cystic or cystic/solid mixed-echo mass with an unclear boundary with the adrenal gland, an uneven internal echo, calcification of part of the cyst wall, and a visible internal blood flow signal (Figure 2A). 2) Subphrenic pulmonary sequestration was characterized by a solid hyperechoic mass under the diaphragm, with a clear boundary with the adrenal gland, a uniform internal echo, no calcification, and abundant internal blood flow signals (Figure 2B). 3) Adrenal hematomas exhibiting a cystic or cystic/solid echo mass with, for the most part, an unclear boundary with the adrenal gland, an uneven internal echo, no calcification, and no obvious blood flow signals (Figure 2C). 4) Adrenal teratomas presenting as an irregular cystic/solid mixed-echo mass, most of which were calcified and had an unclear boundary with the adrenal gland and punctuate blood flow signals, both internally and at the periphery (Figure 2D). 5) Adrenal cysts presenting as a round cystic echo mass, with a clear boundary with the adrenal gland, an uneven internal echo, no calcification, and no blood supply. A summary of the ultrasonographic features of all 36 cases is given in Table 2.

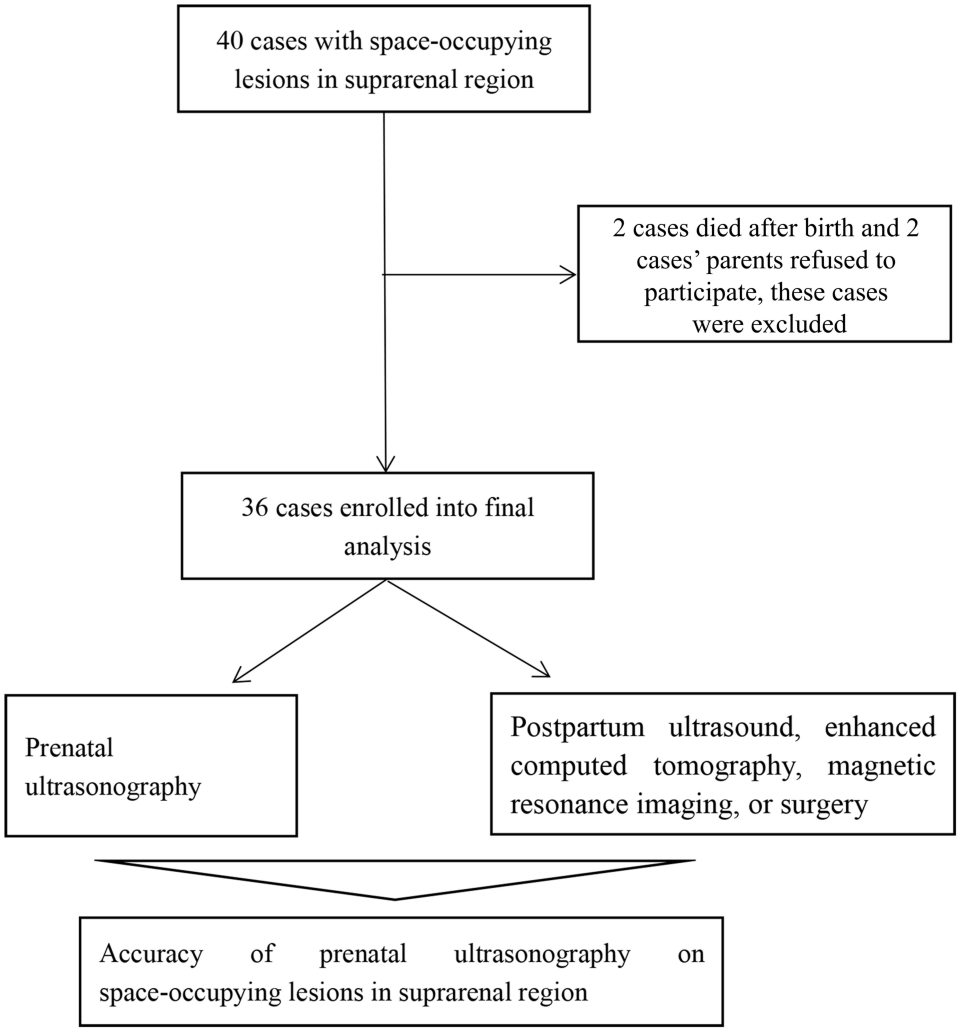

Figure 1 Flowchart of patients' selection.

Gestational Age at First Detection

The mean gestational age at first detection of subphrenic pulmonary sequestration was 22.5 ± 3.1 weeks, which was significantly lower than that of the other conditions (all $P<0.05$). There were no significant differences between adrenal hematomas, adrenal cysts, adrenal neuroblastomas, and adrenal teratomas in mean gestational age (all $P>0.05$). Records of the gestational age at first detection for each lesion type are shown in Table 3.

Table 1 The Coincidence Rate Between Prenatal Diagnosis and Postpartum Diagnosis

Prenatal Diagnosis	Number of Cases	Postnatal Diagnosis		Coincidence Rate
		Conformity	Inconformity	
Adrenal hematomas	10	8	2	80% (8/10)
Adrenal cyst	7	6	1	85.7% (6/7)
Adrenal neuroblastoma	8	5	3	62.5% (5/8)
Subphrenic pulmonary sequestration	7	6	1	85.7% (6/7)
Adrenal teratoma	4	2	2	50% (2/4)

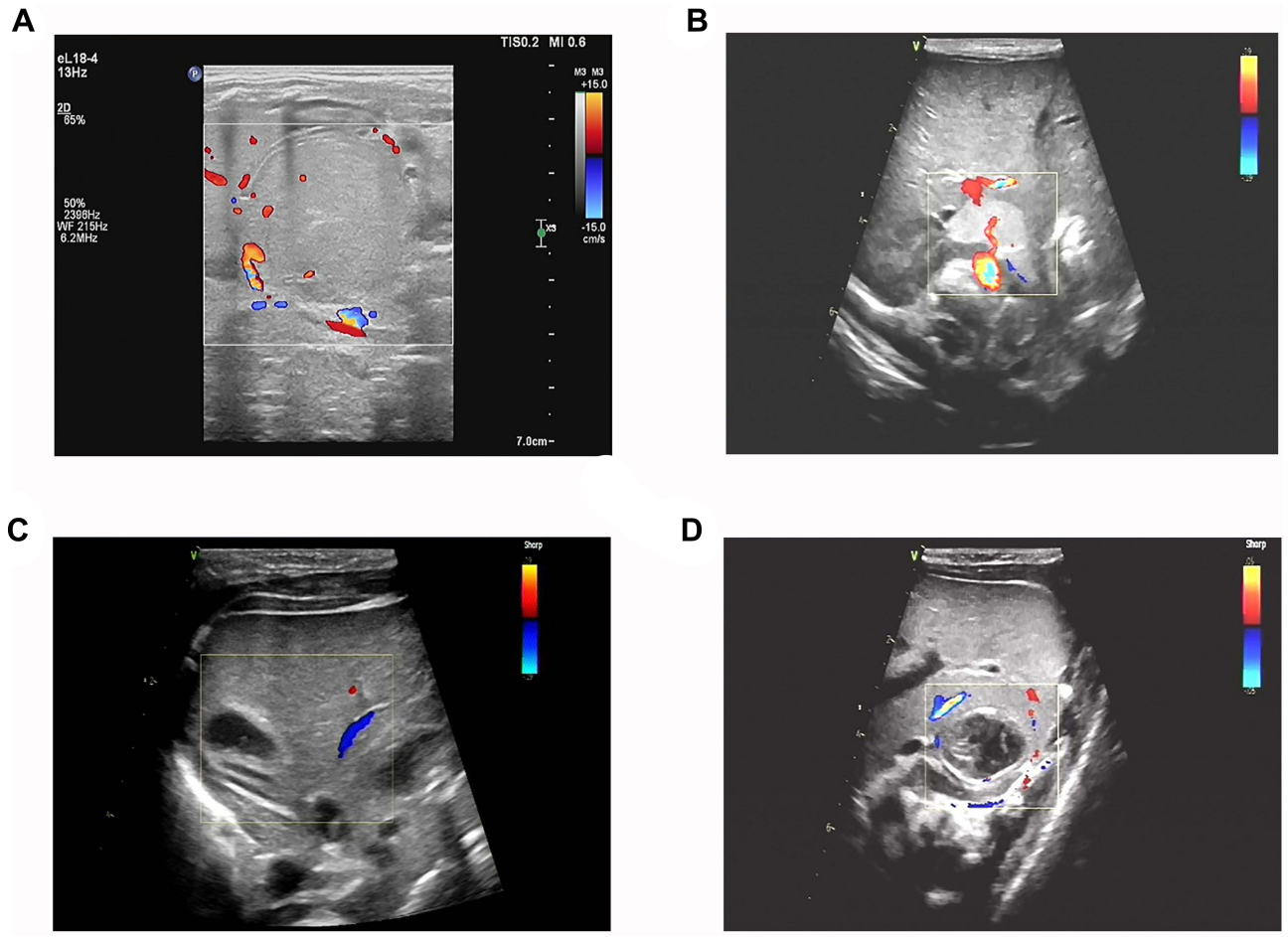

Figure 2 Ultrasonography of typical lesions. (**A**) Adrenal neuroblastoma: presented as an uneven, solid echo mass, approximately 15×18 × 22 mm in size, with a clear boundary and visible striped blood flow signals. (**B**) Subphrenic pulmonary sequestration: a large hyperechoic area, approximately 11×14 × 16 mm in size, was seen under the diaphragm with a cystic dark internal area and blood flow signals supplied by systemic circulation. (**C**) Adrenal hematoma: presented as a cystic echogenic mass, approximately 13×9 × 21 mm in size, with a clear boundary and an internal striped blood flow signal. (**D**) Adrenal teratoma: presented as a mixed-echo mass, approximately 10×10 × 12 mm in size, with an unclear boundary, internal calcification, and punctuate blood flow signals.

Mass Diameter

The mean diameter of adrenal cysts was 15.1 ± 4.2 mm, which was significantly smaller than that of the other conditions (all $P<0.05$). There were no significant differences between adrenal hematomas, subphrenic pulmonary sequestration,

Table 2 Summary of Ultrasonographic Features of 36 Cases of Space-Occupying Lesions in the Adrenal

Lesion (Case)	Total (Case)	Internal Echo			Adrenal Gland Demarcation		Calcification		Echo Changes		Internal Blood Supply	
		Cystic	Cystic-Solid	Solid	Clear	Unclear	Yes	No	Yes	No	Yes	No
Adrenal hematomas	10	8	2	0	1	9	0	10	9	1	0	10
Adrenal cyst	7	7	0	0	7	0	0	7	6	1	0	7
Adrenal neuroblastoma	8	4	3	1	0	8	3	5	6	2	8	0
Subphrenic pulmonary sequestration	7	0	1	6	7	0	0	7	0	7	7	0
Adrenal teratoma	4	0	4	0	1	3	3	1	2	2	4	0

Table 3 Clinical Parameters and Treatment of 36 Cases of Space-Occupying Lesions in the Adrenal Gland

Lesion (Case)	VMA (mg/24h)	AFP (ng/mL)	First Detection of Gestational Age (Week)	Diameter (mm)	Location		Surgery or Not	
					Left	Right	Yes	No
Adrenal hematomas	1.3±0.5	31.8±11.4	33.7±5.2	34.8±6.9	6	4	0	10
Adrenal cyst	1.1±0.4	33.5±12.3	34.1±4.9	15.1±4.2	4	3	3	4
Adrenal neuroblastoma	5.9±1.1	35.6±12.5	34.8±5.4	37.2±6.1	5	3	8	0
Subphrenic pulmonary sequestration	1.4±0.5	38.1±13.7	22.5±3.1	30.3±5.5	3	4	5	2
Adrenal teratoma	1.3±0.4	89.4±16.2	31.9±4.6	31.5±6.4	2	2	4	0

Abbreviations: VMA, vanillylmandelic acid; AFP, alpha-fetoprotein.

adrenal neuroblastomas, and adrenal teratomas in cyst diameter (all $P>0.05$). Records of mass diameter and location for each lesion type are shown in Table 3.

Treatment

Newborns with adrenal teratoma were treated with surgery during which the mass was completely removed. The eight newborns with neuroblastoma had stable adrenal lesions after 1 month postnatal CT follow-up and then underwent adrenal surgery. No subsequent chemotherapy was performed, and no recurrence of the masses was found during follow-up. In three cases of adrenal cyst and five cases of subphrenic pulmonary sequestration, the newborns underwent surgery. Other newborns with these conditions underwent follow-up by enhanced CT examination, and it was found that the adrenal masses gradually decreased in size or even disappeared. Records of treatment for each lesion type are shown in Table 3.

Discussion

As ultrasonography is noninvasive, simple to carry out, and does not use radiation, prenatal ultrasound has become the most common method for the clinical diagnosis of congenital fetal diseases. It is usually carried out before 24 weeks of gestation in cases where fetal abnormalities are suspected.[8] Previous studies have identified the accuracy of prenatal ultrasound in diagnosing fetal neuroblastoma as 51–70%, adrenal hematoma as 72–86%, and subphrenic pulmonary sequestration as 64–81%.[4,9] In the present study, the findings concerning diagnostic accuracy were consistent with those of previous research, with the accuracy of diagnosis of adrenal cyst and subphrenic pulmonary sequestration reaching as high as 85.7%. This indicates that attention should be paid to the value of prenatal ultrasonography as a diagnostic tool.

Prenatal ultrasonography can detect variations in space-occupying lesions in the suprarenal region, including differences in mass, internal echo, and blood flow signals. Lesieur et al proposed a diagnostic orientation of an atypical suprarenal entity according to its location and appearance.[3] A combination of MRI and ultrasound graph would be helpful for diagnosis of suprarenal entity.[6,10]

Approximately 90% of neuroblastomas, which are malignant tumors arising from the neural crest, occur in the adrenal gland, with most located on the right side. The ultrasonographic findings for neuroblastoma vary widely and can be cystic, of homogeneous echo texture, or calcified. Cystic neuroblastomas are the most common, accounting for 50% of all cases, while calcification is less common.[11] There may or may not be blood flow around the lesion, but there is usually no single feeding artery. In contrast, a single feeding artery is usually seen in ultrasound images of subphrenic pulmonary sequestration and is an important diagnostic indicator for this condition. The artery generally arises from the abdominal aorta, and in some cases, multiple arteries can also be seen, most of which drain to the inferior vena cava or vena azygos.[12] Subphrenic pulmonary sequestration is typically diagnosed in the second trimester of pregnancy. In the present study, the mean gestational age at first detection was 22.5 ± 3.1 weeks, which was much earlier than for other lesions.

The incidence of adrenal hematoma in neonates is 1.9 in 1000, which is much higher than that of neuroblastoma (0.058 in 1000), and its occurrence is closely related to perinatal asphyxia, stress response, birth injury, and coagulation disorders.[13] Ultrasonographic findings for adrenal hematoma are related to the time of hematoma formation. A hyperechoic mass is evident in the early stages, becoming progressively anechoic with liquefaction, followed by calcification, after which the hematoma subsides. Adrenal cysts are usually anechoic, with increased posterior echogenicity and well-defined borders, but may contain tissue fragments. Punctate blood flow signals may also be detected in some cases, and calcification of the cyst wall can also occur.[14]

Adrenal teratoma is rare and presents as cystic or solid on ultrasound images, with an uneven internal echo, rich blood flow signal, and occasional calcification. It is difficult to distinguish between neuroblastomas and advanced adrenal hematomas, which is one of the reasons for their low ultrasonic diagnosis rate. In the present study, the diagnostic accuracy of adrenal teratoma was only 50%. Therefore, it is suggested that teratoma should also be considered when neuroblastoma is suspected, especially when the features are atypical.

Given the differing malignancies of lesions in the adrenal gland, selecting the correct treatment strategy is a major challenge for pediatricians. Adrenal hematomas and cysts are often treated conservatively because they are benign lesions with a tendency to self-resolve. However, aggressive surgical resection is recommended when hematomas or cysts affect the surrounding organs, although the specific follow-up protocol remains controversial. Besides, non-surgical treatment was also proposed as a safe alternative for extra-pulmonary sequestration,[15] because several of these lesions might be invisible on imaging which could be categorized as postnatal regression.[6] Fetal neuroblastoma usually has a better prognosis when diagnosed early and may even disappear in utero or shortly after birth. However, in rare instances, neuroblastoma may metastasize to the liver.[16] For adrenal neuroblastoma diagnosed in late pregnancy, surgical treatment is the first choice, followed by chemotherapy in stage III and IV cases. Surgery usually involves a multidisciplinary treatment strategy.[17] In contrast, instances of fetal adrenal teratoma also require aggressive surgical treatment following diagnosis but usually have a better prognosis than neuroblastoma cases and do not require chemotherapy after surgery.[18] In the present study, all newborns with adrenal neuroblastoma and teratoma underwent surgery, and all cases survived until follow-up was completed.

A specific initial diagnosis is not always possible in cases of fetal adrenal gland lesions. In such instances, it has been suggested that newborns should be observed via follow-up for a month, and imaging, histopathological, and cytogenetic examinations should be conducted to confirm the diagnosis if the mass continues to grow or does not decrease.[19] This protocol avoids unnecessary surgery and mitigates the risk of harm to the fetus without delaying effective treatment.

The present study had several limitations. First, it was a retrospective study with unavoidable biases. Second, only a small number of cases were included in the sample. Last, follow-up biases might exist, due to the unwillingness of newborns' parents to disclose accurate health conditions of their babies and unpunctual follow-up at the time-point asked. Therefore, the study's conclusion should be interpreted cautiously.

Conclusion

Prenatal ultrasonography is a useful tool in the differential diagnosis of fetal space-occupying lesions in the adrenal gland and can therefore be used to develop appropriate treatment strategies, thereby improving prognosis. In addition, close follow-up and dynamic observation of mass changes in the adrenal region should be performed in clinical practice, and an aggressive treatment plan should be swiftly implemented if mass enlargement or malignant transformation occurs.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of the Jiangxi Maternal and child Health Hospital. Written informed consent was obtained from all participants.

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Disclosure

The authors declare that they have no competing interests.

References

1. Hsieh CC, Chao AS, Hsu JJ, et al. Real-time and power Doppler imaging of fetal adrenal hemorrhage. *Chang Gung Med J*. 2005;28:860–865.
2. Lin JN, Lin GJ, Hung IJ, et al. Prenatally detected tumor mass in the adrenal gland. *J Pediatr Surg*. 1999;34(11):1620–1623. doi:10.1016/S0022-3468(99)90629-2
3. Lesieur E, Noire A, Maurice P, et al. Prenatal assessment of atypical adrenal glands: a systematic approach for diagnosis. *J Ultrasound Med*. 2020;9999:1–10.
4. Schwab ME, Braun HJ, Padilla BE, Nijagal A. Imaging modalities and management of prenatally diagnosed suprarenal masses: an updated literature review and the experience at a high volume Fetal Treatment Center [published online ahead of print, 2020 Jan 26]. *J Matern Fetal Neonatal Med*. 2020;1–8. doi:10.1080/14767058.2020.1863366
5. Castro P, Paula Matos A, Werner H, et al. Prenatal diagnosis of suprarenal mass by magnetic resonance imaging: a case series. *J Matern Fetal Neonatal Med*. 2019;32(22):3882–3886. doi:10.1080/14767058.2018.1471679
6. Lazow SP, Richman DM, Dionigi B, Staffa SJ, Benson CB, Buchmiller TL. Prenatal imaging diagnosis of suprarenal lesions. *Fetal Diagn Ther*. 2021;48(3):235–242. doi:10.1159/000512689
7. Li JL, Geng XP, Zhang R, Yan C.Fetal adrenal area space-occupying lesions: prenatal diagnosis on ultrasound and prognosis. *Chin J Ultrasonography*. 2016;25(01):65–68. Chinese.
8. Brignole C, Bensa V, Fonseca NA, et al. Cell surface Nucleolin represents a novel cellular target for neuroblastoma therapy. *J Exp Clin Cancer Res*. 2021;40(1):180. doi:10.1186/s13046-021-01993-9
9. Ramareddy RS, Alladi A. Adrenal mass: unusual presentation and outcome. *Indian J Med Paediatr Oncol*. 2017;38(3):256–260. doi:10.4103/ijmpo.ijmpo_33_16
10. Victoria T, Johnson AM, Moldenhauer JS, et al. Imaging of fetal tumors and other dysplastic lesions: a review with emphasis on MR imaging. *Prenat Diagn*. 2020;40(1):84–99. doi:10.1002/pd.5630
11. Xia B, Yu G, Hong C, et al. Clinical analysis of 10 cases with fetal neuroblastoma. *Chin J Appl Clin Pediatr*. 2018;33(8):623–624.
12. Lu BX, Jiang B, Wang XM.Prenatal ultrasonic diagnosis of infradiaphragmatic pulmonary sequestration: case report. *Chin J Med Imaging Technol*. 2018;34(2):274. Chinese.
13. Pace S, Sacks MA, Goodman LF, Tagge EP, Radulescu A. Antenatal diagnosis of retroperitoneal cystic mass: fetiform teratoma or fetus in fetu? A case report. *Am J Case Rep*. 2021;22:e929247. Chinese. doi:10.12659/AJCR.929247
14. Zhang M, He XQ.The value of ultrasound in prenatal diagnosis and prognosis of fetal cystic mass. *Chin J Ultrasound Med*. 2020;36(02):157–160.
15. Robson VK, Shieh HF, Wilson JM, et al. Non-operative management of extralobar pulmonary sequestration: a safe alternative to resection? *Pediatr Surg Int*. 2020;36(3):325–331. Chinese. doi:10.1007/s00383-019-04590-2
16. Psarris A, Sindos M, Dimopoulou A, et al. Prenatal diagnosis of adrenal neuroblastoma - differential diagnosis of suprarenal masses in the third trimester of pregnancy. *Ultrasound Int Open*. 2019;5(3):E93–E95. doi:10.1055/a-1070-8651
17. Fati F, Pulvirenti R, Paraboschi I, Martucciello G. Surgical approaches to neuroblastoma: review of the operative techniques. *Children*. 2021;8(6):446. doi:10.3390/children8060446
18. Obeidat N, Sallout B, ALAAli W. Isolated subdiaphragmatic extralobar pulmonary sequestration: masquerading as suprarenal mass with spontaneous resolution. *Clin Exp Obstet Gynecol*. 2016;43(3):457–459. doi:10.12891/ceog2116.2016
19. Lackova E, Cunderlik A, Ticha L, Gabor M. Fetal adrenal gland enlargement - prenatal and postnatal management. *Neuro Endocrinol Lett*. 2017;38(Suppl1):31–34.