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Case Report

Two case reports of age-associated increased risk for fetomaternal hemorrhage and a literature review

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ABSTRACT

Fetomaternal hemorrhage (FMH) represents a relatively infrequent yet critical obstetric complication. Its subtle onset and absence of distinctive symptoms often render early detection a formidable task. This condition, if unchecked, can culminate in serious sequelae including fetal anemia, edema, and in extreme cases, fetal or neonatal demise. A variety of physiological and pathological elements inherent to pregnancy, coupled with the mother's advanced age, can elevate the risk profile for the development of FMH. In the current paper, we present two case studies involving FMH in maternal age, and couple these with a thorough review of existing literature. Our objective is to meticulously analyze the underlying causes, diagnostic modalities, clinical presentations, and therapeutic interventions pertinent to FMH. Ultimately, our aim is to contribute a valuable resource for guiding practitioners in the accurate diagnosis and effective management of this complex obstetric challenge.

KEYWORDS

fetomaternal hemorrhage (FMH), advanced age, literature review

1 Introduction

Fetomaternal hemorrhage (FMH) is a hidden and rare pregnancy disorder. A group of syndromes caused by various factors leading to the breakdown of the placental barrier, resulting in the entry of fetal blood into the maternal circulation system, causing fetal anemia and maternal hemolytic transfusion reaction, is one of the main causes of non-immune fetal edema. Fetomaternal transfusion is considered to be a common physiological phenomenon, which can occur during pregnancy and childbirth. The incidence of moderate to severe fetomaternal transfusion is 0.3% among all live-born infants [1]. It accounts for 14.0% of fetal deaths [2]. Due to its atypical and covert clinical symptoms, early prenatal diagnosis of feto-maternal transfusion is challenging. This condition often leads to severe complications and adverse outcomes for the fetus and newborn, including fetal distress, stillbirth, neonatal hemorrhagic anemia, hemorrhagic shock, neonatal death, or poor long-term prognosis [3]. Many clinical doctors currently have insufficient understanding of this disease, leading to a low diagnostic rate. We report here two cases of suspected FMH diagnosed in our hospital, discussing the etiology, clinical features, diagnosis, and treatment of FMH. The aim is to enhance the knowledge and management skills of obstetricians in dealing with FMH, improve the early diagnosis rate of FMH, and improve the prognosis of affected children.

2 Case presentation

Case 1: Patient, 27 years old, experienced 2 pregnancies and 1 abortion. Past medical history: In 2010, the patient underwent surgery for "atrial septal defect" with blood transfusion during the procedure, without any transfusion reactions. Presenting complaint: The patient was admitted on July 12, 2020 due to 41 weeks of amenorrhea and decreased fetal movement for 15+ hours. Prenatal examinations: Early and mid-term Down syndrome screening, fetal four-dimensional (4D) ultrasound, oral glucose tolerance test (OGTT), blood biochemistry, and hepatitis B, syphilis, and HIV tests all showed no abnormalities. Blood type of the pregnant woman is A positive (Rh positive). Inpatient fetal heart monitoring shows: baseline 150 beats per minute, suspicious sinusoidal wave (Fig. 1). Upon admission, an ultrasound examination of the fetus was performed, which showed an amniotic fluid index of 89 mm, indicating a normal amount of amniotic fluid. No other abnormalities were detected during the ultrasound

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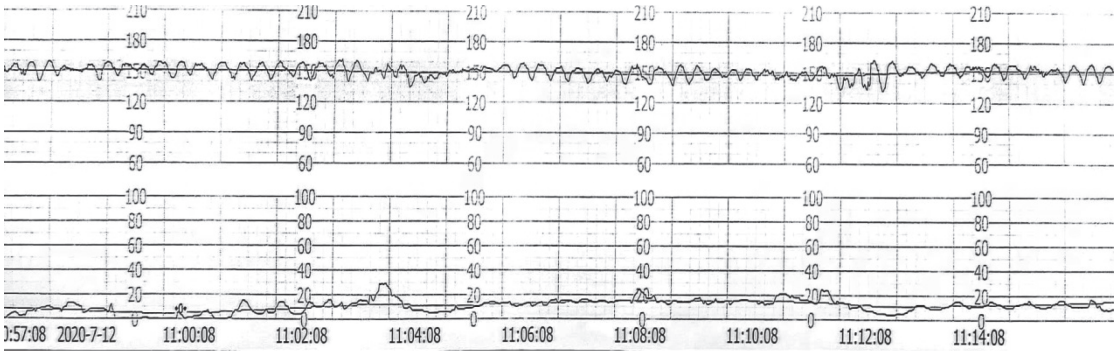

Figure 1 Case 1: fetal heart monitoring (sinusoidal wave). The horizontal axis represents time, and the vertical axis is divided into two parts. The upper half represents fetal heart rate, and the lower half represents uterine contraction pressure. The baseline fetal heart rate refers to the average level of the fetal heart rate within any 10-minute period. The normal baseline fetal heart rate is 110–160 beats per minute. Fetal tachycardia: Fetal heart rate baseline > 160 beats per minute. Fetal bradycardia: fetal heart rate baseline < 110 beats per minute. In this case, the baseline fetal heart rate is 150 beats per minute, and it shows smooth, sinusoidal-like oscillations.

examination. Additionally, the patient's blood test results showed a hemoglobin level of 119 g/L, which is within the normal range. Diagnosis: Fetal intrauterine distress. An emergency cesarean section was performed, during which meconium-stained amniotic fluid of approximately 600 mL was observed. A live female infant was delivered without umbilical cord entanglement, and the placenta appeared normal. The newborn had a normal appearance, pale skin, a heart rate of 60 beats per minute, a weight of 3310 g, and a length of 50 cm. The Apgar score at 1 min was 1, at 5 min was 5, and at 10 min was 7. Arterial blood gas analysis of the umbilical cord revealed a pH of 7.145 and a newborn hemoglobin level of 36 g/L. The newborn was transferred to the neonatology department and received treatment including blood transfusion. On July 14th, the newborn was transferred to Hunan Children's Hospital for further treatment. After the postpartum period, the mother underwent an urgent examination of alpha-fetoprotein (AFP), which revealed a level of 2 389.3 ng/mL. Discharge diagnosis: Fetal-maternal transfusion syndrome. Postoperative placental cord pathology examination showed focal calcification in the placental tissue, with no abnormalities detected in the umbilical cord. The follow-up until March 2024 shows that the prognosis for the newborn is good.

Case 2: Patient, 37 years old, G6P2A3. Past medical history: In 2022, the patient underwent internal fixation surgery for a left hand fracture. Admission reason: “36 weeks and 5 days of amenorrhea, decreased fetal movements for 2 days”. The patient was admitted on July 20, 2023. Prenatal examinations: nuchal translucency (NT) was not performed. Screening for thalassemia was negative. Early-stage Down syndrome screening showed low risk. Pregnancy-associated plasma protein A (PAPP-A) multiples of the normal median (MoM) value was higher than the cutoff value. Mid-term Down syndrome screening showed low risk. Non-invasive DNA testing indicated low risk. Fetal 4D ultrasound, OGTT and hepatitis B, syphilis, and HIV tests were all normal. Maternal blood type: O positive (Rh positive). On the day of admission, outpatient fetal heart monitoring was performed, showing poor variability and no significant accelerations (Fig. 2). Fetal ultrasound revealed one loop of umbilical cord around the neck, but no other abnormalities were found. Post-admission, continuous fetal heart monitoring was performed, which still showed poor variability and no significant accelerations (Fig. 3). Blood routine examination revealed a hemoglobin level of 117 g/L. Diagnosis: Fetal distress. Emergency cesarean section was performed, and clear amniotic fluid of approximately 500 mL was observed during the operation. A live male infant was delivered with one loop of umbilical cord around the neck. The placenta was unremarkable, and the newborn appeared without any abnormalities. The baby had pale skin, weighed 2710 g, and measured 48 cm in length. The Apgar scores at 1, 5, and 10 min were all 8. Umbilical artery blood gas analysis: PH 7.105, neonatal hemoglobin 33 g/L. The newborn was transferred to the neonatal department. Blood type was determined as O positive (Rh positive), and no evidence of hemolysis was found. The newborn responded well to blood transfusion and other treatments and was discharged in a stable condition. Postoperative rapid AFP test: 5694 ng/mL. Hemoglobin electrophoresis: HbF 5.7%, HbA 91.7%, HbA2 2.6%. Discharge diagnosis: Fetomaternal transfusion syndrome. The follow-up until March 2024 shows that the prognosis for the newborn is good.

3 Discussion

3.1 Etiology and pathogenesis

The etiology and pathogenesis of FMH are not fully understood, but it is believed to be associated with damage to the placental barrier. Any intrinsic or extrinsic factors that cause damage to the placental villi can lead to FMH. Possible high-risk factors include placental factors such as placental abruption, placenta previa, placental vessel abnormalities, placental chorioangioma, and choriocarcinoma; iatrogenic factors such as chorionic villus sampling, amniocentesis, umbilical cord blood sampling, external cephalic version, induction of labor with oxytocin, manual placental removal, and cesarean section; maternal factors such as smoking, preeclampsia, autoimmune diseases, and trauma [4]. A study on the incidence and risk factors of FMH in pregnant women in the Changsha area showed that the age of pregnant women who experienced FMH was higher than those who did not experience FMH, and the difference was statistically significant ($P < 0.01$) [5]. Advanced maternal age may be a risk factor for FMH. It is generally believed that FMH occurs due to damage to the placental barrier, with degeneration of the villi. This can lead to a significant difference in blood

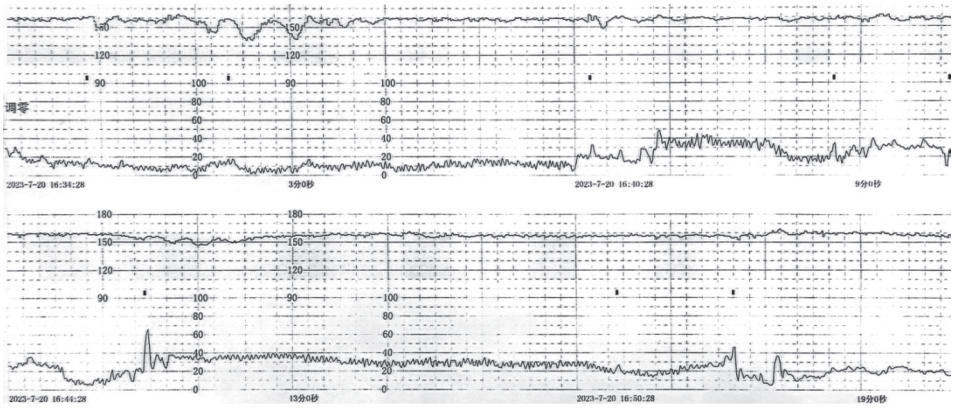

Figure 2 Case 2: outpatient fetal heart monitoring (atypical NST). The upper and lower halves of the graph represent continuous 20 minutes of fetal heart monitoring. The upper curves in both sections represent fetal heart rate, while the lower curves represent uterine contraction pressure. Baseline variability refers to the amplitude change of fetal heart rate from peak to trough per minute. It can be classified based on the degree of amplitude fluctuation as follows: (1) absent variability: complete absence of amplitude fluctuations; (2) minimal variability: amplitude fluctuations ≤ 5 beats per minute; (3) normal variability: amplitude fluctuations between 6 and 25 beats per minute; (4) marked variability: amplitude fluctuations > 25 beats per minute. The graph shows poor baseline variability in fetal heart rate and no significant accelerations.

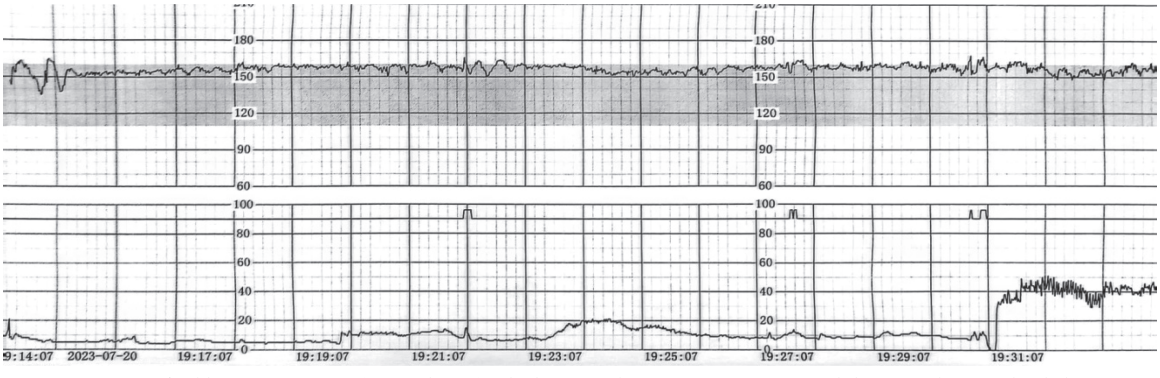

Figure 3 Case 2: inpatient fetal heart monitoring (atypical NST). The horizontal axis represents time, and the vertical axis is divided into two parts. The upper half represents fetal heart rate, and the lower half represents uterine contraction pressure. The graph shows a baseline fetal heart rate of approximately 157 beats per minute, with poor variability and no significant accelerations.

pressure between the mother and fetus, causing fetal blood to directly enter the intervillous space and eventually enter the maternal circulation. Pathological examination of the placenta in cases of FMH has revealed findings such as placental infarction [6], poor development [7], and immaturity of the villi [8]. Additionally, there may be the presence of nucleated red blood cells (nRBCs) in the villous vessels and stroma [9]. The placenta may appear pale in color, and there may be the formation of intervillositis thrombosis (IVT) [10], which is significantly associated with FMH. Increased vascular proliferation, fibrosis of the villi, and reduced distribution of villous vessels in the placental villi have been found to be associated with FMH [9]. Studies have shown that there is expression of vascular endothelial growth factor (VEGF), CD34, and CD31 in the placental villi of FMH cases [11]. In addition, FMH may also be associated with intrauterine infection. Studies have found that the incidence of FMH is higher in cases with intrauterine infection compared to those without intrauterine infection. Furthermore, when comparing patients with intrauterine infection and FMH to those without FMH, there is a significant increase in interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) levels in both maternal blood and umbilical cord blood [12]. These findings suggest the involvement of inflammatory cytokines in the occurrence of FMH. Additionally, it has been reported that gestational diabetes can cause changes in the ultrastructure of the placenta in patients. Syncytiotrophoblast microvilli become swollen and thickened, with fewer, narrower, and shorter inter-villous spaces, and disordered arrangement [13]. However, these risk factors are not present in most severe cases of FMH. In our hospital, there were no such risk factors in both cases. Some studies also suggest that these factors are not the main causes of FMH, but rather increase the risk of FMH in cases of impaired placental permeability [14]. Benirschke et al. [15] suggested that in cases of "spontaneous" FMH without high-risk factors, the bleeding may be caused by minor trauma to the placenta, such as fetal kicking or movement in the uterus, similar to the mechanism of FMH caused by external version. This idea is supported by studies showing an increased incidence of FMH with advancing gestational age [16]. Some researchers believe that as the placenta matures, the syncytiotrophoblast membrane becomes thinner and the capillaries gradually grow towards the periphery of the villi. The pressure inside the fetal capillaries is higher compared to the intervillous spaces of the placenta. This may make a more mature placenta more fragile, and the syncytiotrophoblast layer more susceptible to minor trauma (such as fetal movements) that can disrupt it. This is considered a possible explanation for the etiology of FMH without high-risk factors [17].

3.2 Clinical manifestations

The clinical manifestations of FMH are non-specific and can vary depending on the amount and rate of fetal hemorrhage. There is no universally defined threshold for massive FMH. Some researchers consider FMH to be present when the fetal blood loss exceeds 150 mL or approaches 50% of the fetal blood volume. Others suggest that a fetal blood loss exceeding 80 mL is sufficient for diagnosis [18]. When FMH is small, there may be no noticeable symptoms. However, in cases of significant FMH, the clinical manifestations can include decreased fetal movements, abnormal non-stress test (NST) results, edema, intrauterine fetal demise, and fetal growth restriction (FGR). Abnormal fetal heart rate monitoring can include a low baseline heart rate, decreased variability, absence of accelerations during fetal movement, and the presence of late decelerations or a typical sinusoidal pattern [19]. Decreased fetal movements, a sinusoidal pattern, and fetal edema are known as the classic triad of late-onset FMH. In newborns, severe anemia, bradycardia, heart failure, and shock may be observed. Newborns may also exhibit decreased muscle tone and low Apgar scores. In general, conventional resuscitation measures may not be effective in cases of severe FMH. However, there are instances where resuscitation efforts are successful. Even in these cases, the newborn may still exhibit pale skin throughout the body, which may not be proportional to the degree of asphyxia [20].

3.3 Auxiliary diagnostic methods

3.3.1 Maternal blood AFP testing

AFP is mainly synthesized by fetal liver cells. Some of it can enter the maternal bloodstream through the placenta and fetal blood, leading to an increase in AFP levels during pregnancy. AFP levels start to rise in early pregnancy, reach a peak around 32 weeks, and gradually decrease but still remain at a relatively high level around 33–34 weeks. Generally, AFP levels do not exceed 300 ng/mL [21]. When FMH occurs and the maternal-fetal blood barrier is disrupted, a large amount of AFP can enter the maternal bloodstream, leading to a significant increase in maternal AFP levels. The advantage of AFP testing is that it can be performed in most hospitals, and results can be obtained within 1–2 hours. However, a limitation is that there is no baseline AFP value before the occurrence of FMH for comparison. Additionally, it is necessary to differentiate between FMH-induced AFP elevation and other conditions that can cause an increase in maternal AFP levels, such as liver diseases. In such cases, a liver and gallbladder ultrasound examination can be performed to aid in the diagnosis.

3.3.2 Color Doppler measurement of fetal middle cerebral artery peak systolic velocity (MCA-PSV)

MCA-PSV has been widely used in clinical practice to predict fetal anemia. MCA-PSV ≥ 1.5 MoM indicates moderate to severe anemia, with a sensitivity of up to 100%. Some researchers suggest that MCA-PSV measurement should be routinely used as an auxiliary diagnostic tool for FMH [22]. Color Doppler measurement of fetal MCA-PSV is a non-invasive, repeatable, and rapid method for assessing fetal anemia. It is necessary for ultrasound practitioners to undergo training to acquire the skills necessary to master this technique.

3.3.3 Acid elution test (K–B test)

Kirby–Bauer (K–B) test [23] is based on the fact that fetal hemoglobin is more resistant to acid than maternal hemoglobin. After the maternal blood smear is washed with an acidic buffer solution, only the red blood cells containing fetal hemoglobin are stained with eosin, and the proportion of fetal red blood cells is calculated by counting the stained cells. The K–B test can be used as a diagnostic test for FMH and can provide an estimation of the fetal blood loss. The fetal blood loss (mL) can be calculated using the formula: fetal blood loss (mL) = maternal blood volume × maternal hematocrit × percentage of fetal red blood cells in K–B staining/neonatal hematocrit. The K–B test does not require special instruments or equipment, but it is time-consuming and has low repeatability. Its accuracy can be influenced by factors such as the thickness of the blood smear, acidity or alkalinity, personnel skills, and laboratory conditions. As a result, not all hospitals may offer this test.

3.3.4 The HbF measured by flow cytometry

The quantification of fetal red blood cells in maternal blood can be achieved by labeling them with specific antibodies and analyzing them using automated flow cytometry. This method provides higher accuracy and stability compared to the K–B test. However, it requires specialized equipment and technical expertise, making it more commonly used in research settings. Only a small number of hospitals offer this test, limiting its widespread application.

3.3.5 Maternal blood hemoglobin electrophoresis

In normal circumstances, the HbF content in maternal blood is less than 2%. In cases of FMH, the HbF content increases, and a HbF content greater than 3% in maternal blood is significant for diagnosing FMH. However, hemoglobin electrophoresis results may not be rapid and can be influenced by various factors, limiting its effectiveness in early diagnosis of FMH.

3.4 Treatment and prognosis

The treatment for FMH primarily involves blood transfusion, including intrauterine transfusion for the fetus and postnatal transfusion for the newborn. The timing for the termination of pregnancy should be carefully considered. For pregnancies near full term, active termination should be pursued. For pregnancies less than 32 weeks gestation, intrauterine fetal blood transfusion can be considered to prolong the gestational age and promote fetal lung maturity. However, there are associated risks such as infection, intrauterine fetal demise, and recurrent FMH during the treatment process. Intrauterine blood transfusion should use Rh-negative O-type blood, and cross-match with maternal serum to ensure no agglutination. The transfusion should follow the principle of small amounts multiple times. The transfusion volume should be determined based on the fetal hematocrit obtained from umbilical cord sampling, fetal weight, and gestational age. The transfusion volume usually ranges from 75 to 175 mL, not exceeding 30 mL/kg of fetal weight [24]. A post-transfusion hematocrit close to or exceeding 40% or fetal hemoglobin

reaching 150 g/L can be used as an indicator to end the transfusion [25]. During the transfusion, fetal monitoring should be performed to observe the disappearance of sinusoidal pattern or other abnormal heart rates. Doppler ultrasound should be used to monitor the restoration of peak velocity of blood flow in the middle cerebral artery. Daily fetal movement counts should be recorded, and biophysical profile assessments should be performed every 2 weeks. The decision to perform intrauterine fetal blood transfusion for pregnancies between 32 and 34 weeks should be carefully weighed, considering the potential benefits and risks.

The prognosis of FMH fetus has been reported to be related to factors such as the amount and rate of blood loss and gestational age. Newborn hemoglobin levels are an important prognostic factor for long-term adverse outcomes [26]. A study conducted by Kadooka et al. [27], a group of Japanese researchers, followed 18 FMH newborns for 15 years. Among them, 9 newborns showed adverse outcomes such as cerebral palsy, intellectual disability, attention deficit, hyperactivity, and epilepsy. The study results indicated that the median hemoglobin concentration in the poor prognosis group was 3.6 g/dL, while it was 5.4 g/dL in the good prognosis group (P = 0.01). The study suggested that the less blood loss the fetus experienced during pregnancy, the better the relative prognosis.

4 Conclusion

FMH is rare, and early diagnosis is difficult, most of which is diagnosed after delivery. Clinicians need to strengthen the understanding of FMH, early identification, early diagnosis, active treatment, to avoid the occurrence of adverse fetal outcomes.

Author contributions

Dan Xu was responsible for the conception and overall design of the study, while Dan Xu and Jia Liu collaborated on conceptualization, data curation, and methodology, as well as contributed to the writing. Additionally, Dan Xu and Jie Gong performed formal analysis and were involved in the review and editing process of the manuscript.

Ethics approval

The institutional review board of the Yueyang People's Hospital approved this study. The present study was approved by the ethics committee of The Second Affiliated Hospital of Zhengzhou University (Approval ID: 2021326) and was performed in compliance with the WMA Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects.

Consent to participate

The volunteers were enrolled with written informed consent. All the patients' authorized representatives and those patients who had the ability to communicate with the doctors agreed to participate in the study. The informed consent was obtained in written form.

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Conflict of interests

The authors report there are no competing interests to declare.

References

[1] Maier, J. T., Schalinski, E., Schneider, W., Gottschalk, U., Hellmeyer, L. Fetomaternal hemorrhage (FMH), an update: Review of literature and an illustrative case. *Archives of Gynecology and Obstetrics*, **2015**, 292(3): 595–602. https://doi.org/10.1007/s00404-015-3686-1.

[2] Stroustrup, A., Plafkin, C., Savitz, D. A. Impact of physician awareness on diagnosis of fetomaternal hemorrhage. *Neonatology*, **2014**, 105(4): 250–255. https://doi.org/10.1159/000357797.

[3] Troìa, L., Al-Kouatly, H. B., McCurdy, R., Konchak, P. S., Weiner, S., Berghella, V. The recurrence risk of fetomaternal hemorrhage. *Fetal Diagnosis and Therapy*, **2019**, 45(1): 1–12. https://doi.org/10.1159/000491788.

[4] Zhang, Z. W., Duan, M. Y. Fetomaternal hemorrhage syndrome. *Chinese Journal of Practical Gynecology and Obstetrics*, **2011**, 27(3): 238–240.

[5] Fan, K. X., Zhu, P. H., Wang, Y., Wang, Y. J., Zhang, N. J. Analysis of the incidence and risk factors of fetal-maternal hemorrhage syndrome in pregnant women in Changsha area. *Chinese Journal of Blood Transfusion*, **2022**, 35(10): 1031–1034.

[6] Stefanovic, V. Fetomaternal hemorrhage complicated pregnancy: Risks, identification, and management. *Current Opinion in Obstetrics and Gynecology*, **2016**, 28(2): 86–94. https://doi.org/10.1097/GCO.0000000000000248.

[7] Ravishankar, S., Migliori, A., Struminsky, J., Has, P., Sung, C. J., He, M. Placental findings in feto-maternal hemorrhage in livebirth and stillbirth. *Pathology – Research and Practice*, **2017**, 213(4): 301–304. https://doi.org/10.1016/j.prp.2017.02.005.

[8] Gică, N., Botezatu, R., Demetrian, M., Vayna, A. M., Cimpoca-Raptis, B. A., Ciobanu, A. M., Gica, C., Peltecu, G., Panaitescu, A. M. Severe neonatal anemia due to spontaneous massive fetomaternal hemorrhage at term: An illustrative case with suspected antenatal diagnosis and brief review of current knowledge. *Medicina (Kaunas)*, **2021**, 57(12): 1285. https://doi.org/10.3390/medicina57121285.

[9] Lewis, N. E., Marszalek, L., Ernst, L. M. Placental pathologic features in fetomaternal hemorrhage detected by flow cytometry. *Pediatric and Developmental Pathology*, **2017**, 20(2): 142–151. https://doi.org/10.1177/1093526616687652.

[10] Redline, R. W. Classification of placental lesions. *American Journal of Obstetrics and Gynecology*, **2015**, 213(4 Suppl): S21–S28. https://doi.org/10.1016/j.ajog.2015.05.056

[11] Zheng, Y., Li, D., Li, X., Zheng, A., Wang, F. Spontaneous massive fetomaternal hemorrhage: Two case reports and a literature review of placental pathology. *BMC Pregnancy Childbirth*, **2023**, 23(1): 530. https://doi.org/10.1186/s12884-023-05826-9.

[12] Wu, L. Q., Wang, M. X., Yao, R. Changes in cytokines in intrauterine infection and fetal maternal transfusion syndrome and perinatal outcomes. *Practical Medical Journal*, **2017**, 33(18): 3085–3088.(in Chinese)

[13] Yan, H. C., Xue, J. Q., Dong, H. Y., Yu, H. L., Xu, H. Study on the ultrastructure of placenta in patients with gestational diabetes. *Journal of Xuzhou Medical College*, **2006**, 26(3): 248–250.(in Chinese)

[14] Umazume, T., Yamada, T., Morikawa, M., Ishikawa, S., Kojima, T., Cho, K., Masauzi, N., Minakami, H. Occult fetomaternal hemorrhage in women with pathological placenta with respect to permeability. *Journal of Obstetrics and Gynaecology Research*, **2016**,

42(6): 632–639. Epub 2016 Mar 2 https://doi.org/10.1111/jog.12959.
[15] Benirschke, K., Burton, G. J., Baergen, R. N. Early development of the human placenta. In: Pathology of the Human Placenta. Berlin, Heidelberg: Springer, 2012: 41–53. https://doi.org/10.1007/978-3-642-23941-0_5
[16] Jiao, L., Ghorani, E., Sebire, N. J., Seckl, M. J. Intraplacental choriocarcinoma: Systematic review and management guidance. *Gynecologic Oncology*, **2016**, 141(3): 624–631. https://doi.org/10.1016/j.ygyno.2016.03.026.
[17] Renaer, M., Van de Putte, I., Vermylen, C. Massive feto-maternal hemorrhage as a cause of perinatal mortality and morbidity. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, **1976**, 6(3): 125–140. https://doi.org/10.1016/0028-2243(76)90140-4.
[18] Zizka, Z., Calda, P., Zlatohlavkova, B., Haakova, L., Cerna, M., Jirasek, J. E., Fait, T., Hajek, Z., Kvasnicka, J. Massive fetomaternal transplacental hemorrhage as a perinatology problem, role of ABO fetomaternal compatibility—case studies. *Medical Science Monitor*, **2001**, 7(2): 308–311.
[19] Liao, C. Y., Liao, L. P. Limitations of ultrasound for the diagnosis of fetomaternal hemorrhage: Report of a fatal case. *Taiwan Journal of Obstetrics and Gynecology*, **2015**, 54(1): 95–98. https://doi.org/10.1016/j.tjog.2014.11.016.
[20] Ding, X., Huang, X. H. The impact of fetal-maternal transfusion syndrome on neonates. *Chinese Journal of Obstetrics and Gynecology*, **1998**, 33(1): 44. (in Chinese)
[21] Tao, E., Ye, D., Long, G., Hu, Y., Fu, Q., Yuan, T., Jiang, M. Severe neonatal anemia affected by massive fetomaternal hemorrhage: A single-center retrospective observational study. *J Matern Fetal Neonatal Med*, **2022**, 35(20): 3972–3978. https://doi.org/10.1080/14767058.2020.1845313.
[22] Munoz, J. L., Schleicher, M., Bowersox, N. Integration of fetal middle cerebral arterial (MCA) ultrasonography in acute fetal-maternal hemorrhage. *Obstetrics and Gynecology*, **2019**, 2019: 4363054. https://doi.org/10.1155/2019/4363054.
[23] Chen, J. C., Davis, B. H., Wood, B., Warzynski, M. J. Multicenter clinical experience with flow cytometric method for fetomaternal hemorrhage detection. *Cytometry*, **2002**, 50(6): 285–290. https://doi.org/10.1002/cyto.10154.
[24] Plecas, D. V., Chitkara, U., Berkowitz, G. S., Lapinski, R. H., Alvarez, M., Berkowitz, R. L. Intrauterine intravascular transfusion for severe erythroblastosis fetalis: How much to transfuse. *Obstetrics and Gynecology*, **1990**, 75(6): 965–969.
[25] Tanawattanacharoen, S., Taylor, M. J. O., Letsky, E. A., Cox, P. M., Cowan, F. M., Fisk, N. M. Intrauterine rescue transfusion in monochorionic multiple pregnancies with recent single intrauterine death. *Prenatal Diagnosis*, **2001**, 21(4): 274–278. https://doi.org/10.1002/pd.49.
[26] Wylie, B. J., D'Alton, M. E. Fetomaternal hemorrhage. *Obstetrics and Gynecology*, **2010**, 115(5): 1039–1051. https://doi.org/10.1097/AOG.0b013e3181da7929.
[27] Kadooka, M., Kato, H., Kato, A., Ibara, S., Minakami, H., Maruyama, Y. Effect of neonatal hemoglobin concentration on long-term outcome of infants affected by fetomaternal hemorrhage. *Early Human Development*, **2014**, 90(9): 431–434. https://doi.org/10.1016/j.earlhumdev.2014.05.010.