

Approach an appropriate decision on fetus with endocardial fibroelastosis in collaboration with cardiovascular profile score

A case report

Hualin Yan, MD^{a,b}, Kaiyu Zhou, MD, PhD^{a,c}, Zhang Zhang, MD^d, Chuan Wang, MD^{a,b}, Nan Guo, MD^e, Yifei Li, MD, PhD^{a,*}, Yimin Hua, MD, PhD^{a,c,*}

Abstract

Introduction: Fetal endocardial fibroelastosis (EFE) is a kind of rare fetal cardiac malformation characterized by the diffuse thickening of the ventricular endocardium. The diagnosis of fetal EFE depends on the echocardiographic features which are still confused that how to make an appropriate pregnant decision due to the conflict between high prenatal mortality and acceptable prognosis once after birth. Here, we seriously built a 4-gradation recommendation system based on cardiovascular profile score (CVPS) to supply a prediction of clarified pregnant outcomes with EFE and provide a practical way to offer optimal medical consultation.

Clinical procedure: A suspected case of fetal EFE has been aware at 24th gestational week by fetal echocardiography. The CVPS of this affected fetus dropped to 6 out of 10 points, which indicated a severe heart condition along with the fetus and predicted an adverse fetal prognosis according to our recommendation system. After fully informed consent, the prospective parents determined to terminate pregnancy. Following the induced abortion, postmortem pathological findings confirmed the echocardiographic suspicion of EFE.

Conclusion: According to our experience and previous researches, we could reach a relative clear prediction of the outcomes of the EFE fetuses based on the CVPS of such suspected fetuses, which should lead to approach an appropriate pregnant decision for such fetuses.

Abbreviations: CVPS = cardiovascular profile score, EFE = endocardial fibroelastosis.

Keywords: cardiac function, cardiovascular profile score, fetal endocardial fibroelastosis, fetal outcomes, prenatal diagnosis

1. Introduction

Fetal endocardial fibroelastosis (EFE) is a type of rare fetal cardiac malformation characterized by the diffuse thickness of the ventricular endocardium. The fundamental pathological changes of EFE include hyperplasia of endocardium elastic fibers and collagenous fibers. Its main clinical complication is diastolic

dysfunction, following a significant heart failure which might lead to a fetal demise. Here, we suggest a 4-gradation recommendation for doctors to provide an appropriate suggestion for such fetuses suffered with EFE and their parents. And this study was approved by the Ethics Committee of West China Second University Hospital of Sichuan University.

2. Case report

A 39-year-old woman (gravida 3 para 2, 1 miscarriage and a healthy daughter without any heart diseases) was transferred to our center for the abnormal findings during the routine obstetric ultrasound examination at 24 weeks' gestation. Extended echocardiography screen showed a hypokinetic left ventricle and septum associated with a thickened hyperechogenic endocardium. Dilation had been confirmed of the right ventricle and both ventricles showed poor contractile function on screening (Fig. 1A and B). So a suspected fetal EFE had been identified.

Cardiovascular profile score (CVPS), comprising of 5 categories,^[1] was established to evaluate the fetal cardiac function and has been applied to fetal outcomes prediction regardless of primary diseases. For such fetus, the dilated fetal heart resulted in an increased cardiothoracic area ratio, there were no flows in the left ventricle during ventricle diastole, and end-diastolic velocity of umbilical artery was absent on Doppler flow measurement. Taken together, the CVPS of this fetus was 7 points (Table 1). According to our meta-analysis,^[2] once CVPS dropped to 7 or below, it would demonstrate an adverse pregnant outcome. Such

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HY and KZ contributed equally to this article.

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^a Department of Pediatrics, West China Second University Hospital, Sichuan University, ^b West China Medical School, Sichuan University, ^c Key Laboratory of Women and Children's Diseases and Birth Defects, Ministry of Education, West China Second University Hospital, Sichuan University, ^d Department of Pathology, West China Hospital, Sichuan University, ^e Department of Ultrasound, West China Second University Hospital, Sichuan University, Chengdu, China.

* Correspondence: Yifei Li and Yimin Hua, Department of Pediatrics, West China Second University Hospital, Sichuan University, No. 20, 3rd Section, South Renmin Road, Chengdu, Sichuan 610041, China (e-mail: liyfwcsh@scu.edu.cn [YL] and nathan_hua@163.com [YH]).

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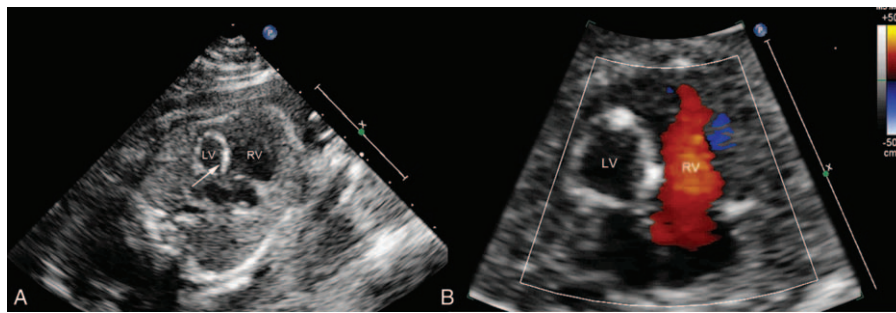


Figure 1. Echocardiogram of the case. (A) Four-chamber view showing hypokinetic LV and septum with thickened hyperechoic endocardium (arrow), and dilated RV at 24 week gestation. (B) Doppler flow imaging during ventricle diastole showing filling of RV, but no flows in the LV. LV = left ventricle, RV = right ventricle.

fetuses always suffered poor fates, even faced intra-utero death. However, the CVPS decreased at 6 points at 27 weeks' gestation (cardiothoracic area ratio increased to 0.56). The total follow-up period was about 3 weeks, but we found the CVPS had already dropped at 6. So we considered that the fetus was under a very severe condition, and if it dropped at 5, the fetus might cause adverse impacts on maternal side. Meanwhile, maternal oral digoxin administration was recommended for the parents and they refused such intervention under fully understanding there would be a bad prognosis of their fetus without treatment. After the fully informed consent, the parents decided to receive a termination avoiding adverse impacts on maternal side.

On pathological examination, the fetus weighed 940.0 g and was 36.5 cm in length, with a 7.1 g heart. Autopsy of the heart revealed the concentric hypertrophy of left ventricle with a thickened wall (4 mm), covered with diffuse white fibrous tissue (Fig. 2A and B). The aortic valve was dysplastic. There was small amount of pericardial effusion. No septal defects and other valvular abnormalities were noticed in the heart. Hematoxylin–eosin stain and Verhoeff elastic stain showed the thickened left ventricular endocardium and hyperplastic elastic fiber, which confirmed the diagnosis of EFE (Fig. 3A and B).

3. Discussion

Fetal EFE was considered to be a reactive process of the endocardium, which can be caused by several factors such as

intrauterine viral myocarditis (mumps, coxsackie virus B^[3]), autoimmune reaction,^[4] and mucopolysaccharidosis.^[5] Meanwhile, Fetal EFE could also be secondary to aortic stenosis or hypoplastic left heart syndrome^[6] and company with dilated cardiomyopathy^[7] or left ventricular noncompaction.^[8]

To the best of our knowledge, there were limited cases of fetal EFE have been published. The prenatal diagnosis of EFE mainly depended on the echocardiographic features—hyperechoic endocardial thickening of ventricular walls. Previous studies have demonstrated that several indicators of echocardiography could identify a fetal EFE.^[9,10] However, the autopsy is still the golden standard for EFE diagnosis.^[9] Luckily, in the past decade, increasing evidences have obtained which revealed that fetal EFE could receive acceptable clarified diagnosis with the advanced echocardiography. Moreover, a kind of 3-gradation system has been built to claim the severity of fetal EFE based on a 74 cases group.^[6] However, abnormalities of heart structure can be combined with fetal EFE, as well as the completed heart block. According to the limited studies and cases, the survival rate of fetal EFE is around 20% and survivals have the capabilities that they could recover after several months or years after treatment.^[7,11] Therefore, it is important to make prudential decision by parents and doctors on whether such fetuses with EFE would be terminated as they might receive an acceptable prognosis once survived from their fetal period.

Although several risk factors for poor outcomes of fetal EFE have been identified, such as fetal hydrops, systolic dysfunction, diastolic dysfunction, significant atrioventricular valve regurgitation,^[7,11] and severe myocardial damage in right ventricle.^[4] However, such factors are mostly description features which are still difficult and confused to provide a clear suggestion for parents and doctors. Even McElhinney et al^[6] established a system to assess the severity of fetal EFE, but it failed to predict the fetal life according to such protocol. Fortunately, with the rapid development and applications of CVPS, many researches have identified its advantages in predicting fetal outcomes with fetal heart disorders originated by kinds of reasons.^[12–14] The CVPS has been built as a 10-point grading system to measure the fetal cardiac function regardless their primary diseases by echocardiography, including 5 reliable categories features (Table 1). A systematic review and other studies have confirmed a final score ≤ 7 would be significantly associated with increased hazard of mortality and adverse outcome of pregnancy.^[12–14] So CVPS has already become a practical tool to evaluate the pregnant prognosis of fetus with most types of cardiac diseases. More important, most of the listed risk factors would induce a

Table 1
Cardiovascular profile score of this fetus with endocardial fibroelastosis.

	Score	Normal	Abnormal findings
Hydrops	2	2	N/A
Venous Doppler (umbilical vein and ductus venosus)	2	2	N/A
Heart size (cardiothoracic area ratio)	1	2	The fetal heart was dilated, and the cardiothoracic area ratio was of 0.45
Cardiac function	1	2	During ventricle diastole, there were no flows in the left ventricle
Arterial Doppler (umbilical artery)	1	2	End-diastolic velocity of umbilical artery was absent
Total	7	10	

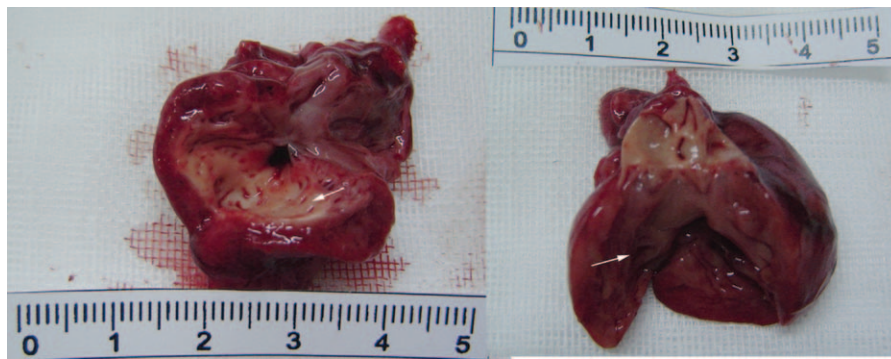


Figure 2. Postmortem feature of the case. (A) Cross-section through left ventricle showing diffuse white fibrous tissue (arrow) covering the inner surface of left ventricle. (B) Cross-section through right ventricle showing no fibrous tissue (arrow).

reduction of CVPS (Table 1). So that it would be great to predict the fetal pregnant prognosis of EFE not only taking the advantages of CVPS itself but also enrolled the identified risk factors together. Although there was limited knowledge on fetal EFE using CVPS, but based on our notable researches on CVPS under fetal heart disease, a 4-gradation recommendation system could be drawn for doctors to provide an appropriate suggestion for such fetus suffered with suspected EFE with a serious discretion. Firstly, once the CVPS of suspected EFE fetus drops to 5 points or less, termination of pregnancy should be strongly recommended because of the adverse impacts resulting from allosteric overload to both fetal and maternal sides, especially maternal aspect, which put the mother in the high-stress conditions resulting in infertility and diabetes. Secondly, if CVPS states between 6 and 7 points, the pregnancy decision should be carefully considered according to the involvement of fetal lesions, the maternal health condition, as well as the family's comprehensive situation. At the same time, the medication administration should be aware by parents as an alternation and recommended. Thirdly, if CVPS dropped, but still stand higher than 7 points, the EFE fetus should be very closely followed up every 2 weeks. Medication intervention is not necessary at that period. Based on our experience,^[15] transplacental digoxin therapy could improve fetal cardiac function and help the fetus survive with the exception of contraindications such as aortic stenosis. Finally, for the suspected EFE fetus with no reduction of CVPS, observation

and dynamic ultrasound evaluation are recommended with a little prolonged interval of 3 to 4 weeks because such fetuses would be more likely to survive prenatally and receive kinds of postnatal treatment according to the experience of our cardiac center. Moreover, as such abnormalities may cause a spontaneous miscarriage, the parents should have the choice of continuing the pregnancy until a natural end. But they also should be fully informed that there might be adverse impacts on maternal side once CVPS dropped under 5. In this case, the entire left ventricle was occupied with thickened fibrous tissue, the aortic valve was dysplastic, and CVPS decreased at 6 points within 3 weeks. So that all aforementioned information indicated a poor outcome.

In summary, once a fetal EFE was suspected, fetal extended cardiac echocardiography should be performed basically, and also a CVPS should obtain additionally, which could provide clinical suggestion according to our 4-gradation recommendation system. A series of following fetal echocardiography should be arranged during continuous pregnancy to get a dynamics recording of CVPS. Whether to apply intrauterine intervention depends on the integration of cardiac function assessed by CVPS. However, as there were still limited cases of fetal EFE and this was the first case using CVPS to provide suggestions for pregnancy decision, additional experience, and external validation should be enrolled for final conclusion making. Also there is little knowledge about the long-term postnatal outcomes, which should be elucidated by more researches.

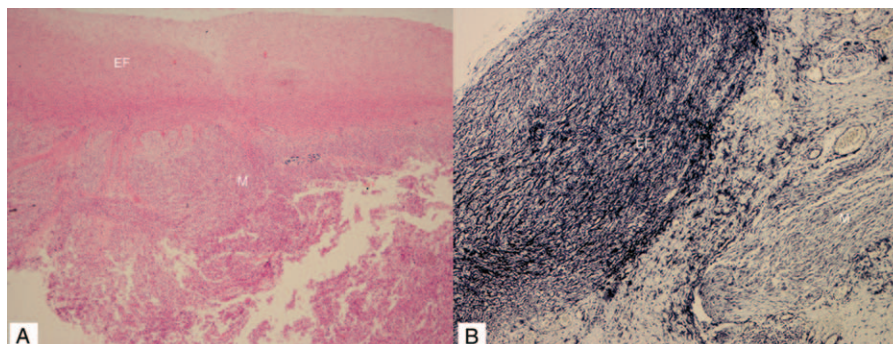


Figure 3. Histology feature of the case. Endomyocardial section showing remarkable hyperplastic EF of endocardium. (A) Hematoxylin and eosin stain $\times 40$; (B) Verhoeff elastic stain $\times 200$. EF = elastic fiber, M = myocardium.

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