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Subchorionic hematoma complicated by different antenatal complications: a case report of four patients with spontaneous abortion and literature review

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Summary

Subchorionic hematoma (SCH) is a specific pathology of pregnancy, as a sonographically-detected, intrauterine, echo-free area located between the membranes and the uterine wall. No reports have described SCH complicated by different antenatal complications in patients with spontaneous abortion. The patients herein present four cases of SCH accompanied by different complications, including Sjogren's syndrome (SS), antiphospholipid syndrome (APS), cervical incompetence (CI), and undifferentiated connective tissue diseases (UCTD). All the four patients with a history of spontaneous abortion delivered healthy babies. Additionally, the authors also reviewed previously reported cases regarding SCH. Appropriate treatment can effectively improve pregnancy outcomes in patients with a history of spontaneous abortion and SCH complicated by other complications.

Key words: Subchorionic hematoma; Spontaneous abortion; Sjogren's syndrome; Antiphospholipid syndrome; Cervical incompetence; Undifferentiated connective tissue diseases.

Introduction

SCH is a frequent finding on routine obstetric ultrasonography, which appears as a hypoechoic or anechoic crescent-shape area between the chorion and the uterine wall [1]. The incidence of SCH varies greatly from 4 to 48 percent of all pregnancies among reported studies [2, 3]. Although the exact mechanism of SCH and its influential factors remain unclear, SCH is associated with an increased risk of adverse outcomes, such as miscarriage, placental abruption, and preterm premature rupture of membranes [4]. Moreover, autoimmune diseases, such as Sjogren's syndrome (SS), antiphospholipid syndrome (APS), and undifferentiated connective tissue diseases (UCTD), are common among women of childbearing age, characterized by an abnormal immunologic reaction against antigens promoted by antibodies and immuno-complex formation [5, 6]. As a group of heterogeneous disorders, these autoimmune diseases have been associated with an increased risk of poor reproductive and/or adverse neonatal outcomes, such as miscarriage, premature delivery, and fetal growth restriction [7]. Specifically, APS is found in about 15% of women with recurrent pregnancy losses (RPLs), suggesting that APS is one of the most frequently acquired etiology for RPL [8]. Furthermore, CI is characterized by the inability to support a full-term pregnancy due to painless dilatation and effacement of the cervix in the second trimester of pregnancy, which complicates roughly 0.2% pregnancies and accounts for approximately 8% of fetal losses in the second trimester, with another typical symptom of preterm birth. However, to be best of the present authors' knowledge, no reports have investigated pregnancy outcomes of spontaneous abortion patients with both SCH and these autoimmune diseases. Therefore, in this paper, the authors report four cases of SCH in patients treated in their institution, with a history of spontaneous abortion accompanied by different complications, including SS, APS, CI, and UCTD, respectively.

Case Report

Maternal characteristics and neonatal outcomes of the four cases are depicted in Table 1. All the four patients provided informed consent for this report. Patient anonymity has been preserved.

Case one underwent spontaneous abortion twice before this pregnancy. Her first pregnancy had no fetal heart and received artificial abortion. Her second pregnancy was also eventful and ended with induced labor because of intrauterine fetal death at week 20. Subsequently, she received comprehensive screening for the etiology of recurrent spontaneous abortion and was diagnosed with SS, accompanied by high platelet aggregation in response to arachidonic acid (AA), high level of ESR, and low value of protein S. As a prophylactic measure, she was given multivit-

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Table 1. — *Clinical characteristics and outcome of four case series complicated by SCH.*

Case	Maternal age, y	Gravida, Parity	History of SA	Complication	Time of detection of SCH	Size of SCH (at time of detection, mm)	Time of disappearance of SCH	Treatment	Weeks at delivery	Birth weight, (grams)	Apgar scores (1/5 min)	Mode of delivery
1	34	G2P0	2	SS	7 weeks	20×24×30	10 weeks	LMWH, LDA, Pred	37^{+2}	3,300	10/10	Vaginal delivery
2	34	G1P0	1	APS	7 weeks	12×16×38	9 weeks	LMWH, LDA, Pred, HCQ	38	3,200	10/10	Vaginal delivery
3	30	G2P0	2	CI	20 weeks	74×63×84	28 weeks	LMWH, LDA, Pred	37	2,860	8/10	Cesarean section
4	35	G1P0	1	UCTD PROM	8 weeks	21×25×23	9 weeks	LMWH, LDA, Pred	36^{+1}	2,615	10/10	Vaginal delivery

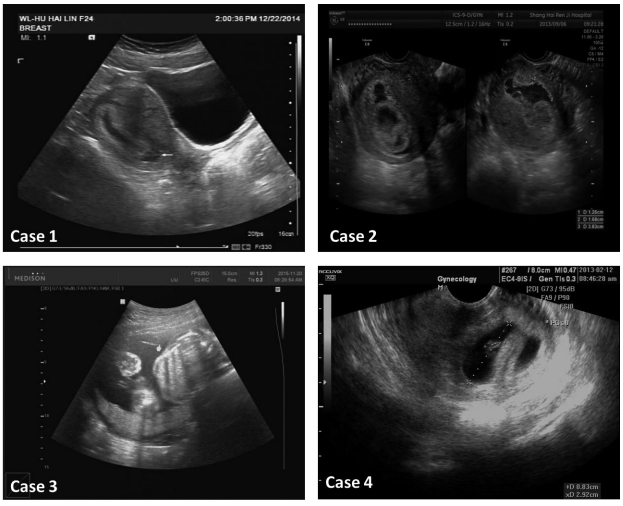

Figure 1. — Antenatal ultrasound presentations of SCH in four cases.

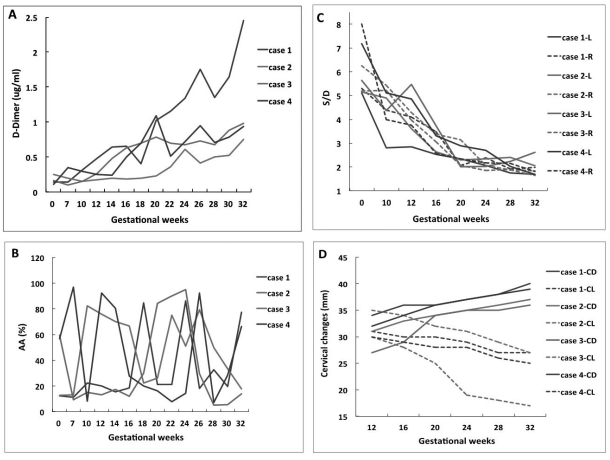

Figure 2. — Summary of D-dimer concentrations (A), AA (B), uterine artery pulsatility index S/D, (C) and cervical changes, and (D) in four cases during pregnancy. L = left; R = right; CD = cervical dilation; CL = cervical length.

amins, Chinese medicine angelica, low-dose aspirin, and prednisone therapy for two months before she was ready for another pregnancy. Dose of aspirin was adjusted every two weeks according to her level of platelet aggregation in response to AA. When she was in a stable condition, a regimen therapy with low-dose aspirin (LDA), low molecular weight heparin (LMWH), prednisone, and multivitamins was established. Meanwhile, she also received treatment with estradiol and progesterone during the first trimester of the current pregnancy. At week 7, an intrauterine cystic echo-free area sited between the uterine wall and the membranes was identified (Figure 1), and an SCH was suspected. At the time, the patient had no pain or bleeding. Follow-up ultrasound examination at ten weeks later documented the disappearance of the hematoma.

Case two underwent one early spontaneous abortion before this pregnancy. Her medical record indicated infertility, and *in vitro* fertilization and embryo transfer was performed in both pregnancies. Diagnosis of primary APS was performed for the detection of triple antibodies positivity after fetal loss in the first pregnancy. Meanwhile, her protein S value was below the lower limit. Therefore, she was given multivitamins, hydroxychloroquine (HCQ), LDA, and prednisone therapy for two months before she was ready for the second pregnancy. Then a regimen therapy with ASA, HCQ, LMWH, prednisone, and multivitamins was established. Meanwhile, she also received treatment with estradiol and progesterone during the first trimester of the current pregnancy. Moreover, at 7 weeks the SCH as an intrauterine cystic echo-free area was identified (Figure 1). At the time, she had slight vaginal bleeding without pain. Repeat ultrasound examination two weeks later documented the resolution of the hematoma.

Case 3 underwent early spontaneous abortion twice before this pregnancy. Both pregnancies had no fetal heart. Thus, she received medications including multivitamins, low-dose aspirin, Chinese medicine angelica, and bak Foong pills for two months to regulate menstrual cycle and improve endometrial blood flow. Thereafter, she received multiple treatments, including ASA, LMWH, prednisone, estradiol, progesterone, and multivitamins to prepare for another pregnancy. Her first trimester pregnancy was uneventful. However, a SCH was formed at week 20 (Figure 1), but she experienced no pain or bleeding at that time. The hematoma decreased gradually in size over time, and at week 28, SCH disappeared. Furthermore, sonographic cervical length (CL) at week 20 was only 25 mm. Therefore, transvaginal cervical cerclage was performed at week 21, and a McDonald suture was in-

serted. Finally, in this patient, a good outcome was achieved with careful surveillance.

Case 4 underwent one early spontaneous abortion. Given that her clinical history was suggestive of a CTD, but did not fulfill the criteria for any defined CTD, the diagnosis of UCTD was performed for positive test for antinuclear antibody (ANA) and dsDNA. Meanwhile, because her pre-pregnancy uterine artery systolic/diastolic (S/D) ratio was high, she received a similar drug therapy as in the third case. A SCH was also found at week 8 but disappeared one week later Figure 1), during which she experienced no pain or bleeding. Nevertheless, premature rupture of membranes occurred at 35+3 weeks. She was then treated with tocolysis and dexamethasone; and finally delivered a baby at 36+1 weeks.

In all the four cases, platelet aggregation in response to AA and D-dimer levels of all the four cases were monitored every two weeks during any subsequent pregnancy. Similarly, uterine artery blood flow and cervical changes were monitored every four weeks. In addition, as expected, pregnancy of all the four cases increased the D-dimer concentration in a stepwise fashion from preconception to the third trimester (Figure 2A). Platelet aggregation in response to AA changed in a wave mode (Figure 2B). By contrast, uterine artery blood flow index S/D gradually reduced with the progression of pregnancy (Figure 2C). Moreover, with the gradual shortening of CL during pregnancy, the degree of cervical dilatation increased.

Discussion

Women with SCH are more likely to have miscarriage and preterm birth. However, little is still known regarding the relationship between intrauterine SCH and other complications during pregnancy. To the best of the present authors' knowledge, this is the first report on SCH complicated by different antenatal complications, including SS, APS, CI, and UCTD in patients with spontaneous abortion.

Although the etiology and physiology of SCH remains unclear, it is believed to result from partial detachment of the chorionic membrane from decidua, and from subsequent abnormal placental implantation. Possible mechanisms of its formation [9] include premature perfusion of the intervillous space before the development of placental adaptations to cope with oxidative stress and shallow trophoblast invasion with resultant friable blood vessels. In addition, previous research found that vessels in the decidua capillaries were atrophied physiologically at 8-14 week of gestation, which could easily cause bleeding due to their fragility at this time [10]. A surface less than one-quarter of the gestational sac area was associated with a better prognosis. Therefore, small SCH tends to be more common in the first trimester and appears to pose no added risk to the ongoing pregnancy [11], which was consistent with the present results; only one case developed SCH at 20 weeks of gestation and remaining three cases developed SCH at first trimester.

Many autoimmune diseases occur frequently in women at childbearing age, posing various potential risks during reproduction, from fertility to pregnancy itself. Furthermore, pregnancy is considered to be an important factor that may alter the course of autoimmune diseases, which is associated with flares of disease activity. Particularly, APS has been widely studied for their detrimental effects on pregnancy, such as fetal losses, premature deliveries, preeclampsia, and IUGR. Recently, researchers have reported the association between SS or UCTD and spontaneous abortion. Moreover, systemic SS is frequently characterized by anti Ro/SSA (70-80%), and afflicted pregnancies may be exposed to a high risk of congenital heart block, idiopathic cardiomyopathy, and neonatal lupus. UCTD is a group of systemic autoimmune conditions not fulfilling the classification criteria for a definite CTD. So far, empirical prophylactic anticoagulation and immunosuppression therapy has always been recommended to treat these autoimmune diseases to improve pregnancy outcomes in recurrent spontaneous abortion patients. There were few case reports and sporadic observations indicating that thrombolytic therapy during pregnancy were associated with maternal and fetal complications, including SCH and abruption placentae [12, 13]. Accordingly, the present authors hypothesized that thrombolytic therapy with aspirin and LMWH may be associated with hematoma formation. A previous study reported that the marked immunomodulatory effect of dydrogesterone is a good choice for preventing abortion in women suffering from SCH [14]. In the present cases, dydrogesterone was used in the first trimester and this may explain the resolution of hematoma in the follow-up ultrasound examination a few weeks later. Additionally, careful surveillance of various blood indexes every two weeks may contribute to the improvement in the pregnancy outcomes of spontaneous abortions patients with SCH. It is well known that changes in pregnancy, especially endocrinological changes influenced by estrogen, may produce a prothrombotic state, which can increase maternal plasma D-dimer concentration progressively from conception to delivery. This is consistent with the present observations of the four cases. Previous studies reported that pulsed Doppler ultrasonography was useful in identifying women with spontaneous abortion who had impaired uterine circulation [15]. It was suggested that poor uterine perfusion leading to decreased trophoblast invasion of spiral arteries and inadequate placentation could be one of the causes of spontaneous abortions among women with autoimmune diseases [7]. Since platelet aggregation in response to AA was found to be higher among patients with RSA before pregnancy, therapy with aspirin to decrease platelet aggregation, either alone or in combination with LMWH to reduce D-dimer levels, might be efficacious if it was started early. Furthermore, prophylactic treatment with either HCQ or daily low-dose prednisone may provide a protective effect for patients with SCH complicated by different autoimmune diseases. Therefore, the present cases indicate that good outcomes could be achieved with careful surveillance and appropriate treatments, which may pro-

vide an important clinical perspective for treatment of spontaneous abortion patients with SCH complicated by different antenatal complications. In patients with SCH, physicians should not abandon the possibility of infants' survival especially in an earlier gestational week. Further investigations based on large numbers of subjects are necessary to confirm the present authors'supposition.

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