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Case report

Autoimmune hepatitis and pregnancy: report of two cases with different maternal outcomes

Gokcen Orgul[1], Esra Uyanik Ozkan[1], H. Tolga Celik[2], M. Sinan Beksac[1]

[1]Department of Obstetrics and Gynecology, Division of Perinatology, Hacettepe University Faculty of Medicine, Ankara, Turkey
[2]Department of Pediatrics, Division of Neonatology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Abstract

Women of childbearing age with autoimmune hepatitis (AIH) are now able to get pregnant. The progress of the disease during pregnancy is not well clarified yet.

The first pregnant woman had cirrhosis secondary to AIH, and she delivered by cesarean section. The patient had severe thrombocytopenia at the time of hospitalization. Unfortunately, she died due to massive thromboembolism at the 24th hour after delivery. The other patient had three recurrent abortions with a diagnosis of AIH. Low-dose low molecular weight heparin and low-dose acetylsalicylic acid along with low-dose prednisolone were administered during the course of the following pregnancies. The following pregnancies ended up with a living child.

There is a high morbidity and mortality risk for both fetus and mother. Hepatic performance of the patients, thrombotic events, inflammatory disorders and autoimmune system activation must be the main concerns together with necessary precautions.

Key words: pregnancy, autoimmune hepatitis, maternal mortality.

Address for correspondence

Gokcen Orgul, Hacettepe Universitesi Tıp Fakultesi Hastanesi, Kadın Hastalıkları ve Dogum Anabilim Dalı Perinatoloji BD, 06100 Ankara, Turkey, phone: 905556066254, fax: 903123051990, e-mail: gokcenorgul@gmail.com

Introduction

Autoimmune disorders and autoantibody positivity are risk factors for obstetric complications and perinatal morbidity and mortality [1, 2]. On the other hand, women of childbearing age with autoimmune disorders are now able to get pregnant and give birth under successful medical management due to advances in this field [3]. Autoimmune hepatitis (AIH) is a rare chronic inflammatory disease with a low incidence (1/100 000) in the general population [4]. AIH is more frequent in females, and pregnancy outcomes are reported in a limited number of clinical studies [5-7].

The progress of the disease during pregnancy is not well understood, and information in the current literature is confusing. Some authors have described worsening of the condition as a potential consequence after conception [8]. Controversially, others have claimed that regression or an unalterable state is also possible during pregnancy [5, 9, 10]. We aim to report our experience with two cases and their opposite pregnancy outcomes.

Case presentations

Case 1

A 31-year-old pregnant woman (gravida 2, para 1) at the 35th gestational week with cirrhosis secondary to AIH was hospitalized due to severe respiratory distress. This referred patient was under prednisolone treatment (4 mg/day) and her antenatal care follow-up visits were undertaken at another health center. An empiric antimicrobial regimen was administered quickly for pneumonia, and all the necessary laboratory tests were performed immediately. She had severe thrombocytopenia ($27 \times 10^3/\mu l$), but liver function tests were within the normal range. The patient was transferred

to the intensive care unit and emergent delivery was planned due to worsening maternal health condition. The patient was delivered by cesarean section (C/S) at the 37th (36 weeks 4 days) gestational week after intravenous immunoglobulin administration and platelet transfusions. The 1760 g female neonate was transferred to the neonatal intensive care unit for necessary medical procedures. Although C/S was uneventful, hematuria was observed starting at the postoperative 6th hour, and low molecular weight heparin (LMWH) administration was suspended until the 12th postoperative hour. Sudden hypotension, bradycardia and chest pain occurred 24 hours after surgery. Emergent echocardiographic findings and clinical/laboratory manifestations confirmed the suspected diagnosis of pulmonary embolism. Consequently, the clinical condition of the patient became critical very quickly, and she died at the intensive care unit due to massive thromboembolism and cardiovascular failure. The neonate was discharged from the neonatal care unit without any complication, and sent back to her home under the supervision of the father and the aunt.

Case 2

A patient with a history of three recurrent abortions and the diagnosis of AIH (at 20 years old) was admitted to our clinic before her fourth pregnancy. This patient had been evaluated carefully and undertaken intensive medical follow-up before her following pregnancies. Low-dose LMWH (0.2 ml enoxaparin) and low-dose acetylsalicylic acid (100 mg/day) along with low-dose prednisolone (4 mg/day) were administered during the course of her fourth and the following (5th and 6th) pregnancies. Various antibody tests for autoimmune disorders were performed. The results were negative for ASMA, AMA, and ALKM, but positive for ANA. Serum liver enzyme changes were not observed during her last 3 pregnancies. Platelet counts were normal before every pregnancy, but decreased during the course of these three pregnancies (the lowest level was $95 \times 10^3/\mu l$). The fourth and sixth pregnancies both resulted in preterm labor (34 3/7 week and 34 4/7 week, respectively), but both infants were healthy without any long-term complications. The fifth pregnancy of the patient was also uneventful, and she delivered at the 37th gestational week (2840 g female newborn) without any maternal or perinatal complications.

Discussion

Autoimmune hepatitis (AIH) is a rare chronic inflammatory disorder, and women with AIH are commonly infertile [9-11]. After recent advances in immunosuppressive treatment and increased clinical experience on AIH, pregnancies in this patient population have started to be reported in the literature [4-6]. There is a high morbidity and mortality risk for both fetus and mother from conception to the end of the puerperium [10-12]. Control of innate and humoral immunity together with hepatic functions is critical, as is the necessity of prevention of "endothelial injury/inflammatory processes" and thrombotic events [13, 14].

Obstetric complications are more common in women with AIH [9], and the probable cause is that the maternal-fetal interface structures (cellular components of intervillous space, such as syncytiotrophoblasts, endovascular trophoblasts, endothelial tissue of spiral veins, superficial epithelial cells of decidua and others) are target tissues for autoantibodies and natural immune cells activated by the disease [15]. Increased first trimester miscarriage and preterm delivery risks have been reported in previous studies, and this seems to be a result of adverse inflammatory changes in the placenta as described above [11, 12]. Thrombosis, which is caused by endothelial damage and complement system activation, is also a major dilemma in these patients. The increased tendency to thromboembolism and its negative impact on perinatal outcome are important, and must be taken under control during pregnancy [13, 14]. Besides this reality, pregnancy outcome is satisfactory only with successful medical therapy, and close antenatal follow-up [7, 11]. We prescribed low-dose prednisolone together with low-dose LMWH in case two, and she delivered three babies (under treatment) after three pregnancy losses. Clinicians should consider low-dose LMWH administration during pregnancy if there is clinical evidence of increased inflammation and thrombosis.

Massive gastrointestinal system bleeding is a major risk factor that can cause sudden death among pregnant women with AIH [6, 11]. Furthermore, pregnant women with AIH carry a high risk of infection, and sepsis can be a cause of maternal mortality [9]. The other important etiological factor contributing to maternal mortality is thromboembolism in these patients, and maternal deaths related to pulmonary embolism have been reported previously [6, 7]. Pulmonary embolism treatment depends on the hemodynamic status of the patients. Respiratory support and fluid replacement are the first steps followed by empiric anticoagulation with an effective oxygen supply [16]. Here we have presented a patient with the sudden occurrence of pulmonary thromboembolism in spite of severe thrombocytopenia. The disease exacerbation and massive pulmonary

thrombus formation precipitated maternal death during the postpartum period.

In conclusion, a special antenatal care program and perinatal surveillance are necessary for pregnant women with AIH. Patients must be in remission before getting pregnant. Hepatic performance of the patients, thrombotic events, inflammatory disorders and autoimmune system activation must be the main concerns together with necessary precautions during the framework of multidisciplinary follow-up of these patients. A successful pregnancy outcome under effective management is possible, but it is advisable that clinicians counsel patients carefully on the potential complications even before conception.

Disclosure

Authors report no conflict of interest.

References

1. Gleicher N. Maternal autoimmunity and adverse pregnancy outcomes. J Autoimmun 2014; 50: 83-86.
2. Mumusoglu S, Beksac MS, Ekiz A, et al. Does the presence of autoantibodies without autoimmune diseases and hereditary thrombophilia have an effect on recurrent pregnancy loss? J Matern Fetal Neonatal Med 2016; 29: 2352-2357.
3. Quintero OL, Amador-Patarroyo MJ, Montoya-Ortiz G, et al. Autoimmune disease and gender: plausible mechanisms for the female predominance of autoimmunity. J Autoimmun 2012; 38: J109-J119.
4. Manns MP, Czaja AJ, Gorham JD, et al. Diagnosis and management of autoimmune hepatitis. Hepatology 2010; 51: 2193-2213.
5. Hautekeete M. Remission of autoimmune hepatitis during pregnancy: a report of two cases. Liver 1999; 19: 55-57.
6. Heneghan M, Norris S, O'grady J, et al. Management and outcome of pregnancy in autoimmune hepatitis. Gut 2001; 48: 97-102.
7. Westbrook RH, Yeoman AD, Kriese S, et al. Outcomes of pregnancy in women with autoimmune hepatitis. J Autoimmun 2012; 38: J239-J244.
8. Stellon AJ, Keating JJ, Johnson PJ, et al. Maintenance of remission in autoimmune chronic active hepatitis with azathioprine after corticosteroid withdrawal. Hepatology 1988; 8: 781-784.
9. Schramm C, Herkel J, Beuers U, et al. Pregnancy in autoimmune hepatitis: outcome and risk factors. Am J Gastroenterol 2006; 101: 556-560.
10. Werner M, Björnsson E, Prytz H, et al. Autoimmune hepatitis among fertile women: strategies during pregnancy and breastfeeding? Scand J Gastroenterol 2007; 42: 986-991.
11. Terrabuio DR, Abrantes-Lemos CP, Carrilho FJ, et al. Follow-up of pregnant women with autoimmune hepatitis: the disease behavior along with maternal and fetal outcomes. J Clin Gastroenterol 2009; 43: 350-356.
12. Braga AC, Vasconcelos C, Braga J. Pregnancy with autoimmune hepatitis. Gastroenterol Hepatol Bed Bench 2016; 9: 220-224.
13. Zöller B, Li X, Sundquist J, et al. Autoimmune diseases and venous thromboembolism: a review of the literature. Am J Cardiovasc Dis 2012; 2: 171-183.
14. Downing LJ, Strieter RM, Kadell AM, et al. Low-dose low-molecular-weight heparin is anti-inflammatory during venous thrombosis. J Vasc Surg 1998; 28: 848-854.
15. Hekimoglu R, Pergin A, Ugur Y, et al. Impaired Implantation and Hereditary Thrombophila; Expression of LIF (Leukemia Inhibitory Factor) on Extravillous Trophoblasts. Gynecol Obstet Reprod Med 2012; 18: 123-126.
16. Konstantinides SV, Torbicki A, Agnelli G, et al.; Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J 2014; 35: 3033-3073.