Hermansky-Pudlak syndrome in the peripartum period

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Summary: Hermansky-Pudlak syndrome (HPS) is a disease characterized by the triad of oculocutaneous albinism, bleeding diathesis and organ failure secondary to lysosomal accumulation of ceroid lipofuscin. We report the case of a pregnant woman with HPS who had a successful vaginal delivery with the administration of desmopressin.

Keywords: Hermansky-Pudlak syndrome, platelet disorders, pregnancy

INTRODUCTION

Hermansky-Pudlak syndrome (HPS) is an autosomal recessive disorder resulting from abnormal formation or trafficking of intracellular vesicles. Intracellular vesicles such as melanosomes, platelet dense granules and lysosomes are primarily affected. Consequently, HPS is characterized by the triad of oculocutaneous albinism, bleeding diathesis and lysosomal accumulation of ceroid lipofuscin.¹ Bleeding complications resulting from abnormal platelet aggregation can range from mild mucocutaneous bleeding to life-threatening haemorrhage. Ceroid is a lipid-protein complex generated by lipid hyperoxidation and is cytotoxic to cells. Its deposition in organs can result in pulmonary fibrosis, granulomatous colitis and renal failure. Premature death secondary to pulmonary fibrosis occurs in 50% of HPS patients by the fifth decade.^{2,3} HPS occurs worldwide but is most commonly seen in persons of Puerto Rican descent, among whom the carrier frequency is approximately one in 21.⁴ There are eight gene mutations identified to be associated with HPS (HPS1, ADTB3A, HPS3, HPS4, HPS5, HPS6, HPS7 and HPS8/BLOC1S3).^{5,6} HPS1, located on chromosome 10, is the most common mutation and has been found in the Puerto Rican population. A small study has demonstrated that patients with HPS may have lower von Willebrand factor (vWF) activity than patients without HPS; however, the level of vWF activity has not been shown to correlate with bleeding severity.⁷ We describe the case of a woman with HPS presenting with active labour.

CASE REPORT

A 20-year-old Puerto Rican woman, G₁P₀ at 37 weeks of gestation, was transferred to our hospital from a neighbouring state for the management of active labour. She was diagnosed with HPS at age seven after a hand injury, which required treatment with

aminocaproic acid. The patient had oculocutaneous albinism and a bleeding diathesis, but no other organ involvement. She saw a haematologist during her pregnancy and was scheduled for an elective caesarean section at the patient's request during her 38th week of gestation. At 37 weeks of gestation, she presented to a hospital in a neighbouring state with active labour after spontaneous rupture of membranes. Her haemoglobin was 12.7 g/dl, platelet count was 258,000/ μ l, prothrombin time was 12.2 seconds (normal value was 11.0–14.2 seconds), partial prothrombin time was 23.5 seconds (normal value was 22.0–42.0 seconds), international normalized ratio (INR) was 0.94, and bleeding time was >15 minutes (normal = 1–9 minutes). The patient's baseline laboratory data were not available when she was transferred to our facility.

After consultation with the high-risk obstetrical service, a decision was made to deliver vaginally without epidural anaesthesia because of the concern regarding bleeding. The haematology service recommended prophylactic administration of desmopressin (DDAVP) with platelet transfusion as required. Ten hours after presentation, the patient vaginally delivered a healthy non-albino male infant weighing 3000 g with APGAR (Activity, Pulse, Grimace, Appearance and Respiration) scores of 5 and 9 at 1 and 5 minutes, respectively. The patient received DDAVP (0.3 μ g/kg) intravenously immediately after delivery of the shoulders. A platelet function analyzer test (PFA-100) was drawn at baseline and after DDAVP, both of which were normal. The PFA-100 assesses platelet function by measuring the time of formation of a platelet plug when a sample of blood is exposed to a membrane coated with two stimulators of platelet adhesion and aggregation: collagen and adenosine diphosphate (COL-ADP) and collagen and epinephrine (COL-EPI). In this patient, the COL-ADP (normal = 70–120 seconds) and COL-EPI (normal = 75–195 seconds) times were 81 and 135 seconds, respectively, at baseline, and 75 and 86 seconds, respectively, after DDAVP administration. Platelet and plasma vWF activity were not measured. The patient sustained a second-degree perineal laceration which was repaired. Fundal massage was performed and she received 20 units of oxytocin intravenously. The patient did not receive any intramuscular injections. Three hours

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post-delivery, she had a firm uterus but was bleeding moderately from the perineal area. Her haemoglobin and platelets dropped to 9.7 g/dl and 173,000/ μ l, respectively. The patient was subsequently transfused 12 units of platelets over 24 hours postdelivery. Her bleeding resolved, and her repeat haemoglobin and platelets were 10.0 g/dl and 311,000/ μ l, respectively. She was discharged from the hospital on day four. The infant tested negative for HPS.

DISCUSSION

Although her specific gene mutation is not known, our patient most likely had HPS1 as it is the most common mutation and has been found in patients of Puerto Rican descent. Five cases of HPS have been reported in pregnancy. One case described an 18-year-old Puerto Rican woman who presented with known HPS at 40 weeks of gestation. She was given five units of platelets prophylactically and spontaneously delivered a healthy male infant without complications.⁸ Reiss *et al.*⁹ reported two cases of Puerto Rican women, one presenting at 40 weeks and the other at 39 weeks of gestation. One patient received prophylactic platelet transfusion while the other did not; both had uncomplicated deliveries. Another case described a 21-year-old Indian woman who presented at 40 weeks of gestation and was given epidural anaesthesia at her own request. Following a vaginal delivery, she sustained a second-degree tear to the vaginal wall and perineum causing her systolic blood pressure to fall to 60–70 mmHg. The patient was resuscitated with two units of blood and intravenous fluids. Afterwards, the family informed the team of the patient's diagnosis of HPS, and the patient received DDAVP (0.3 μ g/kg). Her bleeding subsided, and the epidural catheter was removed one hour later without complications.¹⁰ Zatik *et al.*¹¹ reported the case of an 18-year-old Hungarian woman with HPS who underwent induction of labour at 41 weeks of gestation secondary to the presence of meconium. She was given prophylactic DDAVP (0.3 μ g/kg) and subsequently required an emergency caesarean for fetal distress. She had a blood loss of 1600 ml and required transfusion of four units of packed red cells and two units of platelets. Her bleeding resolved and she was discharged on postoperative day seven. In a subsequent pregnancy, the patient presented at 39 weeks of gestation with spontaneously ruptured membranes and regular contractions. She was given prophylactic DDAVP (0.3 μ g/kg) and again required caesarean section for fetal distress. She did not have

significant bleeding and did not require transfusion of blood products.

The diagnosis of HPS should be considered in pregnant patients with albinism in order to prevent potential obstetric complications. Pregnant patients with known HPS should avoid aspirin and other anti-platelet agents. Regional anaesthesia should also be avoided to decrease the risk of haematomas. A multidisciplinary approach is necessary to design a delivery plan in advance. There are currently no established guidelines for the obstetric management of HPS. Case reports have demonstrated that prophylactic platelet transfusion or DDAVP administration have been successful in minimizing potential bleeding complications. However, there has also been a case report of a successful, uncomplicated delivery in a woman with HPS who did not receive any prophylaxis for bleeding. Given the rarity of this condition, additional case reports of HPS in pregnant patients may be helpful in guiding the future management of HPS in pregnancy.

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