

CASE REPORTS

Hermansky–Pudlak syndrome in a pregnant patient

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Hermansky–Pudlak syndrome is a multisystem disorder with albinism, bleeding diathesis and visual impairment as the main features. We report a case of epidural analgesia in a pregnant patient, who was subsequently discovered to have this syndrome. We believe this to be the first such report.

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Hermansky–Pudlak syndrome (HPS) is a multisystem disorder characterized by being tyrosinase positive, which means that an individual may present with varied amounts of pigmentation. This manifests as albinism, visual impairment and platelet dysfunction, resulting in prolonged bleeding and ceroid deposition. This can cause progressive symptoms including pulmonary fibrosis, inflammatory bowel disease and kidney disease.^{1,2}

Case report

A 21-year-old Indian primigravida presented at 40 weeks of gestation with spontaneous rupture of membranes. Her antenatal notes revealed a haemoglobin of 8 g dl⁻¹ and serum B₁₂ of 177 ng l⁻¹ (normal range 220–700 ng l⁻¹) in the second trimester. She was taking iron supplements and had also received hydroxycobalamin. She had had no other significant medical, surgical or family history. Although of Asian origin, she appeared Caucasian with a very fair complexion. She requested an epidural for pain relief. After routine explanation and verbal consent, the anaesthetist sited the epidural in the usual manner without difficulty and 3 cm of catheter were placed in the epidural space. There was no blood or cerebrospinal fluid in the catheter. The epidural provided good analgesia and she had a normal vaginal delivery of a female infant 6.5 h later. During delivery she sustained a second-degree tear to both the posterior and anterior vaginal wall and perineum, and also developed a vulval haematoma. At this time, her vital parameters were stable and estimated blood loss was 250 ml. The tear was sutured in the delivery room under epidural analgesia.

After apparently achieving haemostasis, there was a small but continuing blood loss and further exploration in theatre

was planned. At this time, her haemoglobin was 11.3 g dl⁻¹, platelets 327 × 10⁹, INR 1 and APTT 1.1. For the procedure the epidural was topped up with bupivacaine 0.25 %, fentanyl and lidocaine 2%. Re-exploration of the tear revealed no active bleeding, but a continuous ooze from the raw areas was noted. The vagina was packed with swabs. The patient's systolic blood pressure was 60–70 mm Hg and estimated blood loss was 1800 ml. She received two units of blood and 1 litre of gelofusine, with improvement in her blood pressure. Whilst the patient was being treated, her sister arrived on the delivery suite and informed us of her own confirmed diagnosis of Hermansky–Pudlak syndrome (HPS). A prompt internet search³ revealed the relevant details of HPS, the main features of which include reduced platelet activity and a varying degree of albinism.

There had been no formal investigation of our patient, although she had fair skin comparable with that of her diagnosed sibling, in contrast with other family members who were of dark skin colour. A retrospective history revealed that the patient suffered from recurrent nose bleeds, heavy periods and easy bruising, and had some visual impairment, the exact nature of which was unclear.

The patient's postoperative haemoglobin was 8 g dl⁻¹, platelets 205 × 10⁹, INR 1 and APTT 1.1. She was kept on the delivery suite for close observation, in particular looking for signs to confirm regression of sensory and motor blockade from the regional anaesthetic since, with a possible diagnosis of HPS, she was at risk of an epidural haematoma. Recovery from epidural anaesthesia was normal.

After discussion with the haematologist, the diagnosis of Hermansky–Pudlak syndrome was thought likely, and as the surgical pack had to be removed, it was decided to cover the

procedure with DDAVP, keeping platelets ready if required. She was given DDAVP $0.3 \mu\text{g kg}^{-1}$ in 50 ml of normal saline i.v. over 20 min. The existing epidural was used to provide analgesia and the pack was removed with minimal blood loss. The epidural was removed 1 h later under the effect of DDAVP. The patient's recovery from sensory and motor blockade was again normal. Follow-up with the haematologist was arranged and subsequent investigation confirmed platelet storage pool disorder, in keeping with a diagnosis of HPS. The bleeding time was prolonged to >20 min (normal 2–9 min), secondary platelet aggregation was impaired and there was a reduction in platelet nucleotides associated with an increased ATP/ADP ratio.

Discussion

Hermansky–Pudlak syndrome is characterized by platelet storage pool disorder in association with partial or complete albinism. It occurs worldwide, with a prevalence of 1 in 500 000–1 000 000 in a non-Puerto Rican population. Prevalence in northwest Puerto Rico is 1 in 1800.⁴ There are a variety of genotypes. Hence skin colour ranges from white to olive, but is usually a shade lighter than that of other family members. Hair colour ranges from white to brown. These patients can have nystagmus, photophobia, strabismus and decreased visual acuity. Iris colour may be blue, green or brown. HPS can result in variable bruising, epistaxis, gingival bleeding, heavy periods and post-partum haemorrhage. Additionally, pulmonary fibrosis, granulomatous colitis and renal failure may occur in this syndrome and have been attributed to the accumulation of ceroid in lysosomes. The fibrosis is a progressive restrictive lung disease with a variable time course.^{2,5,6} A bleeding colitis resembling Crohn's disease may present in the second decade.⁷

Currently, the *sine qua non* for diagnosis of HPS is absence of dense bodies on electron microscopy of platelets,⁸ although the diagnosis is usually made by characteristic platelet aggregometry tracing, with absent or impaired secondary wave and deficiency of platelet nucleotides. 'Dense bodies' store ATP, ADP, calcium and serotonin which, when released, activate other platelets and enhance the aggregation response. Standard laboratory tests, including PT, APTT and platelet count, are usually normal but the bleeding time is often prolonged. Thromboelastograph® data may provide a useful tool for monitoring response to treatment, although they would not classify the nature of the platelet disorder. Co-inheritance of von Willebrand's disease should also be excluded.

HPS is inherited in an autosomal recessive manner. Various genes are known to be associated with it, mainly *HPS1*, *AOTB3A*, *HPS3* and *HPS4*, but mutations in other genes may also be involved. Correlations between specific HPS mutations and clinical presentation are not convincing, although *HPS3* mutations have milder symptoms than those with *HPS1* mutations.⁹ The albinism of *HPS3* is characterized

by such minimal hypopigmentation that occasional patients have carried a diagnosis of ocular albinism rather than oculocutaneous albinism. *HPS4* resembles *HPS1* in the variability and severity of the oculocutaneous albinism and bleeding diathesis.¹⁰ There is a suggestion that the pulmonary disease can occur because of any HPS mutation.⁶

Management of individual cases depends on the clinical picture exhibited. In our patient, on the advice of the haematologist, we used DDAVP to cover further surgical procedures, including the removal of the epidural catheter. DDAVP is often used in the treatment of mild haemophilia or von Willebrand's disease as it causes a 2–5-fold increase in release of factor VIII and von Willebrand's factor from stores. The mechanism of its action in platelet storage pool disorder is unclear. The response to DDAVP is not guaranteed and platelet transfusions may need to be given.

With prior knowledge of this patient's condition, we would have avoided regional analgesia. Alternatives would include all the non-invasive methods of analgesia, such as TENS (transcutaneous electrical nerve stimulation), Entonox or intravenous PCA (patient controlled analgesia) with fentanyl. For Caesarean section, which would only have been planned for obstetric reasons, general anaesthesia would have been offered. DDAVP is best avoided in the antenatal period because of the theoretical risk of inducing uterine contractions, but it could be given immediately after delivery. The third stage of labour should be managed actively.

In summary, an apparently fit primipara requested an epidural for labour analgesia and later required repair of a second-degree tear. After 3 h of surgical exploration in theatre, a possible explanation of the continued oozing was discovered in a positive family history of HPS. Prior knowledge of this history would have allowed diagnosis antenatally and a properly organized birth plan would have been agreed. As it was, the chance for genetic counselling before conception was lost, the patient was put at considerable risk of epidural haematoma, and she could have been spared a 3 h exploration of the continued ooze from her second-degree tear. Our patient had oculocutaneous albinism, which went unnoticed. However, she suffered no neurological or other deficits. HPS is the most common of all the syndromes occurring with albinism; hence a high index of suspicion should be maintained in any such patient.

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Anaesthetic management of the newborn with multiple congenital epulides

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Epulis of the newborn is a granular cell tumour that originates from the dental alveolar mucosa. We report a case of a neonate with multiple congenital masses of the alveolar mucosa who presented for surgery with a potential airway problem. Intubation was achieved uneventfully using a gaseous induction with a large facemask and displacement of the epulides to allow cautious laryngoscopy.

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Epulis of the newborn is a granular cell tumour which originates from the mucosa of the dental alveolar ridge in newborn infants. It presents as a pedunculated soft tissue mass, which may be a single lobe or multilobular, and can be up to several centimetres in diameter. Its striking clinical presentation was described in 1871 by Neumann,¹ who coined the term 'congenital epulis' after the Greek *epoulis* (gumboil). The first case report in the English language was published in the *British Medical Journal* in 1884.² It is a benign tumour of uncertain cellular origin and aetiology, which has a histological association with granular cell myoblastomas.³

Congenital epulides are reported more commonly in females than males (>8:1),^{4–6} perhaps implicating a hormonal component to their genesis. Difficulties with breast-feeding and respiratory obstruction are common, meriting surgical intervention; prenatal swallowing impairment

presenting as polyhydramnios has also been reported.⁷ Only 10% present as multiple polyps and the maxilla is a more common site of origin than the mandible (3:1).⁴ Classically, epulides will arise on the pre-incisor alveolar margin.

Although congenital epulides are not normally associated with other congenital abnormalities, they have been described in conjunction with neurofibromatosis⁸ and polydactyly.⁹ There are several reports of ultrasonic prenatal detection of oral masses in the third trimester^{7,8,10} which were subsequently diagnosed as congenital epulides at term.

Case report

A 2-day-old girl born at term by Caesarean section was scheduled for removal of five congenital oral masses in a