Hermansky–Pudlak syndrome presenting with subdural haematoma and retinal haemorrhages in infancy

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The most common cause of subdural haematoma together with retinal haemorrhages in an infant is 'shaken-baby syndrome'[1–3]. Whilst a bleeding diathesis is considered in the differential diagnosis, this is an extremely rare cause.

CASE HISTORY

A 7-week-old infant, who had been born at term with a 'difficult' delivery by forceps rotation and Ventouse extraction resulting in a large cephalo-haematoma, was taken to his general practitioner with a 10-day history of vomiting and screaming episodes and was diagnosed as having infantile colic. Two days later he was seen at his local casualty department with bleeding from one nostril, hypothermia (35.2 °C), a bulging anterior fontanelle and drowsiness. There was no history of trauma other than at birth. Fundoscopy of the eye, performed by the local paediatrician without dilatation of the pupils, was judged normal. There were no signs of external injury. He had two generalized tonic clonic seizures. A computed tomographic scan showed an acute left occipital subdural haematoma, and he was transferred to Great Ormond Street Hospital for Children with a Glasgow coma score of 9. There were less than a dozen haemorrhages at the posterior pole of the right eye, not extending into the retinal periphery. These were subhyaloid domed, intraretinal dot and subretinal with one haemorrhage on the optic disc. One haemorrhage was seen at the left macula. There was no suggestion on history or examination that this was a case of shaken-baby syndrome. A skeletal survey was normal. He had had one dose of oral vitamin K in the neonatal period and was partly bottle-fed. A coagulation profile was within normal limits for age (prothrombin time 15 s, control 14 s [normal range 12–17]; activated partial thromboplastin time 40 s, control 34 s [29–52]; thrombin clotting time 11s, control 10 s [8–12]; fibrinogen $3.4\,g\,L^{-1}$ [1.7–4.0]). Platelet count was $339 \times 10^9\,L^{-1}$ [150–450]; however, the bleeding time was grossly prolonged at more than 15 min (normal up to 10 min). A test dose of DDAVP (desmopressin acetate) corrected his bleeding time but caused hyponatraemic seizures[4]. When platelet function studies showed reduced aggregation with ADP and a mixed defect of nucleotide storage and release (see Table 1) a diagnosis of Hermansky–Pudlak syndrome (HPS) was suggested. HPS is an autosomal recessive inherited disorder characterized by oculocutaneous albinism, tissue accumulation of coroid pigment and a bleeding diathesis due to platelet abnormality. Electronmicroscopy of platelets showed normal features with alpha granules and some dense bodies present. The child had white blond hair, but apart from his retinal haemorrhages the eye examination was normal for age with no signs of albinism.

Just before his second birthday the health visitor detected a squint and he was managed by his local ophthalmologist. He was a healthy well-cared-for child with no sequelae from his neonatal illness. Further review at the age of 3 years reveals that his hair is now light brown; he does not have iris translucency or nystagmus. However, in favour of a diagnosis of HPS are the findings of a 20 dioptre esotropia, with reduced visual acuity of 0.4 (crowded LogMar), foveal hypoplasia, and blond fundi. He also has crossed asymmetry of the flash visual evoked potential on uniocular recording, consistent with the chiasmal anomaly common to all forms of albinism[5]. Absence of iris transillumination is not unusual in HPS or in ocular albinism with brown irides, but absence of nystagmus is rare in albinism. We have another child in our care who has steady fixation, yet has all the other features of HPS and is from pedigree where the three other affected members do have nystagmus. The patient in this report does not have any known Puerto Rican or Swedish ancestry.

Table 1 **Platelet studies (normal ranges in parentheses)**

	Platelet nucleotide content	***Platelet nucleotide release***
ADP	10.5 (17–47)	5.5 (15–27.5)
ATP	42.5 (35–55)	1.5 (7–15)
ADP/ATP ratio	4.0 (1.2–2.5)	0.27 (0.43–0.79)
Total	53 (52–102)	7.0 (22–45)

ADP=Adenosine diphosphate; ATP=adenosine triphosphate

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COMMENT

Intracranial haemorrhage is infrequent after accidental head trauma in children with a congenital coagulopathy[6]. This child had had a traumatic delivery followed by seizures. It is possible that the few haemorrhages at the posterior pole of the eye were the result of birth. However, in normal infants, birth haemorrhages should have resolved before 6 weeks of age; in most cases, this happens within a few days. The more sinister retinal findings of macula schisis or paramacular folds[7], often seen in cases of shaken-baby syndrome, were absent. It has been suggested that seizures may be a cause of retinal haemorrhage in neonates. Most studies produce negative evidence, yet only include older children[1,3]. One child who had seizures from 10 days was found to have unilateral retinal haemorrhages at 23 days[1]. The presence of a bleeding disorder does not exclude coexisting child abuse.

We believe that in this case birth trauma, seizures and a mild bleeding disorder together were sufficient to explain the subdural haematoma and retinal haemorrhages. We emphasize the importance of including an assessment of platelet function in neonates presenting with suspected shaken-baby syndrome. Platelet dysfunction can be tested with template bleeding time (which involves a cut in the skin) but this is being replaced by the platelet function analyser[8]. This is the only report of Hermansky–Pudlak syndrome presenting in this manner, as it is usually a very mild disorder. The minor bleeding diathesis in HPS is primarily attributable to deficiency of platelet dense bodies/granules[9]. However, α1-antitrypsin deficiency can give rise to late haemorrhagic disease of the newborn, with a peak incidence between 2 and 12 weeks of age, and occasionally presents with intracranial haemorrhage[10]. Intracranial haemorrhage occurs in up to 4% of newborns with haemophilia[11] and has been reported in factor XIII deficiency[12].

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Sucking noise and collapse after central venous catheter removal

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Air embolism after insertion of a central venous catheter is a well-known hazard[1]; air embolism after catheter removal is less well recognized.

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CASE HISTORIES

Case 1

A woman of 42 was referred for possible lung transplantation because of end-stage respiratory failure due to lymphangioleiomyomatosis. Preoperative assessment, including right and left heart catheterization, disclosed no contraindicating factors and she subsequently received a right single lung transplant. Three episodes of acute allograft rejection were treated successfully and she was then well until the fifth postoperative year when she was admitted for treatment of bilateral cavitating pneumonia. *Staphylococcus aureus* was isolated, and computed tomography scanning of the chest revealed[2] multiple cavities in the transplanted and native lungs. Her immunosuppression consisted of cyclosporin (whole blood monoclonal antibody trough levels 250–350 ng/mL), azathioprine 2 mg/kg per day and prednisolone 10 mg per

day. Because venous access was poor, a right internal jugular venous line was inserted for antibiotic administration. Seven days later a new line was inserted in the left internal jugular vein and seven days subsequently the line was resited on the right side. A permanent indwelling catheter was not fashioned since she was expected to require intravenous antibiotics for only 2–4 weeks more. The patient recovered from the pneumonia and one week after insertion the line was removed. At the time of removal she was fully conscious and supine with her head resting on one pillow. A sucking sound was heard and she immediately became breathless, lost vision in both eyes and reported paraesthesia throughout her lower limbs and trunk. She was transferred to the intensive care unit and subsequently recovered completely.

Case 2

A man aged 67 had a mechanical aortic valve replacement (AVR) for bacterial endocarditis, and his postoperative recovery was complicated by pneumonia, septicaemia and multiple organ failure. He needed prolonged mechanical ventilatory support via a tracheostomy and total parenteral nutrition. His slow recovery necessitated the insertion of multiple central venous catheters, alternating between right and left internal jugular and subclavian veins, for administration of antibiotics and nutrients. We did not wish to insert a permanent indwelling catheter because of his history of endocarditis. Total parenteral nutrition was discontinued 172 days after surgery as his gut function recovered, and at that time (12 days after the line was inserted) it was decided to remove his central venous line. The patient had been well and mobile during the preceding week. At the time of removal he was fully conscious with normal vital signs, supine with head resting on one pillow. Immediately after removal of the central venous line a sucking sound was heard and he immediately became bradycardic then unresponsive; there was a sustained cardiorespiratory arrest with electromechanical dissociation. Cardiopulmonary resuscitation was successful. Haemodynamic stability was maintained with an infusion of adrenaline (4 μg/min) and he was transferred to the intensive care unit. On chest radiography there was no pneumothorax, on electrocardiography there was no evidence of myocardial infarction, and on 2D echocardiography the prosthetic aortic valve was functioning normally. There was no clinical evidence of deep venous thrombosis. The patient recovered completely and was discharged home ten days afterwards.

COMMENT

Air embolism after removal of central venous catheters, which we believe to be the cause of both these incidents, is a rare but potentially fatal complication[3]. Air readily gains access through an opening when pressure in the veins falls below that of atmospheric pressure. This is particularly facilitated when the patient is sitting upright, breathing deeply or inspiring forcefully after an episode of coughing—all of which tend to lower the intrathoracic pressure. By contrast, when the patient is in the Trendelenburg position (head down) the pressure in the central veins rises to atmospheric pressure or above and this prevents intake of air.

When a central venous catheter has been in place only briefly—for example, during a routine cardiac or thoracic operation—removal does not leave a track and the tissues collapse to make an effective seal. When, however, catheters are used for longer periods, removal can leave a fibrinous track that communicates between vein lumen and atmosphere. Unless the track is sealed with airtight dressings or pressure gauze dressings, air can easily gain access and cause massive air embolism.

The second patient had had multiple central lines over a long period. Although the sites were rotated, we suspect that a fibrinous track had formed. Electromechanical dissociation occurred immediately after removal of the central line, when a sucking sound was heard. Air embolism was the only plausible explanation for this incident, in a patient who had been well beforehand.

In the first patient, track formation may have been facilitated by her steroid therapy. This complication has been reported previously in lung transplant patients[4]. The right to left shunting of air is not easily explained but may have been at the pulmonary level: the cavitating pneumonia, causing extensive injury to the allograft and to the native lung with lymphangioleiomyomatosis, might have given rise to abnormal arteriovenous communications. Another possibility is that pulmonary hypertension secondary to hypoxia and lung injury facilitated shunting across a patent foramen ovale that had been unrecognized at preoperative cardiac catheterization.

In neither of these cases was the line removed with the patient in Trendelenburg position nor was an occlusive dressing employed. We now continuously educate our medical and nursing staff about the need for these precautions.

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Femoral vein obstruction with an arthritic hip

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In a woman with a swollen leg and dilated veins, the probable diagnosis is deep vein thrombosis. Appearances can be deceptive.

CASE HISTORY

A woman of 50 was referred with a two-week history of swelling of the left leg. On examination it was swollen to mid-thigh level with visible superficial dilated veins. The provisional clinical diagnosis was deep vein thrombosis. Venography of the left leg did not show any evidence of thrombosis, from calf to iliac veins, but external compression was observed on the femoral vein at the inguinal level (Figure 1). A Duplex ultrasound scan confirmed the absence of femoral vein thrombosis and revealed a 3.4×2.0 cm hypoechoic mass behind the common femoral vein consistent with a 'cyst'. A computed tomographic (CT) scan showed a cystic lesion behind the left femoral vein and artery and in front of the hip joint, characteristic of an enlarged iliopsoas bursa (Figure 2). Under CT control 20 mL of yellow clear fluid was aspirated; no atypical cells were seen and there was no microbial growth after 48 hours of incubation. When contrast was injected into the cyst cavity it passed freely into the hip joint. The underlying hip showed mild osteoarthritic changes on plain X-ray. At follow-up 10 weeks later, the left leg swelling had reappeared. An ultrasound scan showed a further collection of fluid, so the bursa was surgically excised.

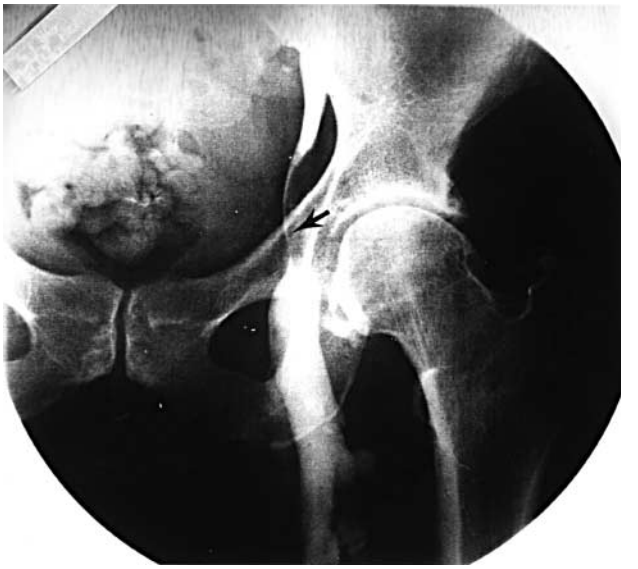

Figure 1 **Venogram showing external compression of the left femoral vein at the inguinal level (arrow)**

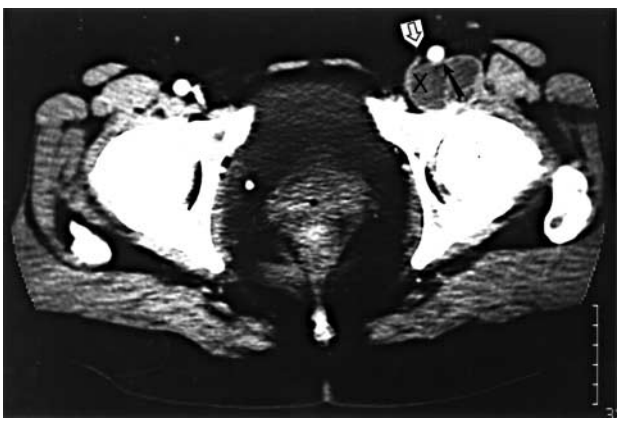

Figure 2 **A contrast computed tomographic examination showing cystic mass (X) posterior to the left femoral vessels which are displaced anteriorly and medially.** The mass is just anterior to the hip joint and is septated. The left femoral vein (white arrow) is seen to be patent although distorted and compressed. The left femoral artery is also seen (black arrow)

COMMENT

The iliopsoas bursa is the largest synovial bursa in the body. It communicates with the hip joint by a defect in the thinnest part of the capsule, between the pubofemoral and iliofemoral ligaments. Amongst its commonest associations are osteoarthritis[1] and rheumatoid arthritis[2] of the underlying hip, although trauma, gout, pseudogout, tuberculosis and avascular necrosis have been reported as well. A recent paper describes a loose hip prosthesis causing a mass in groin and a collection of titanium and polyethylene debris within the iliopsoas bursa[3].

The earliest and the most frequent symptom associated with iliopsoas bursitis is hip pain. Other signs and symptoms are due to compression of the femoral vein or nerve[4] or of lower limb lymphatics. A palpable groin mass is not uncommon. The condition is investigated by a combination of ultrasound and CT or magnetic resonance scanning. Ultrasound helps to confirm the existence of a cyst and can be used to aid needle aspiration. Magnetic resonance is better than CT for detecting the presence of hip effusion, although both provide anatomical definition and can

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demonstrate the communication between the bursa and the joint cavity[5]. In our case, after performing a duplex ultrasound scan and a venogram, we used CT for imaging and then guiding a needle for aspiration and injection of dye into the bursa—to determine the extent of the bursa and display the communication with the hip joint. Plain radiographs of the hip should be done to assess the degree of articular damage, if any. The definitive treatment for iliopsoas bursitis is surgical excision[5], although recurrence rates after aspiration and injection of steroids are said to be low.

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Reversible dementia in Paget's disease

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Neurological syndromes associated with Paget's disease of the skull include cranial nerve compression, spinal cord compression, cerebellar compression and vertebrobasilar insufficiency[1]. Reversible dementia is unusual.

CASE HISTORY

A woman of 79 was admitted for investigation of falls, worsening dementia and urinary incontinence. Three years earlier, Paget's disease had been diagnosed, mainly affecting the skull; alkaline phosphatase at that time, 944 U/L. The recurrent falls and urinary incontinence had begun a year after this, and she had needed several hospital admissions. Investigations, including 24-hour electrocardiography, had been normal but on consecutive admissions there had been a gradual decline in her mental state. She was housebound and needed a Zimmer frame to walk. There was no medical history of note, other than hypertension controlled with bendrofluazide 2.5 mg daily.

Her pulse was regular, blood pressure was 140/90 mmHg with no postural drop and her abbreviated mental test score was 5/10. Apart from an ataxic gait, findings on examination, including optic discs, were normal. The only abnormal finding was an alkaline phosphatase of 1246 U/L. The provisional diagnosis, in view of the triad of dementia, ataxia and urinary incontinence, was normal-pressure hydrocephalus secondary to Paget's disease. This was confirmed with a computed tomographic head scan which showed marked pagetic changes of the skull with dilated lateral and third ventricles (Figure 1); the foramen magnum and the fourth ventricle appeared small.

She was referred to the neurosurgical unit where a ventriculoperitoneal shunt was inserted, the opening cerebrospinal fluid (CSF) pressure being normal at 15 cm. A magnetic resonance brain scan after the procedure showed that the ventricles had greatly decreased in size while confirming the platybasia with a small foramen magnum which flattened both the anterior aspect of the pons and the fourth ventricle (Figure 2).

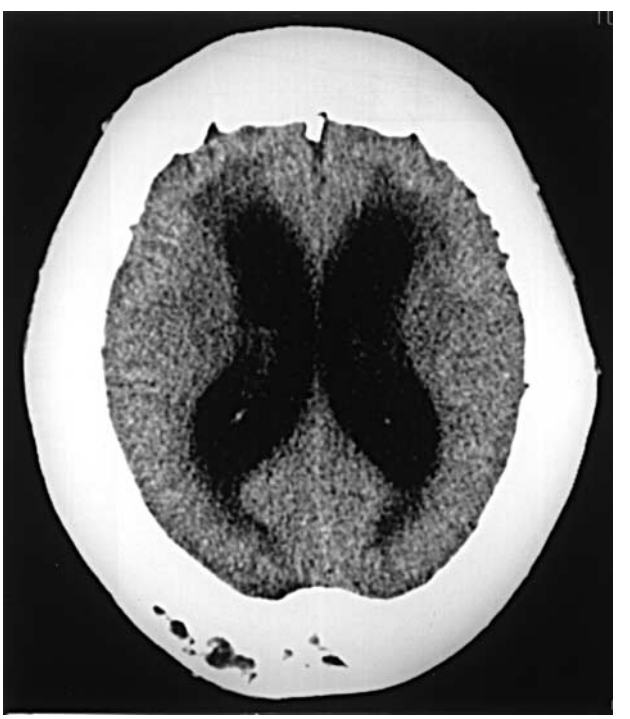

Figure 1 **Preoperative computed tomographic scan**

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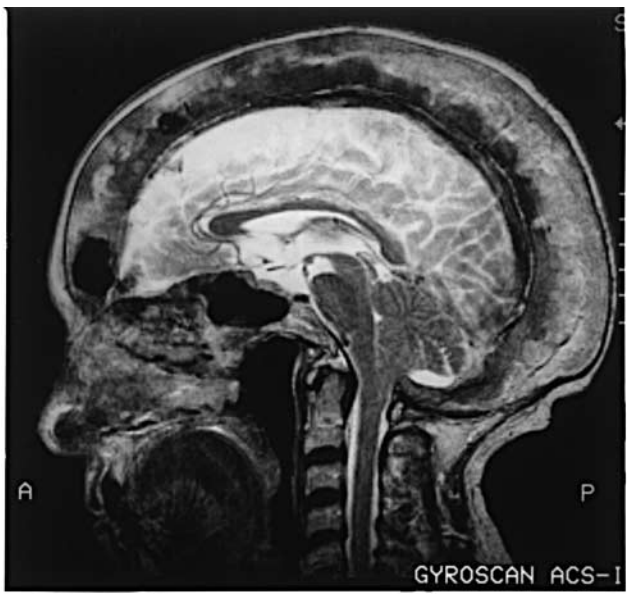

Figure 2 **Postoperative magnetic resonance scan**

Postoperatively she received intensive physiotherapy and a course of intravenous pamidronate (30 mg/week for 6 weeks). When discharged from hospital her abbreviated mental test score was 10/10, she was continent and she was walking with a stick. Her alkaline phosphatase was 615 U/L. Oral etidronate (5 mg/kg daily) was prescribed. She continued to improve and on follow-up in the outpatient clinic she was well oriented and independent and had had no falls.

COMMENT

Paget's disease is found in 6% of hospital patients over the age of 55 years in the UK[2]. It is commoner in men but skull involvement is more frequent in women, being present in 30% of those affected[2]. Less than a third of people with skull involvement will have evidence of basilar impression and a smaller number will go on to develop normal-pressure hydrocephalus[2].

Normal-pressure hydrocephalus develops in Paget's disease as a consequence of obstruction of the posterior fossa cisterns and narrowing of the Sylvian aqueduct[3]. Gottschalk first reported this in 1973[4] and successful treatment by ventriculo-atrial shunt was described in 1974[2].

In view of the mechanism in cases such as this, we might expect the CSF pressure to be raised rather than normal. In fact, continuous CSF pressure monitoring over 24 hours reveals that pressures in such patients do intermittently rise[5]. Perhaps we should revert to the original term of occult hydrocephalus[6,7] to describe this condition. Other causes of normal-pressure hydrocephalus due to partial obstruction to the outflow channel include colloid cysts, cholesteatomas, metastases involving the third and fourth ventricles, aqueductal stenosis and cerebellar tumour or haematoma[8]. Some 20% of patients with normal-pressure hydrocephalus have partial ventricular outflow obstruction[8].

All patients with Paget's disease should be carefully followed up since bisphosphonates are effective both for treatment and for prevention of complications. Where the skull is affected, a watch must be kept for occult hydrocephalus.

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