Pneumococcal sepsis: should we look for asplenia?

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Asplenic individuals are at risk of developing overwhelming bacterial sepsis with capsulated organisms such as *Streptococcus pneumoniae*,¹ against which pneumococcal vaccination or antibiotic prophylaxis can provide life-saving protection. Opportunities to identify such individuals should thus be vigorously pursued.

CASE HISTORY

A well-nourished male infant, age 22 months, reached our intensive care unit in uncompensated septic shock following a 3-day illness of diarrhoea and vomiting (with fever for 2 days). Despite vigorous resuscitative efforts that included antibiotics (ceftriaxone), early intubation and ventilation, fluid resuscitation (100 mL/kg), maximal inotropic support including vasopressin, and corticosteroids, the child died six hours after admission. *Streptococcus pneumoniae*, sensitive to ceftriaxone, was isolated from antemortem blood cultures and pneumococcal antigens were detected in postmortem blood samples.

After the death, we discovered that the child had had one previous invasive pneumococcal infection (meningitis) at 10 months of age from which he had recovered fully. At that time his immune status had been assessed. Serum complement, immunoglobulins and IgG subclass levels were all normal, but evidence for asplenia was not sought. At necropsy the child was found to have only vestigial splenic tissue—very small nubbins which histologically showed occasional follicles and haemorrhagic red pulp but consisted mainly of fibrous scar tissue. The appearance of the spleen was consistent with infarction at some stage, either *in utero* or *ex utero*, and a rather thin hilum at risk of torsion indicated the possible mechanism. There was no history of splenectomy or sufficient trauma, nor any history of sickle cell disease or other potential cause of autosplenectomy to explain these findings. The adrenals showed extensive haemorrhage. There was no evidence of pneumonia or meningitis.

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COMMENT

Clinicians are well versed in the need for protection against *S. pneumoniae* where the spleen is known to be absent, either through functional asplenia as in sickle-cell anaemia or acquired asplenia after trauma or surgery. Congenital asplenia may occur as an isolated condition, in recognized malformation syndromes or in family clusters.² Where a syndrome or family history alerts the clinician to possible asplenia, confirmatory investigations should lead to effective prophylaxis. Our patient had no siblings and had no family history of pneumococcal disease. Individuals with isolated congenital asplenia are, by contrast, brought to the clinician's attention only when they have experienced one or more episodes of invasive infections from capsulated bacteria.³ Some clinicians judge that, even after a single episode of *S. pneumoniae* sepsis, investigation for asplenia is mandatory.⁴

Asplenia is diagnosed through two easy and non-invasive investigations—a search for Howell–Jolly bodies on blood smears, which are characteristic of but not specific for asplenia, or abdominal ultrasound. Can this be reasonably achieved? During the past 12 months, in our institution, *S. pneumoniae* was isolated from samples from normally sterile sites in 16 child patients, which by inference would necessitate the same number of additional abdominal ultrasound examinations, a further case load of only one or two per month. This together with 16 additional blood smears in a year should be easily achieved within current resource. The yield is likely to be low: in one study of 2498 paediatric patients with invasive pneumococcal disease only 0.8% were known to have asplenia⁵ (though the authors did not apparently search actively for asplenia). Nevertheless, there is likely to be a major benefit for the rare affected patient—particularly since the conjugate pneumococcal vaccines are likely to add to the protection given by antibiotic prophylaxis.

This case provides a reminder to pursue asplenia as a potential underlying mechanism for invasive bacterial infection in children. We believe that abdominal ultrasound should be performed in addition to the blood tests usually recommended for immune function screening after such an episode. Such a guideline, if widely instituted, might not only prevent deaths but also provide information on the incidence of unrecognized asplenia presenting with invasive pneumococcal infection.

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Pseudophaeochromocytoma in two young Africans

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Patients with essential hypertension may present with a clinical syndrome mimicking phaeochromocytoma.

CASE HISTORIES

Case 1

An African man aged 36 was seen as an emergency with dysphasia, left facial weakness and a left hemiparesis. Hypertension had been detected by his general practitioner six months earlier and treated with bendroflumethiazide, but blood pressure control had been erratic, with frequent episodes of headache, palpitations and sweating. On admission he had a blood pressure of 240/120 mmHg, bounding tachycardia and a heaving displaced apex. Proteinuria was 2+ but there was no papilloedema. The chest radiograph, electrocardiogram and echocardiogram indicated left ventricular hypertrophy. CT of the brain revealed infarcts in the right caudate and thalamic nuclei.

Labetalol was prescribed for the hypertension but the blood pressure fluctuated widely, reaching peaks of 250/150 mmHg. A suspicion of phaeochromocytoma was supported by raised 24-hour urinary excretion of noradrenaline, metadrenaline, and hydroxymethoxymandelic acid (HMMA) (Table 1). However, when labetalol was stopped, the results of repeat tests were normal. Plasma renin activity (PRA) was 3.60 pmol/L (reference range 1.1–2.7) and aldosterone 120 pmol/mL/h (100–450). Abdominal CT was normal and on further investigations

no secondary cause of hypertension could be found. Subsequently, blood pressure control was achieved with an angiotensin-converting enzyme inhibitor and an alpha-blocker and he made a gradual neurological recovery.

Case 2

An African man of 30 was referred by his general practitioner for investigation of episodic dizziness, headaches, palpitations, sweating and tremors. Symptoms occurred in stereotypic fashion several times a day, sometimes lasting up to an hour and leaving him exhausted. There were no obvious precipitating stresses. A borderline raised blood pressure had been documented on several past surgery visits. Two of his sisters had hypertension. There was no proteinuria or papilloedema. The electrocardiogram was consistent with left ventricular hypertrophy but other investigations, including CT of the brain, yielded nothing of note.

He was admitted for exclusion of phaeochromocytoma. Inpatient monitoring revealed a pattern of symptomatic hypertensive episodes with blood pressure peaks of 200/140 mmHg. 24-hour urinary catecholamines on two separate days were normal (Table 1). PRA was within normal limits at 1.20 pmol/L, as was aldosterone at 310 pmol/mL/h. Other secondary causes of hypertension were excluded and his symptoms and blood pressure control improved on verapamil and atenolol.

COMMENT

Phaeochromocytoma should be considered in the evaluation of patients with symptomatic hypertensive episodes because it is potentially fatal if unrecognized. Confident exclusion of this condition can prove challenging. The diagnosis rests on demonstration of supranormal amounts of catecholamines or metabolites in urine or plasma. However, most of the widely used tests are prone to both false-negative and false-positive results. The most reliable biochemical screens for phaeochromocytoma are 24-hour urine estimations of catecholamines, metanephrines and vanillylmandelic acid (VMA) as well as plasma catecholamines and metanephrines.¹ Of these, VMA has the lowest sensitivity (64%) but its specificity is high (95%); 24-hour urinary catecholamines have better sensitivity (86%). The plasma metanephrines (sensitivity 99%, specificity 89%) have been advocated as the test of first choice but are not widely available.¹

In both our patients, phaeochromocytoma was excluded by the finding of normal urinary catecholamines. However, hypertensive patients with equivocal biochemical screens require further testing and the pentolinium suppression test is the preferred pharmacodynamic test. Pentolinium suppresses sympathetic overactivity in patients with

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