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Necrobacillosis with pancytopenia

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Abstract

Two young children whose presentation with necrobacillosis caused considerable diagnostic difficulty resulting in referral to an oncology unit are described. In both cases their severe suppurative multisystem illness was complicated by pancytopenia. One had bone marrow infarcts and severe endocarditis in addition to pulmonary involvement and the other had osteitis which resulted in a deformed humerus.

Necrobacillosis, the septicaemic illness caused by *Fusobacterium necrophorum* was first described as a uniformly fatal illness by Lemierre in 1936.[1] It is a severe feverish illness particularly affecting previously healthy young adults who classically develop multisystem abscesses with predominant pulmonary involvement after initial sore throat.[1] Other manifestations involving the upper respiratory tract, and apparently isolated metastatic infection can occur.[2] Staphylococcal infection is often considered.[3] However, it remains unknown to many clinicians and has been described only rarely in children. We have recently seen two children with differing features of this condition, but both had haematological involvement and have been left with significant long term morbidity.

Case reports

CASE 1

A previously healthy 2 year old boy was referred to his local hospital with a two month history of lethargy, anorexia, and weight loss with progressive fever, cough, and pallor. He had fever with minimal left sided consolidation on a chest *x* ray film for which he was treated with intravenous penicillin and flucloxacillin. Haematological investigation showed a haemoglobin concentration of 31 g/l, mean corpuscular volume 68 fl, white cell count 12×10^9/l with 54% neutrophils, and platelet count 71×10^9/l. The blood film showed anisocytosis with teardrop poikilocytosis. Insufficient blood was obtained to measure the serum ferritin concentration. Serum B12 and folate were normal. The patient was transfused and then was referred with suspected disseminated malignancy. Bone marrow examination revealed gross myeloid hyperplasia with the neutrophils showing severe toxic changes. There was depressed erythropoiesis and virtually no stainable iron was found. Several large areas of necrosis were present in the marrow biopsy specimen. There was no evidence of malignancy and the appearances were suggestive of a severe toxic insult.

Intravenous azlocillin and gentamicin were commenced, but after 72 hours of continued fever were changed to vancomycin and ceftazidime, to which metronidazole was added when an anaerobe was reported on the original blood culture. Purulent fluid drained from both a right pyopneumothorax and a chest wall abscess was sterile. On day 6, the anaerobe was confirmed as *F necrophorum* sensitive to metronidazole and penicillin to which he was changed. He had a respiratory arrest associated with the development of a right pneumothorax and worsening right sided consolidation. He was admitted to intensive care for ventilation where his course was complicated by bilateral pneumatocoeles that resolved slowly. He had two seizures, but no evidence of cerebral abscess was found. A new ejection systolic murmur was noted at the apex, but no structural lesion was evident on cross sectional echocardiography. He was successfully extubated after two weeks and antibiotic treatment was continued for a further week. Before discharge the peripheral blood count, including mean corpuscular volume, was within normal limits and no evidence of immune deficiency was found. Two months later he was admitted in acute cardiac failure secondary to severe mitral incompetence, which was thought to be due to endocarditis occurring during the original illness. He remains well after mitral valve replacement.

CASE 2

A 5 year old girl was admitted to her local hospital with a one week history of malaise, fever, and diarrhoea for which she had been treated with amoxycillin. On examination she was feverish and looked pale and a diagnosis of haemolytic uraemic syndrome was suspected. Haematological investigation showed a haemoglobin concentration of 78 g/l, mean corpuscular volume 77·3 fl, white cell count 19×10^9/l with 86% neutrophils, and platelet count 47×10^9/l. Her electrolytes and creatinine were normal and there was no red cell fragmentation. The anaemia and thrombocytopenia were thought to be consistent with toxic marrow depression. Intravenous chloramphenicol, cefuroxime, and ampicillin were commenced but she remained feverish. On day 6 a painless swelling developed in her left mastoid region and pus drained from her left ear. A left cortical mostoidectomy and drainage of a Bezold's abscess was performed. At the same time *F necrophorum* was isolated from her original blood culture and treatment with penicillin, metronidazole, and ceftazidime was commenced.

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Despite appropriate antibiotics she remained unwell and feverish for a further two weeks. During this time radiological investigations, including a bone scan and computed tomogram, failed to show further abscesses. She deteriorated and developed rigors, bone pain, headache, irritability, and photophobia. The white blood cell count was now $2{\cdot}4\times10^9$/l, with a neutrophil count of $1{\cdot}4\times10^9$/l, although her platelet count was improving. She was referred for exclusion of underlying immunodeficiency or malignancy. The clinical features were felt to be compatible with disseminated necrobacillosis, and she was reinvestigated for the presence of metastatic abscesses. Antibiotic treatment was changed to penicillin, metronidazole, and imipenem. Despite the lack of clinical signs and symptoms radiological studies revealed severe active osteitis of the right humerus with mild osteitis on the left. However, no evidence of cerebral abscess was found. Bone marrow examination was normal.

After six weeks in hospital, her temperature settled and her full blood count returned to normal. She was discharged home to complete eight weeks of antibiotics. Clinically she made a good recovery, although osteitis has led to a severe deformity of the right arm which may require surgical correction.

Discussion

Many of the commonly described clinical features of this syndrome were seen in our patients: severe protracted feverish illness with rigors, metastatic abscesses, initial diagnostic difficulty with frequent changes of antibiotic treatment, and a slow clinical response.[3 4] However, haematological abnormalities, apart from leucocytosis, have been thought not to occur in necrobacillosis,[5] although patients with a severe infection may have anaemia.[1] Neither pancytopenia, which occurred in both patients, nor bone marrow necrosis which occurred in one, have previously been described in this disease. It is possible that underlying iron deficiency contributed to the severity of the anaemia in case 1.

Review of the literature on necrobacillosis is complicated by frequent changes in nomenclature of the organism. This disease classically occurs after a sore throat, although a primary focus of infection is not always evident. It is unknown why this normal oral commensal becomes invasive. Otitis media and mastoiditis are common presenting features in infants, but rare in adults, and may be associated with central nervous infection in any age group.[2] Septic thrombophlebitis and metastatic abscess formation commonly result in pneumonia and empyema. Bone or joint infection as well as hepatic and renal involvement are frequently found.[1] Bacterial endocarditis has been reported as a rare complication in adults with necrobacillosis. Acute endocarditis of previously healthy valves has been described.[6] The need for mitral valve replacement is more unusual.

F necrophorum has a typical appearance on microscopy but may be mistaken for bacteroides. It can be difficult to culture and requires strict anaerobic conditions.[3] Although the organism is sensitive to many antibiotics, in vitro sensitivity does not correlate well with the clinical response, which is characteristically slow. It is widely suggested that metronidazole is the drug of choice, and that penicillin should be added for a microaerophilic streptococcus which may be grown concurrently.[2] The optimal duration of antibiotic therapy is unknown.

This report highlights the need to consider anaerobic infection, including necrobacillosis, in previously healthy children who develop severe suppurative infection. The early institution of appropriate antibiotics and awareness of the associated complications may help to reduce the morbidity of this rare but serious illness.

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