Back pain and Staphylococcal bacteraemia in haemodialysed patients—beware!

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Introduction

Staphylococcal infections are frequent in haemodialysed patients, and Staphylococcus aureus bacteraemia is associated with significant morbidity and mortality in these patients [1]. The most common port of entry for Staphylococcal bacteraemia remains cannulation of the permanent dialysis access, or the use of central-vein catheters [2]. Haematogenous complications of Staphylococcal bacteraemia include endocarditis, pericarditis, pneumonia and empyema [3]. This article describes two patients in which methicillin-resistant S. aureus (MRSA) bacteraemia was complicated by metastatic foci of infection in both bone and the nervous system. Both patients complained of severe back pain, the importance of which will be discussed.

Cases

Patient 1

A 67-year-old man began chronic haemodialysis in July 1994 because of end-stage renal failure. In June 1995 his radiocephalic fistula thrombosed and a polytetrafluoroethylene graft was inserted into his right forearm. This graft thrombosed in October 1995 and an attempt at thrombectomy was unsuccessful. A temporary double-lumen haemodialysis catheter was inserted into the left internal jugular vein.

Five days after insertion of the central-vein catheter the patient became acutely ill, with a high fever, chills and leucocytosis. The catheter was immediately removed and intravenous vancomycin and gentamycin commenced. Subsequent blood and catheter tip cultures ‘grew’ methicillin-resistant Staphylococcus aureus (MRSA). Haemodialysis was maintained via temporary femoral-vein catheters. Intravenous vancomycin was continued for 3 weeks and stopped only after blood cultures had become sterile.

However, during this period the patient started to complain of severe, low, central back pain. On physical examination no neurological deficit was elicited, but 45° hip flexion produced central back pain. Initial lumbar vertebral X-rays were normal. Over the ensuing month the back pain continued unabated; the patient lost 5 kg in weight and his serum albumin fell to 3.1 g/l. A technecium bone scan was negative.

In late November 1995 the patient had further fevers and MRSA was again isolated from blood cultures. Despite removal of the indwelling catheter and reinstitution of combined vancomycin and clindamycin therapy the patient’s condition deteriorated. A CT scan of the lumbar spine disclosed complete destruction of the body of L5, with a large paraspinal mass producing pressure on the dural sac. A diagnosis of pyogenic vertebral osteomyelitis, with spinal-cord compression, was made. Surgical intervention was deemed necessary but the patient’s family refused. The family requested that the patient be discharged, and he died shortly thereafter at home. Post-mortem was refused.

Patient 2

A 79-year-old woman with end-stage renal failure was admitted because of fever and a purulent exit site discharge from a temporary central-vein catheter. She had been on maintenance haemodialysis for the preceding 4 months. In 1981 she had undergone a total left-knee replacement. Two weeks previous to the present admission the patient had a stenotic section of her radiocephalic fistula surgically corrected. Recovery had been uneventful and the patient was discharged with the temporary central-vein catheter.

On initial examination the patient was alert, but febrile. Murmurs were heard over the cardiac apex and the right carotid artery. The catheter was removed, and intravenous cefazolin and gentamycin commenced. A transthoracic echocardiogram showed calcification of the posterior mitral valve leaflet with mitral insuffi-
ciency. Within 48 h MRSA had grown in blood cultures. Intravenous vancomycin was started.

On the third hospital day the patient complained of severe back pain in the area of the cervical spine. A few hours later, physical examination revealed a left Horner’s syndrome and flaccid paralysis of the left arm. A CT of the cervical spine was non-diagnostic. Magnetic resonance imaging (MRI) of the cervical spine (Figure 1) showed thickening of the anterior and posterior epidural tissues between C5 and C7. Infiltration of the left paravertebral tissues, including the region of the spinal nerves and rami, from C4 to C7, was also seen. A diagnosis of pyogenic infection, possibly abscess, of the cervical epidural space was made.

The consulting neurosurgeons felt that there was no abscess formation, and, therefore, surgery was not undertaken. Fusidic acid and rifampin were added to the antibiotic regime. However, over the next few days fever remained high, MRSA was subsequently cultured from the patient’s prosthetic left knee and leucocytosis ‘peaked’ at 34,000/mm3. Ultimately the patient developed cardiorespiratory failure and died, 8 days after admission.

On post-mortem an epidural abscess extending from C3 to C6, with necrosis of the surrounding connective tissue was seen. No vertebral osteomyelitis was evident. Cholesterol emboli, of both the kidneys and pancreas, were an unexpected finding.

Discussion

*Staphylococcus aureus* can induce rapid bone destruction, with osteomyelitis being a known complication of *S. aureus* bacteraemia [4,5]. In one tertiary hospital setting, 34/162 patients with Staphylococcal infections had osteomyelitis [6]. In children this occurs most often in long bones, while in adults vertebral osteomyelitis is becoming increasingly frequent [3]. As in the first patient outlined here, the diagnosis of vertebral osteomyelitis is often delayed and this delay may lead to spread of the infectious focus, spinal-cord compression and neurological deficits [4,7]. Thus, if the diagnosis is to be made early, a high degree of suspicion must be present. The major and most frequent symptom is back pain [2,3,7–9]. It occurs in up to 85% of patients, and can be both unrelenting and debilitating. Neurological problems will occur only at a late stage of the disease, either because of complete destruction and collapse of the vertebrae involved, or because of pyogenic spread into the epidural space.

In this era, MRI or CT scans of the suspected vertebral area are the preferred tests to be performed [4,7,9]. Plain X-rays are of little diagnostic value in the early stages of the disease. Technecium bone scans may also give false-negative results, especially when the osteomyelitic process is predominantly destructive, without any osteoblastic activity. In these situations, however, sequential gallium scans may prove helpful, both for initial diagnosis and also as a means of assessing cure, or recurrence at a later date [10]. The advantages of MRI examination, however, are three-fold. First, diagnosis can be made as early as the second week of the disease [11]. Secondly, the criteria for MRI diagnosis of vertebral osteomyelitis are uniform, and include decreased vertebral-body signal intensity on T1-weighted images, loss of endplate...
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Definition and increased disk signal intensity on T₂-weighted images [12]. Thirdly, repeated MRI examinations may be a method of showing complete or incomplete resolution of the problem [11].

Treatment of vertebral osteomyelitis must be preceded by a correct bacteriological diagnosis. Positive blood cultures are sufficient for appropriate antimicrobial therapy to be commenced, but when microbiological diagnosis is uncertain, CT-guided needle biopsy of the involved vertebrae is warranted [13]. In those patients with Staphylococcal vertebral osteomyelitis, intravenous cloxacillin remains the mainstay of therapy. In MRSA infections, vancomycin must be used, and preferably in combination with rifampin or clindamycin. The duration of antibiotic therapy is controversial. However, when Raad et al. [14] summarized 55 catheter-related S. aureus bacteraemia, it became clear that only those patients treated for 10 days or fewer, relapsed. Therefore, S. aureus bacteraemia should be treated for at least 14 days, while it seems prudent to treat S. aureus osteomyelitis for at least 2 months. Finally, central-vein catheters should be removed when S. aureus bacteraemia is present [6].

Indications for surgical intervention include a search for the right histopathological and bacteriological diagnosis, persistent pain, bacteraemia that does not respond to adequate antibiotic therapy, abscess formation and neurological deficits [7,9,15]. Both anterior and posterior approaches have been advocated, but the basic aims of surgery include debridement of necrotic bone and surrounding tissue, drainage of associated paraspinal abscesses, and spinal fusion. Primary bone grafting is indicated when bone resection has been extensive. It may allow earlier mobilization of the patient [9,16,17]. In one study, Arnold et al. [9] described 33 patients who underwent surgery. Twenty-eight patients had a neurological deficit; 11 had severe paraparesis and 10 of these patients achieved good functional recovery. On the whole, surgery can relieve pain, improve neurological problems and allow for quicker rehabilitation, even in elderly patients [16,18].

Spinal epidural abscesses are also becoming increasingly frequent, especially in intravenous drug users and in patients who undergo epidural analgesia [19]. Two recent articles highlight this problem in haemodialysed patients [20,21]. Obrador and Levenson [20] detail 12 cases. Nine patients had infection of their permanent or temporary central-vein access. Staphylococcus aureus was cultured in all patients. The leading presenting symptom was back pain, irrespective of the spinal level involved. Fever was present in only 5/12 patients. Abscess progression was manifested by neurological deficits such as sensory loss, sphincter dysfunction and frank paralysis. Diagnosis was confirmed by either MRI (80% sensitivity) or CT-myelogram (100% sensitivity). Treatment was based upon prolonged antibiotic therapy and decompressive surgery. Five patients were operated on within 1 week of the onset of the pre-operative neurological problem. Three of these patients recovered completely. However, of the six patients in whom surgery was delayed, all were left with severe residual neurological deficits [20]. In 1996, Kovalik et al. [21] described their experience in 10 haemodialysed patients. Eight patients had central-vein catheters. ‘Salvage’ of the central-vein catheter, because of recent Staphylococcal bacteraemia, was attempted in five patients. This ‘salvage’ protocol included antibiotic therapy without catheter removal. Three of these patients subsequently developed Staphylococcal epidural abscesses.

The two above-mentioned articles are in complete agreement with more comprehensive reviews of spinal epidural abscesses. Back and radicular pain are the first clues to proper diagnosis, but progression to eventual paralysis can take place rapidly [22–24]. Contrast-enhanced MRI is the preferred method of investigation for both early diagnosis and as a means to confirm resolution of the abscess [22,23,25,26]. If enhancement is still evident despite obvious clinical improvement, this is probably indicative of chronic fibrotic tissue, and not of active disease [27]. In these situations, gallium scintigraphy may be helpful [28].

Treatment policy is based on lengthy antibiotic therapy, and decompressive surgery [22,23]. However, if surgery is to be successful, it should be immediate and before paralysis has set in [25,28]. Of five patients described by Mak et al. [29], none regained neurological function after acute complete paralysis had become evident. Non-operative treatment should be reserved for only a small group of patients, in whom no neurological deficit is present and who are evidently responding to antibiotic therapy. The only other indication may be the inability of the patient to survive surgery [22,30,31].

In conclusion, beware of recent-onset and severe back pain in haemodialysed patients with a recent or current episode of Staphylococcal bacteraemia. Importantly, fever does not have to be present in haemodialysed patients with vertebral osteomyelitis or spinal epidural abscesses. MRI has a number of advantages when used as a diagnostic tool. It can be used early, is highly sensitive and is non-invasive. However, if clinical suspicion still exists despite a non-diagnostic MRI, then CT-myelography should be performed promptly. In both vertebral osteomyelitis and epidural abscesses microbiological diagnosis is a necessity, but commencement of empirical anti-Staphylococcus aureus therapy in haemodialysed patients is a logical and correct thing to do. Surgery plays a central role in the successful treatment of both conditions and should be performed as soon as neurological problems are apparent. A non-surgical approach, especially in patients with epidural abscesses, is fraught with danger. The two patients described here died; one because of a long delay in diagnosis, the second, possibly, because of non-surgical intervention.

Finally, recent work has shed light on interesting aspects of S. aureus infection and its ability to cause bone destruction [5,32,33]. In vitro studies, using a murine calvarial-bone-resorption assay, have shown that cell-surface-associated proteins of S. aureus are
capable of stimulating target cells to release potent osteolytic cytokines, such as interleukin-1 and tumour necrosis factor. This bone resorption can be inhibited by a specific interleukin-1-receptor antagonist or by a monoclonal antibody to tumour necrosis factor [5].

References