Rapid postoperative onset of neurological dysfunction

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A 69-year-old woman with severe rheumatoid arthritis was admitted with rigors 3 weeks following a left total knee replacement. She had a severe deforming arthropathy with an unstable cervical spine and had had multiple joint replacements. She was being treated with prednisolone and penicillamine. The left knee was slightly warm but there was no effusion or restriction of movement. There were no signs of meningitis. She had a superficial pressure sore over the 8th thoracic vertebra. Urinalysis showed proteinuria and she had a leucocytosis. She was treated with co-amoxiclav (625 mg 8 hourly, oral) for suspected urinary tract infection and flucloxacillin (500 mg 6 hourly, oral) for possible staphylococcal septicaemia in view of the pressure sore and recent joint replacement. Urine and blood cultures were subsequently negative. Her condition deteriorated over the next day and her antibiotic regimen was changed to cefotaxime (1 g 8 hourly, intravenously) and vancomycin (1 g 12 hourly, intravenously) as empirical treatment of septicaemia of undetermined origin. She responded well, but four days later she dislocated her right total hip replacement whilst turning over in bed (an event which had happened twice previously). The hip was relocated under spinal anaesthetic using marcaine in dextrose. Initially the anaesthetist aspirated clear cerebrospinal fluid (CSF) but aspiration following introduction of marcaine revealed purulent CSF. Examination of the CSF revealed 40 red blood cells/mm³, 2920 white blood cells/mm³ (98% neutrophils) and Gram-positive cocci were seen on microscopy.

A few hours postoperatively she became unrousable and had developed neck stiffness. Neurological examination at this time was very difficult in view of her condition, though her left plantar reflex was equivocal. However, because of the paucity of neurological signs, the neuro-radiologists felt that magnetic resonance imaging (MRI) was not indicated. Within a week, her ankle, knee and plantar responses became absent. Sensory examination remained difficult to interpret because of poor cooperation but it was felt that there was abnormal sensation from L4 down.

Questions

- 1 What is the diagnosis?
- 2 What other conditions are in the differential diagnosis?
- 3 What is the treatment of choice for this patient?

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Answers

QUESTION 1

Spinal epidural abscess (SEA). CSF taken intra-operatively yielded a pure growth of methicillin-resistant *Staphylococcus aureus* (MRSA). A initial diagnosis of MRSA meningitis was made immediately post-operation and antibiotic therapy was changed to vancomycin (1 g 12 hourly, intravenously) and rifampicin (600 mg 12 hourly, oral). However a neurologist who examined the patient 48 h later felt that she had a loculated cauda equine SEA. Five days later an MRI scan was performed and provided an equivocal result ('cauda equina roots are ill-defined and suspicious'). We postulate that a SEA developed secondary to epidural anaesthesia, caused by MRSA that was colonising the skin at the puncture site. However, the possibility that she acquired the infection via blood from other sites cannot be excluded. When she underwent her spinal puncture for hip re-location (4 weeks after the original operation), we postulate that the needle penetrated the loculated SEA, causing pus to enter the sub-arachnoid space, precipitating the sudden worsening of her condition. SEAs usually extend for four or five vertebral segments, but may extend for the whole length of the spinal cord.¹ MRSA colonisation was documented in several different body sites within a week of her initial CSF isolate, including a pressure sore over the 8th thoracic vertebra. The patient responded well to the treatment and recovered fully after 3 weeks of therapy

QUESTION 2

Primary postoperative meningitis (without pre-existing suppuration). This diagnosis was less likely due to the relatively short interval between the operation and the onset of clinical symptoms.²

QUESTION 3

Urgent neurosurgical referral and antibiotics with anti-staphylococcal activity. The CSF Gram stain suggested staphylococcal sepsis, which was shown to be caused by MRSA. Vancomycin is the drug of choice for MRSA infections.³ However, sustained improvement was achieved only after her second spinal puncture and the administration of intravenous vancomycin and oral rifampicin. This combination has been used to treat serious MRSA infections such as endocarditis,³ and some *in-vitro* studies have shown synergism between these agents against MRSA.⁴ There are few data on the clinical efficacy of this combination in comparison to vancomycin alone, or other agents, in the treatment of MRSA infections of the central nervous system,^{5,6} due to the rarity of the condition. However, there are reports demonstrating the enhanced clinical efficacy of vancomycin plus rifampicin to treat methicillin-resistant *Staphylococcus epidermidis*

meningitis, particularly when the vancomycin is given by the intraventricular route.⁷ Given the poor penetration of vancomycin into CSF and the excellent penetration of rifampicin, the addition of the latter agent to the antimicrobial regimen, would seem rational.

With the inexorable increase in the incidence of MRSA infection in the UK, vancomycin, with or without rifampicin, may soon become the antibiotic of choice in cases of suspected staphylococcal infection in hospitals with high endemic rates of MRSA infection/colonisation. This has obvious cost implications for clinical practice.

Discussion

SEA is a comparatively rare condition in which *S. aureus* is the most common causative organism.¹ Spinal epidural infection usually occurs as a result of either haematogenous spread from cutaneous infection, pyelonephritis, or pneumonia, or by direct extension from a local site, such as vertebral osteomyelitis.¹ It has also followed epidural anaesthesia, lumbar puncture and back trauma.⁸⁻¹⁰ Abscesses most commonly occur in the thoracic and lumbar regions, which have large epidural spaces with an extensive blood supply.¹ Fever, spinal tenderness, and back pain are the most commonly reported clinical features of SEA.⁸ Our patient complained of spinal tenderness on palpation but no back pain and was afebrile throughout. The absence of pain and temperature is consistent with previous reports of SEA.¹⁰ Prior to the advent of MRI and computed tomography, clinical investigation of suspected SEA included lumbar puncture and myelography, both of which can precipitate extension of the abscess into the subarachnoid space, causing septic meningitis.⁹

The treatment of choice for SEA remains urgent surgical drainage, combined with antibiotic therapy appropriate for the organisms isolated. A few case reports of SEA managed non-surgically have been reported.^{11,12}

Colonisation and infection with MRSA is now a global problem in hospitalised patients and those in long-term residential care.^{2,13} However, MRSA meningitis, particularly in the absence of neurological prosthetic devices, is as yet uncommon, with only nine cases reported in the world literature between 1976-96.¹⁴ We believe this is the first published case of an MRSA SEA.

Final diagnosis

Spinal epidural abscess caused by methicillin-resistant *Staphylococcus aureus*.

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Hypertension and renal failure

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A 74-year-old man with a history of intermittent claudication, cigarette-smoking, hypertension, and a successful recent right nephro-ureterectomy for a right ureter transitional cell carcinoma, presented with abnormal renal function and hypertension (plasma creatinine 228 $\mu\text{mol/l}$ and blood pressure 200/100 mmHg on quinapril 20 mg). Fundoscopy showed grade II hypertensive changes. There was no abdominal bruit. There was no blood and only a trace of protein on urine reagent strip testing; phase-contrast urinary sediment microscopy was normal; 24-h protein excretion was 0.2 g (normal < 0.2 g/24 h), and creatinine clearance was 36 ml/min. Prior to the right nephrectomy, renal function had been abnormal (plasma creatinine 184 $\mu\text{mol/l}$).

Ultrasound of his abdomen showed a nonobstructed 9.3 cm left kidney with increased echogenicity and reduced cortical thickness. Isotope renography while on an angiotensin-converting enzyme (ACE) inhibitor showed no activity on the right (nephrectomy) and definite but sluggish excretion by the left kidney. Frusemide 40 mg/day was added, which reduced blood pressure a little (175/90 mmHg), but caused plasma creatinine to rise from 241 to 312 $\mu\text{mol/l}$.

Quinapril was continued at 20 mg daily and lacidipine 4 mg was added. The patient could not tolerate any strength of any other calcium channel blocker, nor a beta- or an alpha-blocker. Blood pressure rose further. Quinapril was increased to 40 mg/day, and plasma creatinine rose again to 386 $\mu\text{mol/l}$. Echocardiography showed significant left ventricular hypertrophy and diastolic dysfunction.

Questions

- 1 Is it likely that this patient has glomerulonephritis?
- 2 What is the most probable reason for the raised blood pressure and worsening renal function?
- 3 What options are available for effecting an improvement?

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