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ORIGINAL ARTICLE

Bacterial meningitis secondary to spinal analgesia and anaesthesia

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KEYWORDS
Bacterial meningitis;
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Abstract
Introduction: Although rare, infectious complications from spinal analgesia and anaesthesia (SA) can have serious morbidity and mortality. This study describes the clinical features and outcome of SA-associated bacterial meningitis in adults seen in a hospital over a 25 yearperiod.
Methods: We reviewed the charts of all patients (aged ≥14 years) diagnosed with SA-associated bacterial meningitis between 1982 and 2006.
Results: Eight cases of SA-associated bacterial meningitis were diagnosed (3.3%bacterial meningitis), with a median age of 62 years (range, 35-80). SA procedures were: morphine infusion pumps with epidural (3 cases) or intrathecal (3) catheters, spinal cord stimulation with epidural neuroelectrode (1), and epidural anesthesia (1). Site of spinal insertion was: cervical (2 cases), thoracic (3), and lumbar (3). The median time to onset of meningitis was 26 days (range, 7-101) after AE. The most common clinical findings were fever (8 cases, 100%), headache (7 cases, 87.5%), and neck stiffness (4 cases, 50%). CSF abnormalities were pleocytosis (8 cases, 100%), elevated protein level (8 cases, 100%), and hypoglycorrhachia (5 cases, 62.5%). The causative organisms were *Staphylococcus epidermidis* (2 cases), *Staphylococcus aureus* (2), *Enterococcus faecalis* (1), *Streptococcus milleri* (1), and *S. epidermidis* and *Pseudomonas fluorescens* (1); one patient had a negative CSF culture. Treatment included antibiotics and to remove the analgesia device in all patients. There was one death (12.5%).
Conclusions: SA is a rare predisposing condition to bacterial meningitis but, due to the seriousness of the infection, it should be considered in the differential diagnosis for any patient who develops fever or headache in this setting

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PALABRAS CLAVE
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Dolor

Meningitis bacteriana asociada a analgesia y anestesia espinal

Resumen
Introducción: Aunque infrecuentes, las complicaciones infecciosas de la analgesia y la anestesia espinal (AE) pueden ser mortales. El objetivo del estudio es describir las meningitis bacterianas asociadas a AE diagnosticadas a adultos en un hospital durante un período de 25 años.
Métodos: Se revisaron las historias clínicas de los pacientes con edad ≥ 14 años que habían sido diagnosticados de meningitis bacteriana asociada a AE entre 1982 y 2006.
Resultados: Se incluyen 8 casos (3,3% de las diagnosticadas durante el periodo de estudio), con una mediana de edad de 62 años (35-80). El procedimiento de AE efectuado fue: bomba de infusión de morfina con catéter epidural (3 casos) o intratecal (3), electroestimulación epidural (1) y anestesia epidural (1). La localización en columna fue: cervical (2 casos), dorsal (3) y lumbar (3). El tiempo transcurrido del inicio de la AE al diagnóstico fue de 7-101 días (mediana de 26). Tuvieron fiebre 8 casos (100%) y cefalea 7 (87,5%), cursando con rigidez de nuca 4 (50%). En líquido cefalorraquídeo se observó pleocitosis en 8 casos (100%), proteínas elevadas en 8 (100%) e hipoglucorraquia en 5 (62,5%). La etiología fue: *Staphylococcus epidermidis* (2 casos), *Staphylococcus aureus* (2), *Enterococcus faecalis* (1), *Streptococcus milleri* (1), flora mixta (*S. epidermidis* y *Pseudomonas fluorescens*) (1), cultivos negativos (1). El tratamiento incluyó antibioterapia y retirada del dispositivo de analgesia, falleciendo un paciente (12,5%).
Conclusiones: La AE es infrecuente como factor de riesgo de meningitis bacteriana, pero la gravedad de la infección obliga a considerarla en el diagnóstico diferencial de la cefalea y del síndrome febril en estos pacientes

Introduction

In recent years both anaesthesia and spinal analgesia (SA) (epidural, intrathecal or subarachnoid, and combined) have reached a wide range of applications in modern medicine. They are used mainly in obstetric, gynaecological, and lower extremity interventions, as well as in the treatment of acute postoperative and chronic pain (neoplastic or of other origin).[1,2] However, these techniques are not free from complications, which can include post-puncture headache, traumatic injuries of the spinal cord and nerve roots, epidural haematomas, and superficial and deep infections: epidural and paraspinal abscess and acute bacterial meningitis (ABM).[3-10] The aim of this study is to describe cases of adults with ABM associated to SA diagnosed in a hospital over a period of 25 years.

Patients and methods

The study was conducted in a third-level university hospital with 485 beds, which currently serves a population of 600,000 and has a Neurosurgery Service and a Pain Unit. We reviewed the clinical histories of all patients aged ≥14 years who had been diagnosed with meningitis during a period of 25 years (1982-2006). These were identified through a computer search of the coded discharge diagnoses database conducted by the Department of Clinical Documentation and Archives. The cases considered to be ABM were those that met previously established diagnostic criteria[11]:

1) ABM of known aetiology in the case of compatible clinical symptoms and positive cerebrospinal fluid (CSF) culture, or negative CSF culture (with hypoglycorrhachia and/or neutrophilic pleocytosis) and positive hemoculture (except coagulase-negative *Staphylococcus*) or presence of Gram-negative diplococci in CSF Gram staining.
2) ABM of unknown aetiology in the case of compatible clinical symptoms, all negative cultures, pleocytosis of more than 100 neutrophils/mm^3 and a CSF Gram staining (except for Gram-negative diplococci) that resulted positive, negative or had not been carried out.

The present study includes ABM cases diagnosed in patients with any type of spinal analgesia device and patients who had received epidural anaesthesia during a surgical procedure. Demographic, epidemiological, clinical, and laboratory data were obtained from their medical histories, as were the treatment used and their progress. The cases of meningitis were considered nosocomial (hospital-acquired) when the disease developed after 48 hours of hospital admission or during the week following discharge. Otherwise, they were considered community-acquired.

Results

During the study period, 239 cases of ABM were diagnosed in adults using the established diagnostic criteria. Of these, only 8 patients had been fitted with spinal analgesia devices

Table 1 Clinical Characteristics, Laboratory Data, Treatment, and Evolution of Patients With Bacterial Meningitis Secondary to Analgesia or Spinal Anaesthesia

Patient	Age/gender	Acquisition	Indication for analgesia/location	Clinical characteristics/procedure-diagnostic time	CSF analysis	CSF culture/device culture/hemoculture	Empirical treatment (antibiotic therapy duration)	Evolution
1	48/M	Nosocomial	Thalamic syndrome/intrathecal catheter (lumbar)	Fever, headache, reduction of consciousness level, neck rigidity/7 days	L: 1.800/mm^3 (N>50%) P: 280 mg/dl G: 20 mg/dl Tinción de Gram: NR	*P. fluorescens*, *S. epidermidis*/*S. epidermidis*/ND	Ceftazidime + Vancomycin + Tobramycin + Rifampicin (17 days)	Cure
2	80/F	Community-acquired	Postherpetic neuralgia and vertebral crushing/epidural catheter (dorsal)	Fever, headache, reduction of consciousness level, neck rigidity/12 days	L: 3.360/mm^3 (N=80%) P: 211 mg/dl G: 68 mg/dl Tinción de Gram: –	*E. faecalis*/ND/ND	Ceftriaxone + Vancomycin (21 days)	Cure
3	35/M	Community-acquired	Vertebral crushing/intrathecal catheter (dorsal)	Fever, headache, reduction of consciousness level/101 days	L: 1.250/mm^3 (N=85%) P: 96 mg/dl G: 20 mg/dl Tinción de Gram: –	-/-/*S. epidermidis*	Vancomycin + Ciprofloxacin (21 days)	Cure
4	74/M	Nosocomial	Neuropathic pain (PNP)/intrathecal catheter (cervical)	Fever/30 days	L: 170/mm^3 (N=65%) P: 82 mg/dl G: 54 mg/dl Tinción de Gram: –	*S. epidermidis*/*S. epidermidis*/-	Vancomycin + Meropenem (20 days)	Cure
5	66/F	Nosocomial	Ankle fracture/epidural anaesthesia (lumbar)	Fever, headache, vómiting/10 days	L: 765/mm^3 (N=70%) P: 76 mg/dl G: 62 mg/dl Tinción de Gram: –	*S. milleri*/ND/-	Ceftriaxone + Ampicillin (14 days)	Cure
6	63/M	Community-acquired	Cervical myelopathy with spastic paraparesis/intrathecal catheter (lumbar)	Fever, headache, vómiting/44 days	L: 770/mm^3 (N=75%) P: 64 mg/dl G: 43 mg/dl Tinción de Gram: –	*S. aureus*/*S. aureus*/*S. aureus*	Vancomycin + Rifampicin (16 days)	Cure
7	47/M	Community-acquired	Post-laminectomy low back pain / epidural electrode (dorsal)	Fever, headache, neck rigidity / 22 days	L: 780/mm^3 (N>50%) P: 135 mg/dl G: 42 mg/dl Tinción de Gram: –	*S. aureus*/*S. aureus*/*S. aureus*	Vancomycin + Ceftazidime (14 days)	Death
8	62/M	Community-acquired	Lumbar ankylosing hyperostosis / epidural catheter (dorsal)	Fever, headache, neck rigidity / 45 days	L: 480/mm^3 (N=30%) P: 168 mg/dl G: 60 mg/dl Gram staining: –	*S. epidermidis*/ND/–	Vancomycin + Ceftazidime (14 days)	Cure

—: negative; CSF: cerebrospinal fluid; F: female; G: glucose; L: leukocytes; M: male; N: neutrophils; ND: not done; P: proteins; PNP: polyneuropathy.

or had received epidural anaesthesia, representing 3.3% of total ABM cases. Table 1 shows their demographic, clinical, CSF analysis, microbiological, and progress data. The median age of these patients was 62 years (35-80). A total of 6 patients (75%) were males. Five meningitis cases (62.5%) were community-acquired and 3 (37.5%) were nosocomial. Implanted devices for pain control (non-neoplastic in all patients) were the morphine infusion pump with an epidural catheter (3 cases) and with intrathecal catheter (3), plus the epidural stimulation electrode (1); 1 patient underwent surgery for an ankle fracture under epidural anaesthesia. The sites of spinal insertion were cervical (2 cases), dorsal (3), and lumbar (3). The time elapsed from the start of SA to the diagnosis of meningitis ranged between 7 and 101 days (median of 26 days).

Clinical manifestations included: fever in 8 cases (100%), headache in 7 cases (87.5%), altered consciousness in 3 cases (37.5%), vomiting in 2 cases (25%), and neck stiffness in 4 cases (50%). Only 1 patient showed local signs of skin infection (patient no. 6). None of the patients developed epidural or paraspinal abscess (ruled out by CT or MRI in 4 cases). The following were observed in the CSF: pleocytosis (8 cases, 100%) with predominance of neutrophils (7 cases, 87.5%), elevated proteins (8 cases, 100%), and hypoglycorrhachia (5 cases, 62.5%). Gram staining was negative in all 7 cases in which it was performed. The aetiology of meningitis was: *Staphylococcus epidermidis* (2 cases), *Staphylococcus aureus* (2), *Enterococcus faecalis* (1), *Streptococcus milleri* (1), and mixed flora *(S. Epidermidis* and *Pseudomonas fluorescens)* (1). The cultures were negative in only 1 patient (no. 3), on whom it was not possible to carry out a lumbar puncture until 2 days after the initiation of antibiotic therapy due to anticoagulation on admission. All patients received antibiotics; these were empirical on diagnosis and subsequently according to the antibiogram (vancomycin and ciprofloxacin in patients with unidentified aetiology) for 14-21 days. In addition, the analgesia device was removed in all patients as part of the treatment. The culture from the removed catheter was positive in 4 of the 5 cases in which it was done (80%). A total of 7 patients recovered without sequelae and 1 died (12.5%) from an infection by *S. aureus*.

Discussion

The frequency with which infectious complications associated with SA are observed varies significantly in the published studies, ranging from 4.3% to 43% for superficial infections and from 0% to 16% for deep infections.[3-10] The main determining factor behind these variations is the type of procedure. In a study that evaluated spinal anaesthesia complications in the UK for 1 year, Cook et al found only 6 cases of meningitis from a total of 707,455 anaesthetic procedures.[3] In contrast, 16% of patients with chronic cancer pain treated with epidural analgesia analysed by Schoeffler et al developed meningitis.[9] In our series, ABM was also a more common complication of chronic analgesia (7 cases) than of anaesthesia (1 case), the latter being a more common medical practice.[3] However, we could not ascertain the number of spinal anaesthesias performed or the devices implanted for spinal analgesia at our hospital over the 25 years studied, to be able to calculate their incidence. Other proposed risk factors for infection include patient factors (age and comorbidities such as diabetes mellitus or immunosuppression), the indication for the procedure (higher in surgical patients compared to obstetric patients, and labour analgesia compared to caesarean section anaesthesia), catheter position (higher with the intrathecal compared to the epidural, and thoracic location compared to the rest of the spine), not adopting strict antiseptic measures during the procedure, technical difficulties during catheter insertion, and catheter permanence time.[3-10]

The etiological spectrum of meningitis associated to SA is wide.[4-10] *Streptococcus* of the viridans group, other species of *Streptococcus*, *Staphylococcus* spp., *Pseudomonas* spp., *E. faecalis*, *Corynebacterium, Acinetobacter,* and even *Aspergillus*.[12] The reported cases secondary to some of the usual causative agents of community-acquired ABM such as *Neisseria meningitides*,[13] and secondary to viruses[14] are more likely to coincide with the procedure than to be related to SA. The mechanisms proposed as a source of meningeal infection are multiple.[4-10] First, the microorganism can be introduced during catheter insertion; this would explain most cases secondary to spinal anaesthesia, caused primarily by *Staphylococcus* spp. and *Streptococcus* spp (the latter being responsible for more than 50% of cases), sometimes originating in the nasopharynx of the physician,[15] which could occur when aseptic measures during the procedure are inadequate (masks should always be used). Second, the catheter can be contaminated by bacteria residing on the skin (with or without simultaneous superficial infection) and they can subsequently migrate along the skin surface to the subarachnoid space,[16] this would explain most of the infections secondary to chronic spinal analgesia, with *Staphylococcus* spp. being the most common aetiology. Third, there can be a haematogenous spread from a distant source of infection, with contamination of the subarachnoid space occurring with the passage of blood to it during the puncture.[17] Finally, the infusion of contaminated material has been the source in a small number of cases, some of which have been fatal.[12] The microbiological aetiology of the meningitis cases presented is consistent with previous publications: the case secondary to anaesthesia was caused by *S. milleri,* whereas *Staphylococcus* spp were isolated in 5 of the 7 cases secondary to chronic analgesia (one of the cases with mixed infection) and *E. faecalis* were isolated in another. In 1 of our patients, the aetiology was not identified, which also occurs in up to 36% of reported cases.[6]

The time elapsed from the SA to the onset of meningitis is variable.[4,5] The cases secondary to subarachnoid anaesthesia (median of 17 hours, range from 1 hour to 10 days) and combined anaesthesia (median of 18 hours, range from 8 hours to 3 days) develop more rapidly. Cases caused by epidural anaesthesia, especially those that occur in patients with chronic analgesia devices, may develop weeks or even months after the SA. This variation in time is explained by the fact that the mechanisms of infection acquisition are different: direct inoculation during the procedure compared to contamination of the catheter and subsequent bacterial migration through it, respectively. The clinical condition and

CSF biochemical profile of ABM secondary to SA do not differ from those of other bacterial meningitis cases. A differential diagnosis with a lumbar puncture headache and chemical meningitis is compulsory, especially when symptoms appear shortly after the procedure. If the meningitis is associated with an epidural abscess, the patient may also present local pain and neurological symptoms dependent on the location.[6,18] None of the patients presented were diagnosed with epidural abscess (ruled out with imaging techniques in only 4 cases).

The empirical treatment of ABM associated with SA should include vancomycin and a cephalosporin with activity against *Pseudomonas*, due to its aetiological spectrum and the fact that infection acquisition is often nosocomial via a dural puncture.[4,6,19] This combination would also cover *Streptococcus viridans* resistant to beta-lactam antibiotics, which have been isolated with increasing frequency in recent years.[20] Dexamethasone as an adjunctive anti-inflammatory treatment has only shown decreased morbidity and mortality in community-acquired ABM (mainly in those with a pneumococcal aetiology).[21] However, its use is recommended in meningitis cases associated with spinal anesthesia[6] (mainly caused by *Streptococcus* spp.), but not in those associated with chronic spinal analgesia (caused by *Staphylococcus* spp.), because dexamethasone hinders the passage of vancomycin into the subarachnoid space. In addition to antibiotic treatment, removal of the catheter or the entire analgesia device is needed to ensure healing and to prevent recurrences.[19,22] In cases of associated abscess, the need for drainage and decompression neurosurgery[6,18] should be assessed. The prognosis of ABM secondary to SA is more favourable than that of community-acquired meningitis, possibly because it is produced mainly by less virulent bacteria such as *Streptococcus* spp. (not pneumococcal) and coagulase-negative *Staphylococcus*.[4,6,11] The cases presented received empirical antibiotic therapy that was confirmed as appropriate against the isolated bacteria, and all had the analgesia device removed. Only 1 patient died from bacterial infection by *S. aureus*.

In conclusion, although SA is the predisposing factor for infection in a small number of ABM cases, the severity of the disease means that it should be considered in the differential diagnosis of patients who develop cephalalgia. Likewise, it should be considered in the differential diagnosis of the fever syndrome affecting patients who have received spinal anaesthesia or are carriers of chronic spinal analgesia devices.

Conflict of interest

The authors declare no conflict of interest.

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