European Journal of Case Reports in Internal Medicine

Drug-Induced Aseptic Meningitis Following Spinal Anesthesia

Ricardo Paquete Oliveira[1], Mafalda Teixeira[1], Sofia Cochito[2], Ana Furtado[1], Bruno Grima[1], José Delgado Alves[1]

[1]Serviço de Medicina IV, Hospital Prof. Doutor Fernando Fonseca, Amadora, Portugal

[2] Departamento de Pediatria, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, EPE Clínica Universitária de Pediatria, Faculdade de Medicina, Universidade de Lisboa. Lisboa, Portugal

Doi: 10.12890/2019_001334 - European Journal of Case Reports in Internal Medicine - © EFIM 2019

Received: 15/10/2019
Accepted: 23/10/2019
Published: 31/12/2019

How to cite this article: Paquete Oliveira R, Teixeira M, Cochito S, Furtado A, Grima B, Delgado Alves J. Drug-induced aseptic meningitis following spinal anesthesia. *EJCRIM* 2019;**7**: doi:10.12890/2019_001334.

Conflicts of Interests: The Authors declare that there are no competing interest

ABSTRACT

Meningitis is a very uncommon complication of spinal anesthesia, and drug-induced aseptic meningitis (DIAM) is even rarer. We present two cases of DIAM following spinal anesthesia with bupivacaine and ropivacaine, respectively. The patients presented shortly after the procedure with typical meningitis symptoms. Since CSF (cerebrospinal fluid) analysis could not initially exclude bacterial meningitis, they were started on empirical antibiotics. CSF was subsequently found to be negative for viruses and bacteria in both cases, and antibiotics were promptly stopped. Both patients improved rapidly and without neurological sequelae. While it remains a diagnosis of exclusion, it is important to be aware of DIAM as recognition of the condition can lead to shorter admission times and avoid unnecessary use of antibiotics.

LEARNING POINTS

- A diagnosis of DIAM should be considered when a patient who recently underwent spinal anesthesia is admitted with symptoms and CSF compatible with meningitis.
- Clinical and laboratory findings (including CSF analysis) cannot distinguish between bacterial meningitis and DIAM.
- A negative CSF culture and rapid recovery confirm the diagnosis and stopping antibiotics at this point is effective.

KEYWORDS

Aseptic meningitis, drug-induced aseptic meningitis, ropivacaine, bupivacaine

CASE 1

A healthy 44-year-old woman was submitted to ankle arthroplasty under spinal anesthesia (bupivacaine and sufentanyl). There were no breaches in the aseptic precautions, and no anesthetic or surgical complications, and the patient was discharged. One day later she developed an occipital headache with sono and photophobia, vomiting and fever (38°C). On admission, both physical and neurological examinations were normal, except for neck stiffness.

Laboratory tests were remarkable only for leukocytosis (17900/mm^3) and elevated C-reactive protein (CRP) (9.9 mg/dL). A brain computerized tomography (CT) scan was normal. CSF examination showed increased cell count (1116/mm^3 with polymorphonuclear predominance) and hyperproteinorrachia (236 mg/dL) with hypoglycorrhachia (32 mg/dL).

Prior to the microbiology results, a provisional diagnosis of bacterial meningitis was made and the patient was started on empirical antibiotherapy (ceftriaxone and vancomycin). Subsequently, blood, CSF and urine cultures revealed no bacteria and CSF virus panel (Polymerase chain reaction [PCR] for varicella-voster, herpes simplex, Ebstein-Barr and cytomegalovirus) was negative.

There was a rapid and complete clinical improvement in 48 hours. Antibiotics were stopped in less than 72h. The patient was discharged without neurological deficits on day 6.

European Journal of Case Reports in Internal Medicine

CASE 2

A 34-year-old woman was admitted five days after giving birth through vaginal delivery under spinal anesthesia (ropivacaine and fentanyl). She complained of intense low back pain, bifrontal headache and low-grade fever starting on delivery day. On admission she had fever (38.6°C), neck stiffness and Kernig's sign. The rest of the neurological examination was normal. Observation by the gynecology department showed no signs of postpartum complications.

Laboratory tests were normal apart from leukocytosis (13500/mm^3; 85% neutrophils) and elevated CRP (7.4 mg/dL). CSF examination, performed after a traumatic first attempt, showed bloody fluid (invalidating the cell count), hyperproteinorrachia (104.6 mg/dL) and normal glucose (42 mg/dL), with a negative virus PCR panel. Brain CT scan was normal.

Prior to the culture results, the patient was treated empirically for infectious meningitis with IV ceftriaxone, vancomycin and acyclovir.

The patient showed a rapid clinical recovery (in 48 hours). The lab inflammatory markers steadily decreased back to normal. Acyclovir was stopped by day 3 (after a negative CSF virus panel) and antibiotics were stopped by day 5 (after negative blood and CSF cultures). Indeed, on day 3, CSF analysis was repeated and showed 579/mm^3 cells (with polymorphonuclear predominance), 154 mg/dL total protein and 47 mg/dL glucose. Microbiology exams were also negative. The patient was discharged asymptomatic on day 7.

DISCUSSION

Meningitis following spinal anesthesia is an extremely rare event (incidence <0.01%)[1] with potentially serious complications. As with meningitis in the general population, causes can be broadly divided into bacterial and aseptic types, the latter comprising infection by other microorganisms (viruses and some intracellular bateria), meningeal involvement in systemic diseases (autoimmune and neoplastic), and drug-induced forms. Two mechanisms have been proposed for DIAM: direct chemical irritation of the meninges as a result of intrathecal administration of the drug (anesthetics and chemotherapy); systemic immunological hypersensitivity (nonsteroidal antiinflammatory drugs, intravenous immunoglobulin and antibiotics)[2].

It is important to distinguish DIAM from bacterial meningitis, as the latter can lead to neurological sequelae and is a potentially life-threatening condition, demanding urgent treatment. Additionally, establishing an aseptic etiology early can prevent unnecessary treatment and days of hospitalization[3]. That being said, this distinction cannot be made on the basis of patients' characteristics or clinical findings, such as headache, neck stiffness and fever[4,5]. Furthermore, CSF findings are also similar between DIAM and bacterial meningitis: pleocytosis with neutrophil predominance, hyperproteinorrachia and hypoglycorrachia are found in both forms (even though hypoglycorrachia is not always present in DIAM)[5,6]. This means that DIAM remains a diagnosis of exclusion and empirical antibiotics should be started in all cases, and continued until negative CSF cultures are obtained, at which point antibiotics can be stopped. Stopping antibiotics at this point is an effective strategy that also lowers costs and, potentially, antibiotic resistance[5].

In the cases presented, antibiotics were stopped early on, and both followed a typical DIAM course, with rapid clinical recovery and lowering of inflammatory markers, absence of neurological sequelae and no recurrence, substantiating the diagnosis. While some authors have suggested that some previous reports of DIAM could have been viral meningitis[6], it is important to note that in both these cases the most frequent viral agents were excluded using PCR techniques.

In both our patients, we diagnosed aseptic meningitis provoked by the anesthetic used in spinal anesthesia, with bupivacaine being the culprit in the first case, and ropivacaine in the second. Both drugs belong to the amino amide class of regional anesthetics[7]. Bupivacaine may provoke adverse neurological effects (dizziness, altered vision, etc.), but these effects are rare when it is administered correctly. Ropivacaine is a newer drug that shows better sensorimotor dissociation at lower doses and shorter action. While previous bupivacaine-induced aseptic meningitis cases have been reported[6,8] we have found only an isolated incident reported with ropivacaine[6]. While the summaries of the product characteristics for both drugs mention central nervous system adverse effects (ranging from anxiety to seizures), there is no mention of DIAM as a possible complication. In both the incidents described herein, the medical team discussed the case with the anesthesiology department in order to determine the anesthetics used, which was fundamental to the diagnosis.

CONCLUSIONS

Although very rare, meningitis is a possible complication of spinal anesthesia and the possibility of DIAM should always be borne in mind. In the cases presented, the diagnosis of DIAM was based on a high level of suspicion. These cases highlight the need to review drugs recently administered to patients. Only negative CSF definitively confirmed the diagnosis, allowing for a quick withdrawal of the antibiotics, shorter hospital stays and lower costs. Both patients had a fast and complete recovery. To our knowledge this is the first time ropivacaine-induced aseptic meningitis has been described in detail.

European Journal
of Case Reports in
Internal Medicine

REFERENCES

1. Videira R, Ruiz-Neto P, Brandao Neto M. Post spinal meningitis and asepsis. *Acta Anaesthesiol Scanda* 2002;**46**:639–646.
2. Jolles S, Sewell W, Leighton C. Drug-induced aseptic meningitis: diagnosis and management. *Drug Saf* 2000;**22**:215–226.
3. Dubos F, Lamotte B, Bibi-Triki F, Moulin F, Raymond J, Gendrel D et al. Clinical decision rules to distinguish between bacterial and aseptic meningitis. *Arch Dis Child* 2006;**91**:647–650.
4. Moris G, Garcia-Monco J. The challenge of drug-Induced aseptic meningitis. *Arch Intern Med* 1999;**159**:1185–1194.
5. Zarrouk V, Vassor I, Bert F, Bouccara D, Kalamarides M, Bendersky N et al. Evaluation of the management of postoperative aseptic meningitis. *Clin Infect Dis* 2007;**44**:1555–1559.
6. Bihan K, Weiss N, Théophile H, Funck-Brentano C, Lebrun-Vignes B. Drug-induced aseptic meningitis: 329 cases from the French pharmacovigilance database analysis. *Br J Clin Pharmacol* 2019;**85**:240–246.
7. Ruetsch Y, Boni T, Borgeat A. From cocaine to ropivacaine: the history of local anesthetic drugs. *Curr Top Med Chem* 2001;**1**:175–182.
8. Tateno F, Sakakibara R, Kishi M, Ogawa E. Bupivacaine-induced chemical meningitis. *J Neurol* 2010;**257**:1327–1329.