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Case report

Community-acquired *Escherichia coli* meningitis and spondylodiscitis in an adult patient with discoid lupus erythematosus

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ABSTRACT

Acute bacterial meningitis has a high impact on adult mortality worldwide. Community-acquired *Escherichia coli* meningitis (CA-ECM) is a rare and poorly described condition and the available knowledge is based on low evidence research, mainly from case reports. We describe a case of CA-ECM in Portugal in an adult patient with discoid lupus erythematosus under immunomodulatory therapy. A 73-year-old woman was admitted to the emergency department with fever and altered mental status over 48 h. Cerebrospinal fluid analysis showed 185 leukocytes/μL, including 85% neutrophils, hypoglycorrhachia (less than 5 mg/dL) and elevated protein of 423 mg/dL with positive culture for *Escherichia coli*. She was treated with ceftriaxone. Imaging studies also demonstrated spondylodiscitis and arthritis. She responded well to antimicrobial therapy and completed the treatment as an outpatient.

Introduction

Acute bacterial meningitis has a high impact on adult mortality worldwide and its incidence in western countries is approximately 1- to 2- cases per 100,000 inhabitants. The case fatality rate depends on the involved agent and the type of meningitis but can reach up to 30% [1]. *Streptococcus pneumoniae* is the most frequent agent implicated in adult meningitis with a frequency between 9.6%–75.2% [2] and Gram-negative bacilli (other than *Haemophilus influenzae*) represent about 8.7% of all cases with an annual incidence of 2 cases per 100,000 inhabitants [3].

Cases of meningitis caused by Gram-negative bacteria can be classified according to different clinical scenarios, as follows: neonatal meningitis; trauma and neurosurgery; and community-acquired/spontaneous meningitis. This last condition is caused by *Escherichia coli* in 41.9% of the cases [3]. Community-acquired *Escherichia coli* meningitis (CA-ECM) is a rare and poorly described condition, hence the available knowledge is based on low evidence research, mainly from case reports [4].

We describe a case of CA-ECM in Portugal in an adult patient with discoid lupus erythematosus, using immunomodulatory therapy with low doses corticosteroids and azathioprine, for which further investigation lead to the added diagnosis of spondylodiscitis and septic arthritis.

Case report

A 73-year-old woman with discoid lupus erythematosus diagnosed during her youth was admitted to the emergency department with complaints of fever and altered mental status for 48 h. In the previous 5 years, she was treated with prednisolone 2.5 mg/day, azathioprine 75 mg/day and hydroxychloroquine 200 mg/day. There was no history of diabetes mellitus, chronic alcoholism, chronic liver disease, surgical or cranial trauma or previous assistance in healthcare facilities or recent travels. Upon admission, she had a temperature of 39 °C, blood pressure 126/88 mmHg, a heart rate 100 beats per minute and blood glucose 114 mg/dL. Her Glasgow Coma Scale (GCS) score was 13, with scores of 5, 4 and 4 for motor, eye and verbal responses, respectively. She presented psychomotor agitation and physical examination was unremarkable, except for neck stiffness. Motor or sensory deficits were not found during physical examination.

Blood analysis demonstrated no anemia, 9,800/μL leukocytes (reference range 4.5–11.4), 93.1% neutrophils (41%–75%), lymphopenia 4.8% (20%–40%) and thrombocytopenia 100,000/μL (150,000–350,000), renal dysfunction with creatinine 1.24 mg/dL

Abbreviations: CA-ECM, Community-acquired *Escherichia coli* meningitis; CRP, C-reactive protein; CSF, Cerebrospinal fluid; CT, Computed tomography; *E. coli*, *Escherichia coli*; ESR, Erythrocyte sedimentation rate; GCS, Glasgow coma scale; HIV, Human immunodeficiency virus; MRI, Magnetic resonance imaging; PCR, Polymerase chain reaction; PET, Positron emission tomography; RT-PCR, Reverse transcription polymerase chain reaction; STIR, Short-TI inversion recovery; SUVmax, Maximum standardized uptake value; WBC, White blood cell.

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(0.6–1.1), elevated inflammatory markers with erythrocyte sedimentation rate (ESR) 96 mm/1 h (1–20), C-reactive protein (CRP) 42 mg/dL (<0.5) and hypoalbuminemia 1.9 g/dL (3.4–4.8).

A lumbar puncture was performed and the cerebrospinal fluid (CSF) was turbid macroscopically. Empiric antimicrobial therapy was prescribed with ceftriaxone 2 g twice daily, ampicillin 200 mg/kg/day q4h and acyclovir 45 mg/kg/day q8h. Cytochemical analysis showed 185 leukocytes/μL, including 85% neutrophils, hypoglycorrhachia (less than 5 mg/dL) and elevated protein of 423 mg/dL. Capsular polysaccharide antigens were negative and, because PCR and RT-PCR assays for detection of human herpesviruses and enteroviruses in CSF were also negative, acyclovir was discontinued. Cultures of CSF revealed *E. coli* resistant to ampicillin, amoxicillin/clavulanate and trimethoprim/sulfamethoxazole but susceptible to piperacillin/tazobactam, all cephalosporins, carbapenems, aminoglycosides and quinolones. The same agent with the same susceptibility profile was identified in blood cultures. Antibacterial therapy was de-escalated to ceftriaxone. Azathioprine and hydroxychloroquine were stopped, and prednisolone 2.5 mg was maintained. Computed tomography (CT) scan of the brain, chest, abdomen, and pelvis showed no deep infection or evidence of neoplasia.

The patient improved with total regression of neurological symptoms in the first week after antimicrobial therapy initiation, however, high-grade fever persisted (39 °C) for 3 weeks despite antimicrobial therapy use. There was a reduction of CRP (10 mg/dL) but ESR remained high (>120 mm/1 h). Abdominal, renal and vesical ultrasonography as well as a CT scan of the chest, abdomen and pelvis were performed at 2 weeks of hospital admission to exclude the presence of abscess collections or other suspicious images of neoplasia. All results were normal. Transthoracic and oesophageal echocardiogram did not reveal any suggestive images of endocarditis. Infectious diseases serologies and autoimmunity markers were all negative.

A positron emission tomography (PET)-CT scan of the body revealed an increased uptake of 18F-fluorodeoxyglucose in bone and osteoarticular topography involving T4 vertebral body with soft tissue attainment (SUVmax = 7.3), transition of the posterior elements of L2/L3 (SUVmax = 4.6), right slope of the S2/S3 transition (SUVmax = 5.2), left sacroiliac joint with ipsilateral muscle attainment (SUVmax = 6.4) and right glenohumeral joint (SUVmax = 4.7). These hypermetabolic alterations were suggestive of osteomyelitis and multifocal arthritis. A magnetic resonance imaging (MRI) of the vertebral column showed T4/T5 vertebral bodies involvement by inflammatory tissue involving the spongy bone, hypointensity in T1-weighted and hyperintensity in T2-weighted/STIR with contrast enhancement and coexistence of involvement of the intervertebral disc (Fig. 1). MRI of the sacroiliac joints revealed at the level of the left iliac and the left anterior and superior slopes of the S1 wing, a non-homogeneous spongy hypodensity pattern at T1-weighted, with marked hyperintensity at T2-weighted with fat suppression, demonstrating contrast enhancement/uptake, in an area of trabecular oedema, which is also associated with enlargement of the articular interline and small joint effusion suggestive of sacroiliitis (Fig. 2).

After 4 weeks of admission, prednisolone was increased to 40 mg/day and hydroxychloroquine was introduced in the same dosage that the patient used to take. She was afebrile and inflammatory markers were reduced. Antibacterial therapy was extended to 8 weeks with clinical and radiological improvement.

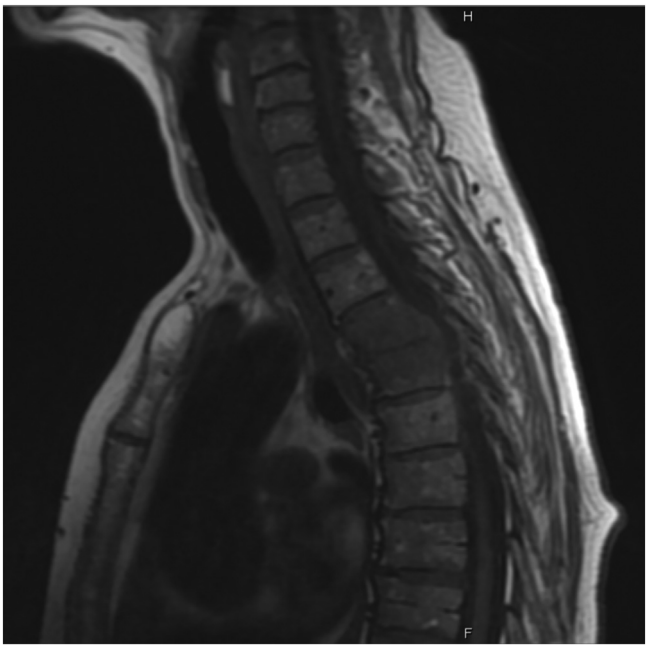

Fig. 1. The T1-weighted sagittal MRI of the vertebral column showed inflammatory involvement of T4/T5 vertebral bodies and coexistence of intervertebral disc involvement.

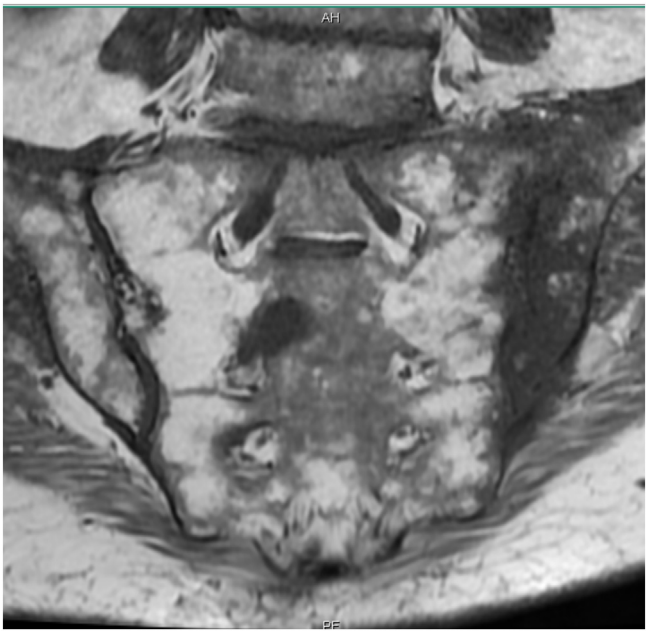

Fig. 2. The T1-weighted coronal MRI of the sacroiliac joints showed a left non-homogeneous spongy hypodensity pattern, associated with enlargement of the articular interline and small joint effusion.

Discussion

CA-ECM in adults is rare, ranging from 0.7% of all diagnosed cases of acute bacterial meningitis in the Netherlands to 3.6% in the United States and 7% in Spain [3,5]. A recent report by Bichon et al. described a worldwide total of 45 cases occurred from 1946 and 2017 with an average report of one case per year across the world [4]. In Portugal, these numbers are unavailable, even in the neonatal and neurosurgery scenarios, where the incidence could be greater.

The occurrence of CA-ECM is often linked to risk factors such as alcoholism with cirrhosis, uncontrolled diabetes, disseminated strongyloidiasis, HIV infection, chronic organ insufficiency and chronic obstructive pulmonary disease. Long-term corticosteroids were reported as a risk factor as well as immunosuppressive drugs

[5]. Hematological and solid neoplasms are also risk factors associated with this condition but there is no reference in literature to connective tissue diseases [6]. Our patient was using low doses of prednisolone which should not cause immunosuppression, but the underlying disease *per se* and the long term use of other immunosuppressive therapy might have resulted in the predisposition to develop an infection in the central nervous system.

Clinically, an observational study conducted by Bodilsen et al. found that CA-ECM patients usually present a GCS between 10- and 15-points, which matches the one identified in our patient. The presence of neck stiffness was identified in 72% of all patients of the mentioned study. The meningitis triad: mental status alteration, fever and neck stiffness, described here, was only observed in 25% of the cases according to the same author's study. In terms of laboratory tests, the WBC count ranged from 6,300/μL to 20,900/μL and the CRP ranged from 8 mg/dL to 32.1 mg/dL. Agent isolation in blood cultures was identified in 76% of the patients. CSF alterations showed leukocytes count between 125/μL to 7773/μL, proteins 2.3 g/L to 6.0 g/L and abnormal cranial imaging in 23% of patients [6].

The prompt start of antimicrobial therapy is the single factor with the most impact in survival in any case of acute bacterial meningitis. In this case, empirical treatment was rapidly initiated and included two antimicrobials, ceftriaxone and ampicillin. CA-ECM is very rare and was not considered in initial diagnosis, moreover the isolated *E. coli* demonstrated to be sensitive to ceftriaxone but resistant to ampicillin. One major concern in treating Gram-negative bacilli is the emergence of strains producing extended-spectrum beta-lactamases, so it is important to consider local antimicrobial resistance patterns. Yang et al. reported 15 patients with *E. coli* meningitis, and all presented some degree of resistance to broad-spectrum cephalosporins. Although their casuistic was composed mainly by post-neurosurgical meningitis, it is known the increased resistance of *E. coli* to cephalosporins in Taiwan, where these cases were originated from [7].

Bacterial meningitis is caused either by direct extension of a contiguous focus or in consequence of bacteremia [8]. The exact source of infection in CA-ECM is unknown but it is described that the focus of bacteremia is originated from genitourinary or gastrointestinal tracts. The overall case fatality rate observed is higher when compared to spontaneous meningitis caused by others agents, mainly because of systemic and neurological complications [3]. It is important to exclude secondary implantation sites, as in our case, despite the guided treatment and the good anti-inflammatory response, the patient persisted with fever. We performed a more extensive diagnostic workup which included the search of endocarditis with a transoesophageal echocardiogram, PET-CT scan and MRI to find intra-abdominal or osteoarticular focus. We discovered a spondylodiscitis which was also described in a report of Kohlmann et al. and Dobson et al. [9,10].

Regarding the limitations of the case, it should be noted that the findings identified in MRI and PET-CT cannot categorically be related to an infectious process because a biopsy was not performed, so the findings may be related to her underlying disease.

Conclusions

CA-ECM in an adult is a rare entity which usually occurs in the presence of predisposing factors. This case demonstrates the change that can be observed in the meningitis epidemiology with the dissemination of immunosuppressive therapy using in different disorders. Other important clinical aspect is the frequency of secondary distant sites of infection and the possibility of resistant strains.

Authors' contribution

FV drafted the manuscript and obtained consent from the patient. VJ collaborated in this manuscript production. MC and JP critically revised the manuscript. All authors read and approved the final manuscript.

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Author's statement

FV drafted the original and reviewed manuscript and obtained consent from the patient. VJ collaborated in the original manuscript and help to reviewed. MC and JP critically revised the original and reviewed manuscript. All authors read and approved the original and reviewed manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

Not applicable.

Competing interests

None of the authors have any competing interests.

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