Mycobacterium mageritense meningitis in an immunocompetent patient with an intrathecal catheter

Meningitis por Mycobacterium mageritense *en una paciente inmunocompetente portadora de un catéter intratecal*

Dear Editor,

Mycobacterium mageritense is a non-pigmented rapidly growing microorganism identified as a new species in the year 1997 in Madrid, Spain.[1] Since 2002, there are several published papers of clinical infections caused by *M. mageritense* (e.g., sinusitis, pneumonia, skin and soft tissue infections, and catheter-related bacteraemia).[2–6] Different antimicrobials (doxicicline, ciprofloxacine, amykacine, imipenem, linezolid and trimethoprim/sulfamethoxazole) have been used for the treatment of these infections. We report here our experience with an immunecompetent patient diagnosed of *M. mageritense* meningitis likely associated to an intrathecal catheter.

In July 2008, a 39-year-old woman was admitted at her reference hospital because of fever. She was carrier of an intrathecal catheter (with a reservoir for epidural analgesia); also, she was taking several psychotropic drugs because of posttraumatic back pain and left radiculopathy (following a car crash). There was a purulent discharge in the reservoir area. Therefore, both the epidural catheter and the reservoir were removed. Microbial cultures (three set of blood, the exudates and the catheter tip) were all negative. An empirical combination of intravenous (IV) vancomycin and gentamicin was prescribed during 14 days. There was total resolution of fever and the patient was discharged from her reference hospital.

Twenty days later (August 2008), she developed a new fever (38.5 °C), headache and somnolence, and the back pain increased significantly. She was remitted to our hospital. The cerebrospinal fluid (CSF) study showed a count of 246 leukocyte/μL (60% of mononuclear's cells), 33 mg/dL of glucose, 155 mg/dL of protein, and the adenosinedeaminase (ADA) was 29 U/L (normal range: <9 U/L). CSF usual stains, bacterial cultures and LCR serology (VDRL, *Brucella* sp., *Listeria monocytogenes*, *Coxiella burnetii*, *Leptospira* sp., and *Borrelia* sp.) were all negative. A Mantoux test was negative. Chest X-ray was within normal limits. Empirical treatment with rifampin, isoniazid, pyrazinamide and ethambutol in standard doses was prescribed. Twelve days after, the patient developed a sudden facio-braquio-crural hemiplegy. NMR study showed several ischaemic infarcts (at the protuberance and right intern capsule). The first CSF culture in Löwenstein medium (August 2008) was positive for a mycobacterium. The isolate was sent to the National Reference Laboratory for Mycobacteria and identified by phenotypic methods as colonies non-pigmented after 3 days of incubation at 22, 30, 37 and 42 °C, negative for Tween Hydrolysis and heat-stable catalase test, positive for arylsulfatase activity at 3 days, and for nitrate reductase. Furthermore, it was identified as *M. mageritense* by PCR-RFLP of hsp65 gene.[8] The strain showed three fragments (240, 130 and 85 bp) by BstEII restriction enzyme digestion and three fragments (145, 120 and 60 bp) by HaeIII restriction enzyme digestion. In addition, the identification was confirmed by sequencing of 16S rRNA gene. Susceptibility testing was made by the proportions method (on Agar 7H10) that showed resistance to isoniazide, streptomycin, ethambutol, rifampicin, P.A.S., kanamycin, cycloserine and ethionamide. Pirazinamide susceptibility on MGIT 960 was made following the manufacturer recommendations. The susceptibility to other drugs (amikacin, norfloxacin, ofloxacin, ciprofloxacin, imipenen, linezolid, trimetil-sulfametoxazol, capreomycin, doxiciclin, claritromycin, amoxicillin-clavulanic and tobramycin) was made by E-TEST (on Mueller-Hinton agar).

Table 1
Mycobacterium mageritense infections.

Localization and type of infection	Reference
Upper respiratory tract and pneumonia	
Female patient of unknown age	2
Severe sinusitis in a 51-year-old man	2
HIV-Infected 42-year-old man	2
Pneumonia in a 36-year-old woman	4
Pneumonia in a 54-year-old immune-compromised woman	7
Catheter-associated bacteraemia	
A 32-year-old immune-compromised woman	2
A 26-year-old pregnant woman	5
Skin and soft tissue infections	
Wound infection after liposuction (37-year-old woman)	2
Wound infection in a 25-year-old man	2
Furunculosis in two women (43- and 56-year-old)	3
Late-onset posttraumatic infection in *tsunami* survivor	6

The initial antitubercular therapy was changed to linezolid (600 mg/12 h), doxicicline (100 mg/12 h), and moxifloxacin (400 mg/12 h) all by IV route. There was a good clinical response but the patient developed nausea and vomiting. Linezolid was switched to oral cothrimoxazole (one strength tablet BID) because of a probable interaction with psychotropic drugs,[9] and vomiting ceased completely. A new CSF study was normal. Nowadays, after 1 year of continuous antimicrobial therapy and nearly 4 years after the clinical diagnosis of meningitis, the patient is in a good state of health with a left hemiplegy as neurological sequel.

This rare case of meningitis widens the still small spectrum of *M. mageritense* infections.[2–6] The most likely way of entry of the mycobacterium in this patient could be through the intrathecal catheter. *M. mageritense* is a ubiquitous bacterium. It can be carried on freshwater and seawater.[3,6] It has been recovered from respiratory secretions, blood, wound infections, and some catheters.[2,4,7] In addition, it is able to form biofilms that can provide resistance to several antimicrobials, but the clinical importance of this fact is not well defined[10] (Table 1).

Regarding the clinical course of our patient, she developed a sudden facio-braquio-crural hemiplegy. In our opinion, this neurological manifestation was probably due to cerebral vasculitis. The relationship between mycobacterial meningeal infections and cerebral ischaemic lesions is well known.

In conclusion, acute meningitis opens the narrow clinical spectrum of *M. mageritense* infections. Also, iatrogenic meningitis is frequently secondary to contamination of aerosolized bacteria from environment (e.g., the mouth of medical staff).[11] In this regard, it is necessary to bear in mind the real probability of environmental infections, whatever the origin, in the carriers of catheters.

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Haemolytic uraemic syndrome associated with bloody diarrhoea caused by *Streptococcus dysgalactiae*

Síndrome hemolítico-urémico asociado a diarrea invasiva por Streptococcus dysgalactiae

Dear Sir,

The haemolytic uraemic syndrome (HUS) includes the triad of haemolytic anaemia, thrombocytopenia, and acute renal failure. HUS can be distinguished in typical HUS and atypical HUS (aHUS). Enterohaemorrhagic *Escherichia coli* (STEC), which produces Shiga toxin, and *Shigella dysenteriae* are frequently the cause of bloody diarrhoea, which characterized typical HUS. Atypical HUS defines non-Shiga-toxin HUS and even if some authors include secondary aHUS due to infectious agents (mostly *Streptococcus pneumoniae*), or other causes (malignancy, cancer chemotherapy, transplantation), aHUS designated a primary disease due to a disorder in complement alternative pathway regulation that shows a poorer outcome.[1] Although extremely rare, infections due to *Streptococcus pyogenes* (GAS) with and without diarrhoea have been associated with HUS.[2,3] *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE) causes invasive streptococcal infections, including streptococcal toxic shock syndrome, as does Lancefield group A *S. pyogenes*. Similarly to group A streptococci, SDSE possesses virulence factors including M protein, streptolysins and others.[4] We report the first case of bloody diarrhoea and HUS probably due to SDSE in a three-year-old girl.

The 3-year-old girl was transferred to Puerta del Mar University Hospital with a history of crampy abdominal pain associated with bloody diarrhoea and oliguria. No previous intake of antibiotics was referred. On admission, BUN and serum creatinine were 167 and 3.1 mg/dl, respectively, haemoglobin was 11.3 g/dl and platelet count was 100,000 μl^{-1}. C-reactive protein was 18.18 mg/dl (normal 0–0.5 mg/dl). Serum fibrinogen levels, prothrombin time and partial thromboplastin time were normal. Blood smear showed polychromasia with the presence of schistocytes. She was admitted to the intensive care unit, and antibiotic despite hydratation, her renal function continued to deteriorated and continuous veno-venous hemodiafiltration was started. By the fourth hospital day, C3 levels were 79 mg/dl (normal 90–180 mg/dl), returning to normal levels at the time of discharge, and C4 was 21.6 (normal 10–40 mg/dl). Renal function was not re-established, and at discharge she was treated with continuous ambulatory peritoneal dialysis. There was no familial history for HUS.

In two stools samples cultured on admission and one day after were isolated with pure growth of *S. dysgalactiae* subsp. *equisimilis*. Identification was made in accordance with the differentiating characteristics described by Ruoff et al.,[5] including agglutination positivity for Lancefield group C (DiaMondial Strept kit, France), strong beta-haemolysis, formation of large, glossy colonies and bacitracin resistance. Susceptibility to antibiotics was determined by disk diffusion test according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI, 2011). The isolate was susceptible to penicillin, vancomycin and levofloxacin, and resistant to erythromicin and clyndamicin. No *Salmonella* sp, *Shigella* sp, *Campylobacter* sp, *Vibrio* sp, *Aeromonas* sp or *Yersinia* sp were isolated by culture. Shiga toxins genes, intimin *eae* gene, and virulence factor *ipah* gene, to detect enterohaemorrhagic *E. coli*, enteroinvasive *E. coli* enteropathogen *E. coli* and *Shigella* was performed by PCR (GenoType EHEC, Hain LifeScience, Germany) on stools, with negative results. Blood cultures submitted at the time of admission were also negative. No throat culture was processed.

In 1996, Vandamme et al.,[6] proposed that a novel subspecies, *S. dysgalactiae* subsp. *equisimilis*, was a clinical pathogen. In the present century, the prevalence of invasive and non-invasive SDSE infections has increased gradually year by year.[4,7] The spectrum and clinical courses of SDSE infection show substantial overlap with those of GAS. Haemorrhagic enteritis caused by GAS has been described[2,8] but, at our knowledge, this could be the first case of bloody diarrhoea caused by SDSE, as no other enteropathogenic bacteria were detected by culture or molecular methods. Recently, it has been determined the complete genomic sequence of SDSE strain GGS_124 isolated from a patient with streptococcal toxic shock syndrome (STSS). SDSE shares most of the virulence factor genes of GAS, including streptolysin O, streptokinase, fibronectin-binding, collagen-binding T antigen (FCT-like regions), and NADase and distantly related to streptococcal inhibitor of complement (DRS), although lacks several virulence factors, such as superantigens, cysteine protease SPE-B and the ABC operon.[9]

An important mechanism underlying aHUS involves the complement system, but endothelial cell activation may play an important role too. The association of GAS with HUS is not well known, however, it has several virulence factors that may predispose to microangiopathy. Activation of endothelial cell matrix metalloprotease by GAS extracellular cysteine protease resulted in endothelial cell damage,[10] but SDSE lacks this enzyme. The release of inflammatory mediators in the presence of SDSE infection may play a role in the pathogenesis of HUS.

Although there more studies are necessary to conclude that SDSE can cause bloody diarrhoea and HUS, we consider that it is important to underline the increased clinical importance of this microorganism.