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Meningitis due to carbapenemase-producing *Aeromonas hydrophila*: a case report

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ABSTRACT

Here we describe an unusual clinical presentation of infection due to *Aeromonas hydrophila* and underline the importance of a correct microbiological diagnosis for an adequate treatment. A 6-year-old patient with a history of craniotomy with duraplasty the week before consulted for fever and drainage of serosanguineous fluid from the surgical wound. The laboratory parameters were normal and the computed tomography scan showed no relevant changes. Lumbar puncture: leukocytes: 91/mm^3; proteins: 89 mg/dL; glucose: 36 mg/dL. Treatment with vancomycin and ceftazidime was started. Cerebrospinal fluid culture: oxidase-positive, glucose-fermenting Gram-negative bacillus. Treatment was changed to meropenem. At 72 hours, using a diffusion method and Vitek 2, it was reported as *Aeromonas hydrophila* sensitive to trimethoprim-sulfamethoxazole, ciprofloxacin, cefotaxime, and meropenem. The Blue-Carba method was performed to detect carbapenemases; the result was positive. Treatment was changed to trimethoprim-sulfamethoxazole. The patient completed 21 days of treatment with a favorable clinical course.

Key words: Aeromonas*, meningitis, carbapenemase, beta-lactamase.*

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INTRODUCTION

The *Aeromonas* spp. genus is widely distributed in aquatic environments. It causes a broad range of diseases. Diarrhea is the most common symptom. It has also been associated with a variety of extraintestinal manifestations, including wound infection after traumatic aquatic injury, eye infections, osteomyelitis, respiratory infections after near-drowning, endocarditis, and sepsis. Few cases of central nervous system (CNS) infections have been described in the bibliography.[1–9]

The management of these infections is challenging because of the ability of *Aeromonas* to produce multiple beta-lactamases. Clinical studies have demonstrated differences in antimicrobial susceptibility among species, highlighting the importance of species identification and appropriate susceptibility testing.

The objective of this article is to describe an unusual and severe clinical presentation of infection due to *Aeromonas hydrophila* and to underline the importance of a correct microbiological diagnosis for an adequate antibiotic therapy.

CASE REPORT

This was a 6-year-old female patient seeking care 7 days after a craniotomy with duraplasty due to Chiari malformation. She attended the Emergency Department due to fever and drainage from the surgical wound for the past 24 hours. Upon admission, the surgical wound showed spontaneous drainage of serosanguineous fluid. The lab tests results were leukocytes: 9230/mm^3 (neutrophils: 54, eosinophils: 3, lymphocytes: 34, monocytes: 9); hemoglobin: 13.1 g/dL; platelets: 507 000/mm^3; C-reactive protein: 1.8 mg/L; erythrocyte sedimentation rate: 27 mm/h; blood glucose: 95 mg/dL. The computed tomography scan of the brain showed no relevant changes. The lumbar puncture results showed cloudy fluid; leukocytes: 91/mm^3; proteins: 89 mg/dL; glucose: 36 mg/dL. An empiric antibiotic therapy with vancomycin and ceftazidime was indicated. At 48 hours, the development of an oxidase-positive, glucose-fermenting Gram-negative bacillus (GNB) in cerebrospinal fluid (CSF) was reported. Blood cultures were negative. The antibiotic therapy was changed to meropenem. At 72 hours, using the Vitek 2 system and conventional typing tests, it was identified as *Aeromonas hydrophila* sensitive to trimethoprim-sulfamethoxazole (TMP/SMX), ciprofloxacin, cefotaxime, and meropenem. In addition, colorimetric (Blue-Carba) and phenotypic methods showed the presence of carbapenemase specific to the genus and species, so meropenem was discontinued and treatment was changed to TMP/SMX. A control lumbar puncture was performed with negative results. The patient completed 21 days of treatment with a favorable clinical course and no sequelae.

DISCUSSION

The species of the genus *Aeromonas* have been isolated from a variety of aquatic environments. The most frequent infections are gastrointestinal, with manifestations of gastroenteritis. Despite increased reports of extraintestinal infections, meningitis is an uncommon clinical entity.[1–9]

Meningitis can affect all age groups, it can be community- or hospital-acquired, and most patients have conditions predisposing to infection. In the first review of meningitis cases conducted by Parras et al.,[5] most corresponded to community-acquired cases with bacteremia; newborn infants or children with a history of hematological disease were the most affected groups.

Subsequently, new cases were reported in patients with no history of immunosuppression, blood dyscrasia or bacteremia. A review of the bibliography showed different mechanisms of entry to the CNS and a progressive increase of cases in immunocompetent individuals, such as our patient, who only had a history of a surgery that predisposed her to infection.

Cases of meningitis caused by *Aeromonas* have been associated with leech therapy for the reduction of edema in a skin flap,[2] surgical craniotomy,[8] and traumatic skull fracture.[9] The latter 2 were described in 3 adult patients in association with a solution of continuity as a gateway for the bacteria to enter the CNS. One case was secondary to a craniotomy for a traumatic subdural hematoma; it was attributed to the surgical procedure, and *Aeromonas hydrophila* was isolated in the CSF.[8] The other case had a cranial fracture with cephalohematoma, and *Aeromonas sobria* was isolated in the CSF.[9] Pampín et al,[3] described a patient with meningitis due to *Aeromonas hydrophila* in relation to a CSF fistula secondary to basilar skull fracture with direct exposure to standing water from a puddle.

Few cases have been described in pediatrics. Kali et al.,[6] described 7 cases. With the exception of a case of meningitis associated with ventriculoperitoneal shunt infection after

a myelomeningocele surgery, in the remaining cases, *Aeromonas* species were isolated in both CSF and blood. They were associated with sickle cell anemia, beta thalassemia, and hemoglobin E. Post-operative meningitis resulted from environmental pathogen entry during surgery. The role of water as a source of infection has also been documented, as in the case of meningitis described by Kumar et al.,[4] in an infant fed with supplemental formula without adequate hygiene measures.

Similar to what has been reported in other publications,[5,6] the source of infection in our patient has not been demonstrated. It is assumed that our patient developed a post-operative CSF fistula due to probable exposure to untreated tap water as per the family's account during history taking. It is also possible that the infection was associated with health care, considering the close history of hospitalization and surgery. However, surveillance cultures could not be performed from home water sources or the hospital setting to confirm this.

Aeromonas are oxidase-positive, motile, glucose-fermenting, facultative, anaerobic Gram-negative bacilli. The role of the microbiology laboratory is critical in the management of infection. The initial report of the development of oxidase-positive, glucose-fermenting Gram-negative bacilli rules out the presence of enterobacteria, which are oxidase-negative, and also implies distinguishing other oxidase-positive genuses, such as *Vibrio* and *Plesiomonas*, with simple tests such as susceptibility to O/129, tolerance to various levels of NaCl broth, and ability to ferment inositol.

Treatment is challenging. Most *Aeromonas* strains are resistant to penicillin, ampicillin, carbenicillin, and ticarcillin, and sensitive to TMP-SMX, fluoroquinolones, third-generation cephalosporins, aminoglycosides, carbapenems, and tetracyclines.[10] Susceptibility studies should be guided by the CLSI M45-A2 standard of 2010. Resistance to carbapenems is mainly due to the presence of carbapenem-hydrolyzing *Aeromonas* (CphA), which is an inducible chromosomal metallo-beta-lactamase (MBL) found in some *Aeromonas* species. This carbapenemase cannot always be evidenced in routine antibiograms and can lead to treatment failures. In the case described here, the initial report was a false result of susceptibility to carbapenems. The isolate was sensitive to carbapenems according to the diffusion method and the Vitek 2 system, but, when the Blue-Carba colorimetric method was performed, the presence of carbapenemase was reported, which was inhibited by ethylenediaminetetraacetic acid (EDTA). The genotypic investigation to confirm the type of MBL was not done. Some automated systems, such as those by BioMerieux Vitek, Inc., may not be reliable for the detection of beta-lactam resistance. Therefore, it is recommended to type at the species or complex level, and report as natural carbapenem resistance in species with CphA. The presence of this carbapenemase may also be studied in a complementary manner by a highly-sensitive phenotypic method, such as Blue-Carba test or Carba NP-Direct.[11,12] In addition, two other MBLs, VIM and IMP, have been detected in strains of *Aeromonas hydrophila* and *Aeromonas caviae*, encoded in an integron and a plasmid, respectively.[13,14]

An initial empiric therapy with a fluoroquinolone, third-generation cephalosporin or TMP-SMX would provide reasonable antimicrobial coverage. Given the variable pattern of resistance, some authors propose an empiric combination therapy in the face of severe infection. The guidelines by the Infectious Diseases Society of America suggest a combination of doxycycline plus ciprofloxacin or ceftriaxone for the treatment of severe necrotizing skin infections caused by *Aeromonas* spp.[15] Parras et al.[5] and Kali et al.[6] described children with meningitis with a favorable response to treatment with a third-generation cephalosporin or carbapenem in combination or not with aminoglycosides. However, there are no conclusive data to indicate that this combination therapy is more beneficial than monotherapy. Subsequently, the antibiotic regimen will be adjusted according to the antibiogram.

To conclude, when faced with a severe and unusual infection due to *Aeromonas hydrophila*, we emphasize the importance of a correct species or complex identification and the detection of its chromosomal MBL by complementary phenotypic methods beyond the carbapenem susceptibility values observed in the routine antibiograms. In view of their distinctive resistance pattern, antibiotic therapy, either empiric or targeted, should be used with caution. ■

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