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# Meningitis by a rare *Flavobacterium lindanitolerans* species – a case report

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***ABSTRACT:***

- ***Background:*** *Flavobacterium lindanitolerans*, a Gram-negative rod first isolated from soil samples in 2008, is an extremely rare human pathogen, with only a few reports of infection in humans. Here, we present the second case of meningitis caused by this species.
- ***Case Report:*** A 65-year-old male presented to the Emergency Room with a sudden onset of headache and posterior nasopharyngeal discharge. Computed tomography (CT) scan revealed a fistula in the anterior cranial fossa, resulting in pneumocephalus. The patient subsequently developed a fever and signs of meningism. A lumbar puncture was performed, and the cerebrospinal fluid (CSF) analysis demonstrated an increased leukocyte count, elevated protein levels, and the presence of Gram-negative rods. Bacterial meningitis was diagnosed, and the patient was started on empiric antibiotic therapy. Bacterial colonies were sent to a national reference laboratory for automated identification, which confirmed the species as *Flavobacterium lindanitolerans*.
- ***Conclusions:*** This is only the fourth reported case of F. lindanitolerans identified in human samples since its discovery. Our patient fully recovered after surgical correction of the anterior fossa fistula, which was considered as a possible route of bacterial entry, and a 14-day course of treatment with ceftriaxone. This case highlights the role of F. lindanitolerans as a potential infectious agent.
- ***Keywords:*** *Flavobacterium lindanitolerans*, Meningitis, Gram-negative, Cerebrospinal fluid fistula.
- ***List of Abbreviations:*** CSF – Cerebrospinal fluid; MIC – Minimal inhibitory concentration; CT – Computed tomography; MALDI-TOF – matrix-assisted laser desorption ionization-time of flight.

## INTRODUCTION

In 2008, a novel species, *Flavobacterium lindanitolerans*, was discovered in an Indian village, isolated from soil samples and taken from a highly contaminated waste site[1]. *F. lindanitolerans* is an extremely rare human pathogen, with only a few documented cases of infection in humans. The species was first isolated from a human sample in 2011, identified in an ascites fluid specimen from a Chinese child co-infected with the Enterovirus 71 (EV71)[2]. Since then, only two clinical reports[3,4] involving *F. lindanitolerans* have been documented, both in 2023. One was a case of meningoencephalitis with bacteremia in a splenectomized patient[3], and the other was post-operative endophthalmitis associated with *F. lindanitolerans*[4].

Determining whether a rare bacterial species is a true pathogen or merely a contaminant can be challenging. Case reports of such isolated species in different patients are crucial to clarify their pathogenic potential. Here, we present the second reported case of meningitis caused by *F. lindanitolerans*.

## CASE REPORT

A 65-year-old male patient was admitted to the emergency department of our hospital (ULSGE, Vila Nova de Gaia, Portugal) with a sudden onset of headache and posterior nasopharyngeal discharge. He was afebrile and had no other symptoms. His medical histo-



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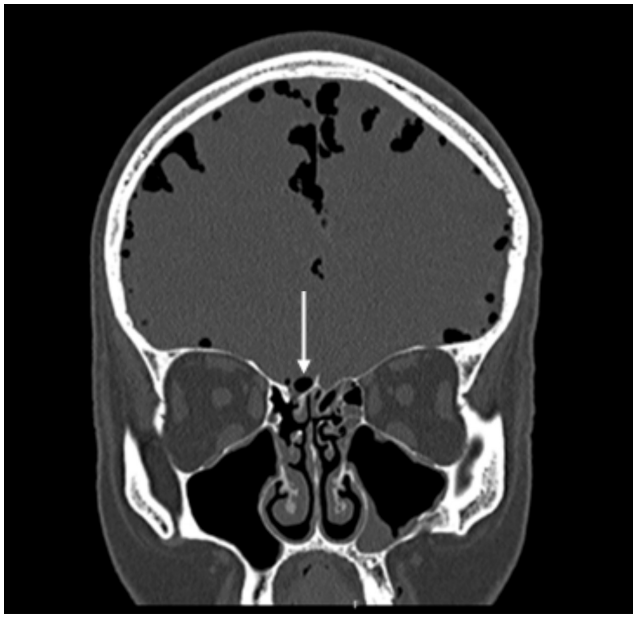

**Figure 1.** CT scan of the head showing a discontinuity on the right side of the ethmoid bone (white arrow).

ry included a past otorhinolaryngology surgery with undisclosed complications. A computed tomography (CT) scan of the head was performed, revealing a discontinuity (fistula) in the anterior cranial fossa caused by a defect in the right side of the ethmoid bone (Figure 1, white arrow). This fistula was leaking cerebrospinal fluid (CSF) into the nasopharynx and had caused extensive pneumocephalus, which was also evident on the CT scan.

Based on these findings, the patient was admitted to the Neurosurgery ward. On the second day of admission, he developed a fever and meningism. A lumbar puncture was performed, and the CSF was sent to the laboratory for cytological, biochemical and microbiological analysis. The CSF results revealed 289 leucocytes per µL (52% polymorphonuclear cells and 48% mononuclear cells), proteinorrachia of 95.9 mg/dL and a glucose level at the lower limit of normal. A Gram stain revealed Gram-negative rods. The complete blood count was normal, but he had a C-reactive protein level of 3.2 mg/dL (reference values: 0-0.5 mg/dL). Hence, the diagnosis of bacterial meningitis was established, and empirical antibiotic therapy with ceftriaxone at meningeal dosage (1 g IV q12 h for 14 days) was initiated.

To perform the cultural exam, the CSF was inoculated on three different growth mediums: Columbia blood agar, Columbia chocolate agar, and MacConkey agar. After a 24-hour incubation period at 37ºC, the agar plates were observed. Both the blood and the chocolate agar showed moderately sized mucoid colonies of a light yellowish color with flat surfaces and regular borders (Figure 2). This phenotype was not frequently observed in our clinical practice. The colonies were oxidase-positive.

Then, we proceeded to the automatic identification of the bacterial species in question by matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry with Vitek MS (bioMérieux, Marcy-L'Étoile, France), but it was unsuccessful. We then tried to identify the bacterial species by Vitek 2 (bioMérieux, Marcy-L'Étoile, France), using the idGN card, also without success. We informed the neurosurgery team that the bacteria was still pending identification and then sent the bacterial colonies to our national reference laboratory (Instituto Nacional de Saúde Dr. Ricardo Jorge). In the meantime, the patient underwent surgery for fistula correction, and a new head CT scan was performed, which showed no presence of the previous fistula and also no pneumocephalus.

The patient completed a 14-day course of ceftriaxone therapy, after which he was discharged due to full clinical and analytical improvement. Only a few days later, the final results of bacterial identification were obtained. The unknown colonies were identified as *F. lindanitolerans* by MALDI-TOF mass spectrometry with MALDI-TOF MS (Bruker Daltonics, Billerica, MA, USA).

Since we were unable to identify the species in advance and the patient was discharged after full recovery, our laboratory did not perform antibiotic susceptibility testing. It should also be noted that without documented clinical breakpoints, it would not have been easy to interpret such results.

## DISCUSSION

Community-acquired bacterial meningitis in adults is caused primarily by *Streptococcus pneumoniae* (53% of cases), followed by *Neisseria meningitidis* (27%), *Listeria monocytogenes* (4%) and *Haemophilus influenza* (3%)[5]. According to the 2016 ESCMID guideline[5] on diagnosis and treatment of acute bacterial meningitis, all other microorganisms account for about 13% of bacterial meningitis cases.

**Figure 2.** *Flavobacterium lindanitolerans* colonies on MacConkey agar.

*Flavobacterium spp* are widely distributed in nature, occurring mostly in aquatic ecosystems of freshwater or seawater, and are responsible for various fish infections[6]. There are only a few reports of *Flavobacterium spp* causing human disease, namely spontaneous bacterial peritonitis[7], pneumonia, and sepsis[8]. As to meningitis, there is only one report of *Flavobacterium*, specifically *F. ceti*, being isolated from the CSF of a patient who had neurosurgery due to a cerebral aneurysm[9].

The present case report is, to our knowledge, the fourth case of *F. lindanitolerans* isolated from a human clinical sample since its discovery in 2008. It is, therefore, a very rare human pathogen. Similar to the case report by Zuburchen et al[3], *F. lindanitolerans* grew on chocolate and blood agar but not in MacConkey, despite being a Gram-negative rod[3]. Moreover, the literature[3,4] shows that the *Flavobacterium* genus comprises oxidase-positive, Gram-negative rods – features we observed in our analysis of *F. lindanitolerans*.

Unlike that case report, our patient fully recovered while being treated with ceftriaxone in meningeal doses. As reported by Zuburchen et al[3], their patient first improved whilst being treated with ceftriaxone, amoxicillin, and acyclovir. Still, some symptoms persisted, which led to minimal inhibitory concentration (MIC) determination for various antibiotic groups, which showed a MIC of 32 mg/L for ceftriaxone and a very low MIC of 1.0 m/L for levofloxacin. Based on these results, they opted for a 21 days course of levofloxacin. In our case, however, the patient had a full recovery under ceftriaxone, which indicates that this antibiotic seemed to be an adequate choice for treating this *F. lindanitolerans* strain.

It is known that *F. lindanitolerans* is a bacteria found in contaminated soil[1]. The fact that this patient had a CSF fistula, i.e., physical communication between his nasal cavities and his skull, means that nasal aspiration could be a possible route of entry for such a pathogen to reach the CSF. Also, although they are rare, reports of this bacterial species as an actual pathogenic agent do exist, which consolidates our belief that *F. lindanitolerans* was, in fact, the causative agent of meningitis in this clinical case and not a mere contaminant.

## CONCLUSIONS

Finally, as the database of MALDI-TOF mass spectrometry increases, the recognition of new or rare bacterial species, such as *F. lindanitolerans,* improves. This allows for a more efficient diagnosis of infections caused by rare pathogens, thereby improving clinical outcomes.

**CONFLICT OF INTEREST:**
The authors declare that there are no competing interests.

**ETHICS APPROVAL:**
The Ethical Committee at ULSGE waived the ethical review and approval for this case report since it only reviews investigation projects, not case reports.

**INFORMED CONSENT:**
Written informed consent was obtained from the patient for participation and publication of this case report.

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All authors contributed equally to the conception and design of the study, acquisition, analysis and interpretation of data, drafting the article, making critical revisions related to the relevant intellectual content of the manuscript, supervision, validation and final approval of the version of the article to be published.

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**DATA AVAILABILITY:**
Data sharing does not apply to this article as no datasets were generated or analyzed during the current study.

**AI DISCLOSURE:**
No artificial intelligence (AI) or assisted technologies were used in the production or writing of this study.

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