# *Enterococcus faecalis*: an unusual cause of meningitis in a child with non-Hodgkin lymphoma

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**Enterococcal meningitis is an uncommon disease in children, most frequently reported in infants or in children with central nervous system pathology. We report a rare case of *Enterococcus faecalis* meningitis in an 11-year-old child with non-Hodgkin lymphoma. The patient during the course of chemotherapy became neutropenic, febrile, agitated, and disoriented with clinical signs of meningeal irritation. Culture of cerebrospinal fluid yielded *Enterococcus faecalis*. The patient was successfully treated with ampicillin without any neurological defects.**

***Key words: enterococcus, meningitis, non-Hodgkin lymphoma.***

Meningitis is an uncommon infectious complication in patients treated for malignancies. Enterococci are saprophytic inhabitants of the gastrointestinal tract[1]. Enterococcal meningitis is an uncommon disease, accounting for only 0.3% to 4% of cases of bacterial meningitis, but is nevertheless associated with a high mortality rate[2]. We report a rare case of *Enterococcus faecalis* meningitis in an 11-year-old child with non-Hodgkin lymphoma.

## Case Report

An 11-year-old boy with B-cell non-Hodgkin lymphoma of the terminal ileum with no bone marrow involvement or distant metastases was referred to our Department from the Pediatric Surgery Department six months after total surgical resection of the tumor. He started chemotherapy according to the NHL-BFM 90 protocol. The treatment consisted of cytoreductive chemotherapy followed by six 5-day courses of alternating chemotherapy courses A and B with a one-week interval between them. Course A included dexamethasone, ifosfamide for five days, 24-hour infusion methotrexate (MTX) and intrathecal MTX with cytarabine and hydrocortisone on the first day, and cytarabine and teniposide on the fourth and fifth days. In course B, cyclophosphamide was used instead of ifosfamide and only doxorubicin was used on the fourth and fifth days.

On the third day of the sixth course and two days after the intrathecal chemotherapy he became febrile (temperature 39.5°C), agitated and disoriented. At that time, the absolute neutrophil count was $<1x10^9$/L in the peripheral blood. Signs of meningismus (neck stiffness and Kernig sign) were evident on clinical examination. A lumbar puncture was performed and analysis of cerebrospinal fluid (CSF) revealed: white blood cell (WBC): 120 cells/mm$^3$ (75% neutrophils and 25% lymphocytes); glucose level: 15 mg/dl; and protein level: 64 mg/dl. CSF examination for ova and parasites was negative.

Pending the results of blood and CSF cultures, empiric treatment with ampicillin, ceftazidime and vancomycin was initiated taking into account the neutropenia, signs of meningeal irritation and the presence of central venous access device (Hickman catheter). Two days later, *Enterococcus faecalis* was isolated in CSF culture. The serial cultures of blood samples remained negative. The minimum inhibitory concentration (MIC) of ceftazidime was ≥8 μg/ml and was discontinued, while MIC of ampicillin

was ≤2 μg/ml and of vancomycin ≤1 μg/ml. The patient's clinical condition improved after two days. Intravenous antibiotic therapy with ampicillin was continued for a total of two weeks. During the antibiotic course, results of repeated analyses of CSF showed significant improvement and sterilization of CSF culture. The patient was discharged after completion of his chemotherapy. During a 12-month follow-up period he remains in good health without any neurological defects.

## Discussion

*Enterococcus faecalis* and *Enterococcus faecium* are the two most frequent species isolated during the course of enterococcal meningitis (76-90% and 9-10%, respectively)[3]. Two different clinical forms of meningitis, postoperative and spontaneous, are usually observed in clinical practice. Postoperative meningitis appears as a nosocomial infection usually associated with neurosurgical procedures and shunt devices. In children it has been most commonly reported in the setting of central nervous system (CNS) pathology such as neural tube defects, head trauma or hydrocephalus[4]. Spontaneous meningitis has been described in infants with diverse conditions such as prematurity, congenital heart disease or recent surgery as well in children with occult CNS malformations such as meningomyelocele or neuroenteric cysts[5]. In adults, it affects patients with severe underlying conditions such as cardiovascular or pulmonary disease, chronic renal failure, diabetes and immunosuppression due to corticosteroid or immunosuppressive therapy, malignancy and human immunodeficiency virus infection[6,7]. In the case presented herein, administration of intrathecal chemotherapy should be recognized as an important risk factor for enterococcal meningitis in the setting of myelosuppressive chemotherapy.

In the majority of adult cases, the usual presentation of enterococcal meningitis is rapid onset of fever, altered mental status, and signs of meningeal irritation. The clinical course of spontaneous meningitis in children is reported as atypical, because neonates account for the majority of patients and CNS symptoms in the clinical presentation of meningitis in the newborn are frequently absent. Incidence of severe complications such as septic shock, coagulopathy or coma is unusual in the course of enterococcal meningitis. In contrast, these severe complications are more common in the course of meningitis caused by more virulent microorganisms such as *Neisseria meningitidis, Streptococcus pneumoniae* or Gram-negative bacilli.

Ampicillin or penicillin is considered the standard therapy for most enterococcal infections since enterococci are classically sensitive to cell wall-active antibiotics such as beta-lactams. Combinations of cell wall-active antibiotics and aminoglycosides such as gentamicin or streptomycin have been shown to have synergistic bactericidal activity and are effective against enterococci, especially in severe infections such as meningitis[8]. Glycopeptides such as vancomycin should be reserved for patients allergic to penicillin or penicillin-resistant strains[2].

In recent years, increasing rates of vancomycin-resistant enterococci (VRE) have been documented in many hospitals[9]. Many of these organisms are multidrug-resistant, making the treatment of VRE a great challenge. VRE are opportunistic pathogens in the hospital environment that are maintained by the selective pressure of widespread use of broad-spectrum antimicrobial drugs. The US Food and Drug Administration (FDA) has recently approved antimicrobial agents with activity against VRE, such as linezolid and quinupristin/dalfopristin. Linezolid is an oxazolidinone antibiotic bacteriostatic against enterococci and with a good CSF penetration. Quinupristin/dalfopristin, a new streptogramin antibiotic, is bacteriostatic against enterococci, and has been used for therapy in severe VRE infections. Unfortunately, resistance to quinupristin/dalfopristin and linezolid is already being reported, and there are few new drugs in development to replace them[10,11]. Taking into account the increasing rates of drug resistance among bacterial pathogens and the limited development of new antibiotics, several factors should be addressed. Among them is the judicious use of broad-spectrum antibiotics along with the strict adherence to infection control practices, which include hand hygiene, barrier isolation precautions, and continuous surveillance of VRE, in order to avoid its progressive dissemination in the hospital environment[12,13].

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