Listeria monocytogenes: a rare complication of Ventriculo-peritoneal shunt in children

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Running title: Ventriculo-peritoneal shunt listeriosis

Key words: Listeria monocytogenes, Real-Time PCR hly-gene, ventriculo-peritoneal shunt
infection, peritonitis, ventriculitis
We report a case of ventricular-peritoneal shunt infection in a 3-year old boy caused by the food-borne pathogen, *Listeria monocytogenes*, subsequent to acute peritonitis. This unusual presentation of CNS-listeriosis underlines the ability of the bacteria to form and survive within biofilms on indwelling medical devices. Bacterial persistence may lead to treatment failure and spreading. We highlight the helpfulness of specific quantitative real-time PCR-hly for the diagnosis and the follow-up of such infection detecting bacterial persistence within medical device despite effective antibiotic treatment. Only the surgical replacement of the VP-shunt will resolve the infection.
Introduction

Hydrocephalus is excessive accumulation of cerebrospinal fluid within the cranium in children. If persistent and progressive, ventriculo-peritoneal (VP) shunt insertion may divert excess of cerebro-spinal fluid (CSF) from the ventricular system into the peritoneal cavity throughout a tube and two catheters inserted at the proximal and the distal ends. (13, 16, 17).

Complications of this indwelling device mainly concern shunt-malfunctions frequently in relation with shunt-infections (13, 16, 17). Central-nervous system (CNS) infections like meningitis, ventriculitis, and brain abscesses may occur starting from cutaneous contamination secondary to the insertion time or all the subsequent manipulations of the proximal or distal catheters (14, 16, 18). Although rare, peritonitis constitutes another complication of VP-shunt (18).

To date, *Listeria monocytogenes* has never been reported as related to VP-shunt infection in children. We describe a case of acute peritonitis in a 3-year old boy caused by this food-borne pathogen, secondary complicated by CNS-infection. We discuss the value of the quantitative real-time PCR on *hly*-gene (Le Monnier et al., manuscript submitted for publication) for the diagnosis and monitoring of this unusual presentation of CNS-listeriosis.

Case report

A 3-year old boy, with antecedent of premature birth and hydrocephalus controlled by a ventriculo-peritoneal (VP) shunt, was admitted to the pediatric emergency department for headaches, abdominal pains, and fever. The clinical signs appeared five days ago, following a stay in Portugal (D -15, Fig. 1). He was rapidly transferred to the infantile neurosurgery department in charge with his follow-up in our hospital. At admission, the physical
examination revealed a temperature of 39°C and an inflammatory aspect along the abdominal scar corresponding to the valve of the VP-shunt, but with no collection. The abdomen was red. The neurological examination did not show any perturbation and the functional controls of the VP-shunt concluded to a permeable and clean system. The intracranial pressure was normal and the hydrocephaly well equilibrated. The biological investigations revealed no inflammation signs and the microbiological cultures of blood, CSF and local samples along the inflammatory tract of the VP-shunt were sterile. Abdominal echography and X-ray CT did not confirm the suspicion of VP-shunt related infection. Then, after five days of hospitalization, the child was discharged home with a symptomatologic treatment for the abdominal pains. A follow-up was programmed a few days after. During, this period, oral 3rd generation cephalosporin was prescribed by the general practitioner for eight days for otitis with no microbiological documentation.

Fifteen days after this first admission, the child was admitted again to the pediatric emergency department for relapsing clinical presentation based on headaches, moderate fever at 38.5°C and asymmetric abdominal pains predominantly on the right hand without transit trouble (D0, Fig. 1). No neurological signs were observed, confirmed by the X-ray CT. CSF cytology and culture ruled out meningitis. However, the abdomen was red. The abdominal scar and the distal part of the VP-shunt tract were inflammatory. Abdominal echography confirmed an hyperechogenic transcutaneous tract of the VP-shunt and revealed ascitis in the right iliac pit but with no argument for an acute appendicitis. The cliche of abdomen without preparation showed a stercoral stasis with no sign of occlusion or small intestine distension. The biology revealed an important inflammatory syndrome with 18,000 white blood cells/ml, predominantly polymorphonuclear cells (58%), and an increased level of C-reactive protein (CRP) up to 48 mg/L. Systemic antibiotics were given associating metronidazole, cefotaxime
and gentamicin. The child was transferred to the infantile neurosurgery department where the peritoneal catheter was exteriorized and sent for microbiological culture. At the proximal end, the indwelling device was modified and reduced to a catheter of external derivation to drain the excess of infected CSF. However, ascitis was spontaneously reabsorbed before the programmed puncture.

One day after the second admission (D1, Fig. 1), the child worsened becoming algic, asthenic with a temperature at 40°C. The X-ray CT carried out at D2, showed ventricular dilatation and increased intracranial pressure evocating of CNS-infection complicating the peritoneal infection. Quantitative culture of the peritoneal catheter retrieved $1 \times 10^3$ *L. monocytogenes* /ml. Ventricular-CSF directly collected at D0 and D2 through the catheter of the external derivation also yielded *L. monocytogenes* by culture. However, CSF collected at D2 by lumbar puncture was sterile by culture but weakly positive using the quantitative real-time PCR on hly-gene (PCR-hly) previously described (Le Monnier et al., manuscript submitted for publication). The complete infectious assessment highlighted a specific anti-Listeria seroconversion reaching the level of 800 UI, characteristic of an evolutive infection (1). All blood cultures collected at this time remained sterile ruling out a hematogenous spreading of *L. monocytogenes*. The antibiotherapy was switched at D3 for amoxicillin (900 mg/day/x4), gentamicin (40 mg/day/x1), and cotrimoxazole (125 mg/day/x2) according to the results of the susceptibility to antibiotics.

At D4, the neurological perturbations worsened combining clinical and biological signs of meningitis despite effective antibiotic treatment. The general state of the child also worsened (D4, Fig. 1). Culture and PCR-hly performed on CSF collected via the catheter of derivation still retrieved high and increasing inoculums of bacteria about $1 \times 10^5$ *L. monocytogenes*/ml.
Specific researches failed to retrieve *Listeria* in feces. This ruled out the hypothesis of persistent bacteria in the digestive tract. Several negative blood cultures ruled out the hypothesis of a persistent circulation of bacteria in the bloodstream. Regarding the persistence of neurological perturbations and the unusual delay for sterilizing the material device, another intervention was programmed at day 7. After endoscopic ablation of free ventricular catheter and replacement by a temporary external derivation, it was processed to a ventriculocisternostomy. CSF collected through the first derivation before intervention still retrieved *L. monocytogenes* DNA by PCR-hly whereas culture remained sterile. The ventricular catheter was sterile with standard cultures but positive by PCR-hly. CSF collected by ventricular puncture during the intervention and those collected through the new external derivation whether at the end of the intervention or later did not detect *L. monocytogenes* neither in culture nor by PCR-hly.

With both accurate treatment and by removing all colonized medical devices, we observed a significant clinical improvement (D8, Fig. 1). All the clinical signs regressed quickly, hydrocephaly became well equilibrated. Afterwards, the unused external derivation was removed at D14 and remained sterile in culture and no *L. monocytogenes* DNA was retrieved by PCR-hly. The child was discharged home at D20 under amoxicillin orally administrated for a total of four weeks.
Complications of ventriculo-peritoneal shunt insertion are usually life-threatening. They consist of mechanical failures, shunt blockage or infections (13, 16). Ventriculo-peritoneal shunt infections in pediatric populations are a recurrent problem with a reported incidence of 5 to 15%, leading to CNS-infection such as meningitis, ventriculitis, and brain abscesses (2, 4, 10, 14, 17, 18). The physiopathologic processes mainly incriminate bacteria of cutaneous flora like *Staphylococcus epidermidis* (40%) and *S. aureus* (20%) and occur within a median of 19 days after shunt insertions (4, 8, 10, 16, 18). Although less frequent, other microorganisms, especially those that cause spontaneous peritonitis (*Streptococci, Enterococci,* Gram-negative bacteria, and anaerobes) could be involved because of weakening peritoneum with long-time peritoneal catheterization (6, 16, 18).

*L. monocytogenes* is already reported to be an unusual agent of spontaneous peritonitis. A review of literature retrieved at least 36 cases of spontaneous bacterial peritonitis caused by *L. monocytogenes* (9, 12, 15). First-line treatment of peritonitis is currently based on third-generation cephalosporins and metronidazole irrespective of some causal agents such *L. monocytogenes* and *Enterococci* (9). These rarer etiological pathogens should be discussed and included in case of first-line treatment failure by associating aminopenicillin to 3rd generation cephalosporin (12). However, to the best of our knowledge, such atypical presentation of *L. monocytogenes* peritonitis, complicated by CNS-listeriosis in ventriculo-peritoneal shunt, have never been described in children and rarely in adults (3, 19).

*Listeria monocytogenes* is a food-borne pathogen, widely found in the environment, that causes severe and life-threatening infections in both human and a large variety of animal species (5). Listeriosis mainly concerns groups at risk including elderly, patients with impaired cell-mediated immunity or underlying diseases (5). However, listeriosis is exceptional in children except in neonates. Such infections result in septicemia, abortions in...
the event of pregnancy, and meningo-encephalitis due to the Central-nervous system (CNS) tropism of the bacteria (11). Then, bacteria can be isolated either in blood cultures and CSF.

However, listeriosis can also occur in less characteristic situations. Although being rare, it is brought back in cases of focal infection, gastroenteritis and medical devicerelated infection for which diagnosis can be difficult. The clinical history of the case reported here began by an abdominal syndrome following a stay in Portugal and may be related to the consumption of ewe raw milk cheese. However, it was difficult to formally prove this mode of contamination at a distance from the initial episode.

Moreover, this observation underlines the ability of *L. monocytogenes* to form and persist within biofilms, especially in the tubes of medical devices such as shunt derivation (3, 19). This faculty, also observed in the food industry, constitutes a problem for the eradication of *L. monocytogenes* despite adapted antibiotic treatment (7). This clearly raises the indication for the withdrawal of material devices during the management of such infections. The outcome of the child was rapidly favorable since the withdrawal of the last external derivation catheters, colonized by high inoculums of bacteria, was complementary to effective antibiotic treatment.

The chronological analysis of the result of standard microbiological cultures and the quantitative results of *hly*-gene amplification, together with the succession of clinical presentation, allowed us to clarify the infectious process. *L. monocytogenes* caused first by a spontaneous peritonitis that conducted to local infection of the distal VP-shunt catheter. Quantitative results of PCR-*hly* highlighted differences in the quantity of *L. monocytogenes* DNA retrieved between ventricular CSF collected through catheter device and CSF collected by lumbar puncture. These results suggested the retrograde ascendant colonization of the proximal catheter, inserted in the cerebral ventricle, starting from the peritoneal cavity and following the subcutaneous VP-shunt device. This colonization then led to CNS-infection.
Sterile blood cultures reinforced this hypothesis excluding a haematogenous route of infection that is classically described for CNS-listeriosis (11).

Quantitative real-time PCR on hly-gene is a powerful tool complementary to standard microbiological culture for rapid and specific diagnosis of *L. monocytogenes* infections (Le Monnier et al., manuscript submitted for publication). In some cases, it compensates the lack of sensitivity of culture because previous antibiotic regimen was given or because of the presence of a low number of viable bacteria in the CSF explained by restricted localization of the bacteria to the brain stem or within material devices as described for this patient.

Moreover, quantitative PCR-hly was a relevant test helpful for clarifying pathophysiological processes leading to CNS-infection, tracing back the contamination route of this atypical presentation of listeriosis. PCR-hly was helpful in the monitoring of the patient by early detection of an increasing rate of *L. monocytogenes* DNA highlighting the persistence of a reservoir of bacteria on medical devices, despite antibiotic treatment and bacterial culture of CSF remain sterile.
REFERENCES


FIG. 1: Chronologic presentation of the microbiologic investigations (culture and PCR-hly), management (intervention and antibiotic treatment) according to clinical presentation.

Consecutive periods of clinical presentations: 1) Gastrointestinal disorders; 2) Gastrointestinal disorders and peritonitis; 3) Neurological perturbations; 4) Deterioration of the general state; 5) General improvement.

Lm: *Listeria monocytogenes*; CSF: cerebrospinal fluid; PCR +: amplification of *Listeria monocytogenes* DNA by PCR-hly; PCR Neg: negative result of PCR-hly.