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Gram-Positive Rods on a Cerebrospinal Fluid Gram Stain

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Cerebrospinal fluid (CSF) access device placement in the pediatric population presents challenges due to the development of infections following placement, access or revision, and/or shunt malfunctions. Here we report an unusual pediatric case of *L. monocytogenes* ventriculitis/VP shunt (VPS) infection and associated pseudocyst with an emphasis on the importance of VPS removal in clearing the infection due to biofilm formation.

Keywords. CNS infection; Gram-positive rod; *Listeria monocytogenes*.

A 3-year-old male with a history of VP shunt (VPS)–dependent hydrocephalus of unknown etiology presented with fever and abdominal distension. Two weeks before presentation, he had been ill with nonbloody, nonbilious vomiting for 1 day and tactile fever for 4 days. Over the following week, he clinically improved but his appetite remained poor. He presented to our emergency department after having 2 days of progressively worsening abdominal distension and pain. His medical history was significant for communicating hydrocephalus diagnosed at 4 months of age in Uganda, where he was born to parents who were refugees from the Democratic Republic of Congo. A right-sided VPS was placed at 8 months of age without subsequent revisions or access. He migrated to the United States at 19 months of age. He was diagnosed with pulmonary tuberculosis at 20 months of age and treated, under direct observation, with rifampin, isoniazid, pyrazinamide, ethambutol (RIPE) and pyridoxine. His immunizations were up to date without associated adverse reactions, and he tested negative for human immunodeficiency virus. His CD4+ and CD8+ T-cell counts were within normal limits for his age, at 1203 cells/uL and 643 cells/uL, respectively. Similarly, his CD19+ B (597 cells/uL) and NK cells (260 cells/uL) were within normal limits.

The family denied any local or foreign travel since immigrating to the United States, foreign visitors, or animal exposures. He did not ingest unpasteurized milk or cheese, cold cuts, or raw or undercooked meat, but he ate vegetables from the local supermarket. He had a diffusely tender abdomen with distension, hypoactive bowel sounds, and guarding on examination. His peripheral leukocyte count was 7.2 thou/mL, his hemoglobin was 11.8 g/dL, and his platelet count was 637 thou/mL. He had hyponatremia (129 mmol/L) and hypoalbuminemia (2.8 mg/dL), but the rest of his complete metabolic panel was unremarkable. His C-reactive protein was elevated at 18.1 mg/dL. Abdominal ultrasound revealed a large, multiloculated, septated cystic lesion encompassing part of the shunt catheter including the tip, consistent with a CSF pseudocyst (Figure 1). Computed tomography of the head showed stable ventriculomegaly compared with previous imaging. We externalized the lower portion of his VPS, drained the pseudocyst, and sent the fluid for culture. His ventricular fluid was straw colored, with a leukocyte count elevated to 585/UL with 23.3% neutrophils, 28% lymphocytes, 45% monocytes/macrophages, and 3.7% atypical/reactive lymphocytes. His ventricular fluid glucose was 37 mg/dL, and his protein was 60 mg/dL. A lumbar aspiration was not performed.

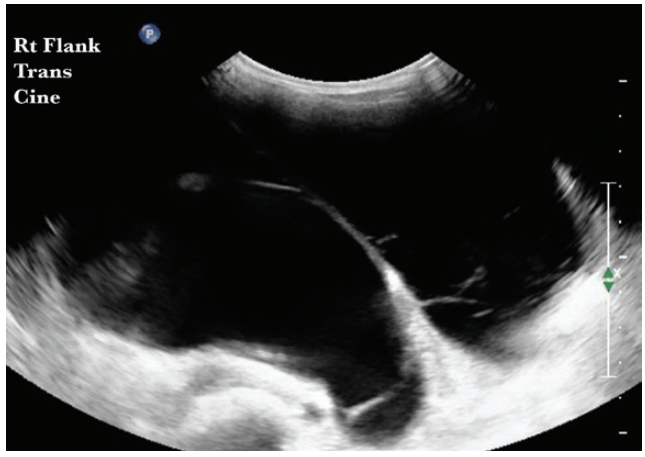

Figure 1. Abdominal ultrasound showing CSF pseudocyst.

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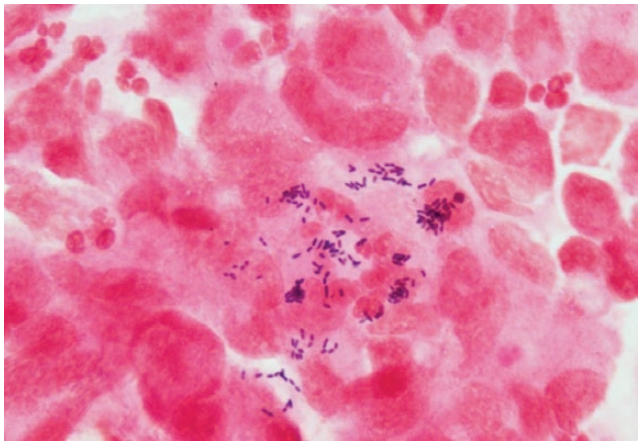

Figure 2. Cytospin-prepared Gram stain of the patient's cerebrospinal fluid with Gram-positive rods in the CSF later identified as *L. monocytogenes* (original magnification, ×1000).

He was empirically treated with parenteral vancomycin 20 mg/kg every 8 hours and ceftriaxone 100 mg/kg every 24 hours. A blood culture was not obtained prior to initiating antibiotics. We observed short Gram-positive rods in the CSF (Figure 2), and added ampicillin 75 mg/kg every 6 hours to the regimen. The ventricular and abdominal pseudocyst fluid cultures grew *L. monocytogenes* on blood and chocolate agar plates within 24 hours. Susceptibility testing was performed using the MicroScan Pos Combo 33 Panel and interpreted with CLSI M45-A2 guidelines, which demonstrated that both isolates were susceptible to ampicillin and penicillin. We discontinued vancomycin and ceftriaxone and removed the entire right-sided VPS, with temporary placement of an external ventricular drain (EVD). After 7 days of therapy, we placed a new VPS on the left side. He received a total of 3 weeks of parenteral ampicillin. Due to rapid sterilization of cultures after initiation of ampicillin and clinical improvement, we did not initiate intraventricular antibiotics. At the follow-up appointment 10 days after hospital discharge and after completion of his antibiotic course, he had no residual symptoms.

Cerebrospinal fluid (CSF) access devices may be complicated by infection and/or mechanical shunt malfunction [1]. The organisms associated with CSF access device infection are frequently biofilm producers and require shunt removal for resolution of the infection [2]. *Listeria* spp. VPS infection is extremely rare and has only been briefly described in the literature (Table 1) [3–5]. We suspect that our patient had undiagnosed listeriosis and seeded his VPS hematogenously.

L. monocytogenes creates and survives within biofilms on implanted medical devices [3]. Ampicillin and penicillin remain the preferred therapeutic agents, with a duration of at least 3 weeks of therapy and removal of the infected device [3, 6]. There is no consensus on the duration of time that must elapse prior to VPS replacement with *Listeria* spp. infection, though Infectious Disease Society of America guidelines recommend a waiting period of 2–10 days based on the organism, CSF cell count, chemistry, and cultures [6]. If an infection does not respond well to systemic antibiotics, intraventricular therapy should be considered [6]. In the event of penicillin allergy or other contraindication,

Table 1. Features of Reported Cases of *Listeria* spp. VPS Infection

Reference, Year	Age	Country	CSF Parameters/ Neuroimaging	Diagnosis	Treatment and Duration	Surgical Intervention	Outcome
Karli, 2014	9 mo	Turkey	WBC 480/mm^3, protein 46 mg/dL, glucose 35 mg/dL/ not reported	CSF and ascites fluid cultures with *Listeria innocua*	CRO → AMP, GEN, CRO → AMP, GEN, MEM Duration: AMP: 3 wk MEM/GEN: 2 wk	Day 4: VPS removal and EVD placement Day 20: EVD removal and VPS replacement	Survived
Le Monnier, 2011	3 y	France	Reported as normal/ ventricular dilatation	Ventricular fluid and peritoneal catheter cultures with *Listeria monocytogenes,* quantitative real-time PCR for *hly* gene	CFM → CTX, GEN, MTZ → AMX, GEN, SXT → AMX Duration: AMX: 4 wk	Day 0: peritoneal catheter removal Day 7: ventricular catheter removal and EVD placement Day 14: EVD removal	Survived
Dominguez, 1994	65 y	USA	WBC 471/mm^3, protein 55 mg/dL, glucose 25 mg/dL/ moderate hydrocephalus without edema → Severe obstructive hydrocephalus with right frontal hypo dense lesion	CSF, blood, and shunt tubing cultures with *Listeria monocytogenes*	CFZ → SXT (PCN allergy) Duration: SXT: 3 wk	Day 0: VPS removal and EVD placement Day 8: EVD removal and VPS replacement	Survived

Abbreviations: AMP, ampicillin; AMX, amoxicillin; CRO, ceftriaxone; CFM, cefixime; CTX, cefotaxime; CFZ, cefazolin; GEN, gentamicin; MEM, meropenem; MTZ, metronidazole; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

trimethoprim-sulfamethoxazole and fluoroquinolones may be used following susceptibility testing. Studies have shown that levofloxacin and moxifloxacin are rapidly bactericidal and achieve effective central nervous system concentrations in vitro and in animal models [7–9].

Biofilms are comprised of microorganisms embedded within an extracellular polymeric matrix that they produce [10–12]. They contribute to the development of chronic infections, particularly when an indwelling foreign body is present due to poor antibiotic penetration in biofilms and deactivation of antibiotics by some biofilm components. This results in higher minimum inhibitory concentrations [10]. As such, *Listeria* spp. infections of medical implants are challenging to treat and require removal of the infected device or prolonged suppressive therapy if it cannot be removed [13–15]. *Listeria* spp. VPS infection is rare but should be considered along with *Propionibacterium* spp., *Bacillus* spp., *Corynebacterium* spp., and *Mycobacteria* spp., with adjustment of the empiric therapeutic regimen if Gram-positive rods are observed in the CSF. In addition, the infected shunt should be removed.

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