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Spontaneous spondylodiscitis and epidural abscess due to Listeria monocytogenes in a middle-aged patient with gentamicin related side effects: A case report and a review of literature

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ABSTRACT

Introduction: Primary spondylodiscitis due to *Listeria monocytogenes* (LM) is a rare condition.
Research question: We present a case of spontaneous LM spondylodiscitis with an epidural abscess in a middle-aged man, who reported no gastrointestinal infection.
Material and methods: We identified 5 spinal infection cases due to LM in the literature, with 3 diagnosed as primary spondylodiscitis.
Results: The patient was treated with surgical decompression, debridement, and antibiotic therapy. Blood cultures remained negative throughout the case and microbiological cultures were obtained during surgery. The patient developed side-effects of prolonged gentamicin therapy but made a recovery from his spinal complaints at 6-months follow-up. Listeriosis is a relatively rare food-borne disease with a wide spectrum of presentation. Surgeons should consider more aggressive therapy for spinal infections and recognize the uncommon manifestations. We identified 3 primary and 2 secondary LM spondylodiscitis cases in the literature. Antibacterial treatment of LM spondylodiscitis varied in agents and duration, but no side-effects were previously reported. Gentamicin treatment requires care and attention to complications.
Discussion and conclusion: Listeria monocytogenes is a rare cause of primary spondylodiscitis. Further studies are needed to establish a safe treatment protocol for treatment with gentamicin and LM spondylodiscitis.

1. Introduction

Listeria monocytogenes (LM) is an aerobic and facultatively anaerobic gram-positive rod. LM causes primarily invasive disease, including central nervous system infection, bacteremia, or febrile gastroenteritis. Invasive LM infections occur more often in neonates, pregnant women, elderly and immunocompromised patients (Radoshevich and Cossart, 2018). Mortality of LM infection remains high and is around 20–30% (de Noordhout et al., 2014).

LM can also lead to soft tissue and joint infections (Diaz-Dilernia et al., 2019). Primary spondylodiscitis due to LM is a rare condition. We identified 5 spinal infection cases due to LM in the literature, with 3 diagnosed as primary spondylodiscitis.

We describe a case of spontaneous LM spondylodiscitis with an epidural abscess in a middle-aged man treated with surgical decompression, debridement, and antibiotic therapy.

2. Case

A 55-year-old male presented to the hospital with severe lumbar pain that was irradiating to both legs. The patient's medical history included type 2 diabetes, ocular myasthenia, hypertension, atrial fibrillation, and gastroesophageal reflux disease. His regular medications were bisoprolol 10 mg q.d., amiodarone 200 mg q.d., atorvastatin/perindopril/amlodipine 20/10/5 mg q.d., metformin 850 mg b.i.d., pantoprazole 40 mg q.d., pyridostigmine 180 mg b.i.d. The patient worked as a cruise ship repairman. He traveled frequently and recently visited Singapore and Bahamas.

Three weeks prior to hospitalization the patient tripped and fell on his back. The next morning, he woke up with a strong back pain that was

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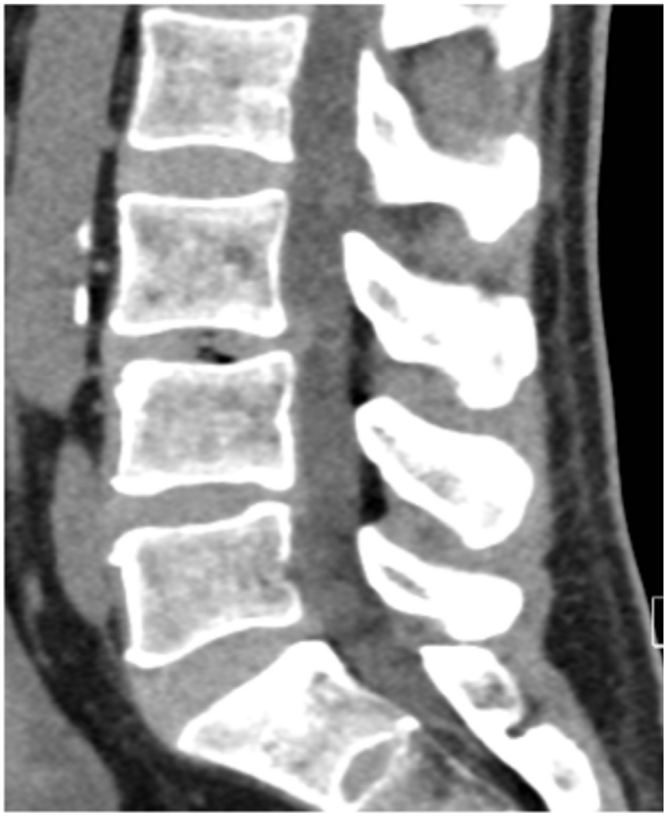

Fig. 1. CT scan of L3-L4 and L4-L5 discs with signs of degeneration and protrusions.

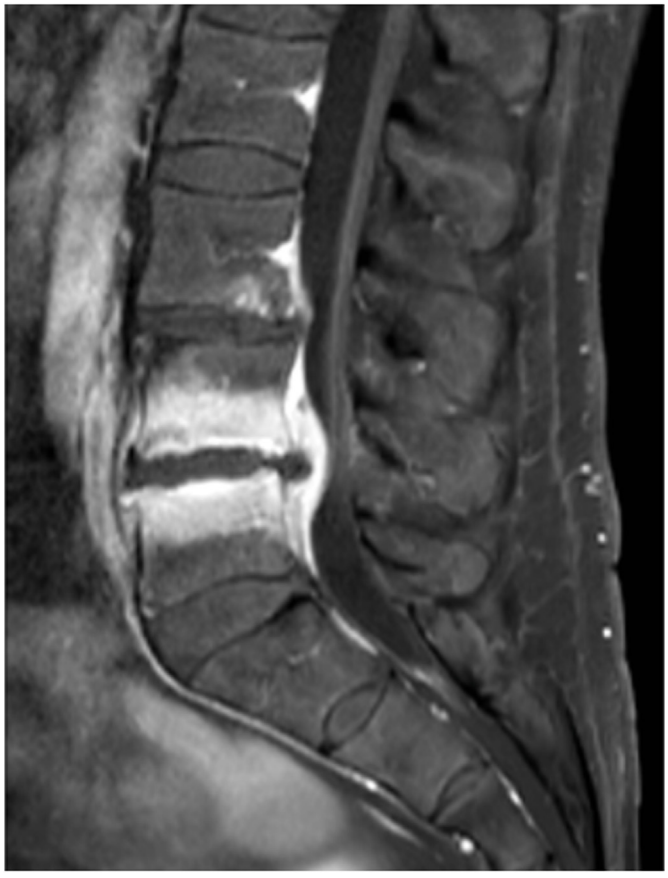

Fig. 2. MRI with gadolinium contrast of spondylodiscitis at L4-L5 level, a forming epidural abscess causing dural sac compression at the same level, and contrast enhancement of L3, L4 and L5 vertebral bodies.

irradiating to the legs. The patient felt that his right leg was more painful and weaker. He turned to the emergency department, where a computed tomography (CT) scan was performed. The CT scan showed L3-L4 disc degeneration, L4-L5 disc protrusion and no spinal fracture or other bony changes (Fig. 1). The patient was prescribed pain medications and discharged home. No blood analysis was performed. Two days later he became febrile and bedridden due to backpain. Three weeks after his fall he was seen by a neurosurgeon in the outpatient department. The patient reported a backpain of VAS 10 (visual analog scale) with severe cramps in his paraspinal and thigh muscles. The patient could not walk without assistance and was able to actively raise his straight legs to only 15°. Distally his leg strength was moderate. Hypoesthesia was localized to L4 and L5 dermatomes in the right leg. Lasègue test was positive at 5° on both sides. Muscle strength and reflex tests were hard to interpret due to severe pain and muscle cramps. On hospitalization the patient did not have any fever. Blood tests showed a total white cell count of 10.7×10^9/L with normal neutrophil count (67%), C-reactive protein level of 14 mg/L and sedimentation rate of 82 mm/h. An emergency MRI revealed spondylodiscitis at L4-L5 level with an epidural abscess causing dural sac compression, contrast enhancement of L3, L4 and L5 vertebral bodies, and abscesses in the paraspinal muscles (Fig. 2). Echocardiography findings showed no pathology. No other infection sites were identified. The patient had no history of gastrointenstinal infection during the recent year.

On admission, empiric antibacterial therapy was started, after blood cultures, with intravenous oxacillin 2 g every 4 h. The next day the patient was operated due to severe pain and neurologic deficit. Laminotomy at L4-L5 level was performed with decompression of the dural sac, drainage of epidural abscess, and debridement of the disc space. After surgery complaints improved and VAS decreased to 6. Microbiological cultures obtained during surgery returned positive for *Listeria monocytogenes*. Blood cultures remained negative. Antibiotic treatment was changed to ampicillin 2 g every 4 h combined with gentamicin 320 mg once daily intravenously (dose later increased to 400 mg once daily

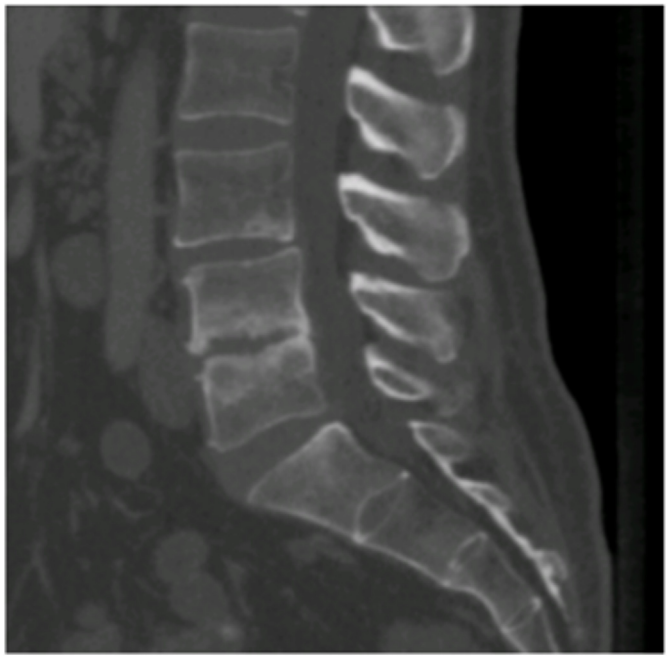

Fig. 3. Follow-up CT scan at 9-months after treatment showing with signs of fusion.

Table 1
Review of previous *Listeria monocytogenes* spondylodiscitis.

Author	Age, gender	Comorbidities	Others infection	Location	Diagnosis	Treatment	Complications
Duarte et al., 2018 (Duarte et al., 2019)	65, male	Diabetes	Perianal abscess	L5, sacrum	Perianal abscess cultures	ceftriaxone (2 g/day), ampicillin 2 g q.i.d. 2 weeks, oral amoxicillin 1 g q.i.d. 3 months	not reported
Hasan et al., 2017 (Hasan et al., 2017)	63, male	not reported	Bioprosthetic aortic valve endocarditis, bacteraemia	L4/5	Blood cultures	benzylpenicillin 14.4 g/day 6 weeks and rifampicin 300mg b.i.d. 4 weeks, amoxicillin 1 g t.i.d. 18 weeks	not reported
Aubin et al., 2016 (Aubin et al., 2016)	92, male	not reported	Bacteremia	L3-L4, L4-L5 and L5-S1	Blood cultures	amoxicillin 200 mg/kg/day 6 days, gentamicin 5 mg/kg/day for 6 days, trimethoprim sulfamethoxazole (30 mg/kg of sulfamethoxazole daily)	not reported
Khan et al., 2001 (Khan et al., 2001)	69, male	not reported	not reported	L5/S1	Epidural abscess cultures	ampicillin and gentamicin	not reported
Chirgwin and Gleich, 1989 (Chirgwin and Gleich, 1989)	57, male	diabetes, asthma	not reported	T5	Bone tissue cultures	cefamandole, ampicillin 12 g/day and tobramycin for 6 weeks	not reported

according to blood concentration levels). Histologic material from the disc space was described as necrotic hyaline cartilage tissue with inflammation.

After 3 weeks of combined antibacterial treatment the patient developed imbalance and oscillopsia that were attributed to gentamicin ototoxicity. The patient exhibited moderate bilateral hearing loss, which could be related to history of diabetes and working in a loud environment. No previous studies were available for comparison. Antibacterial treatment was switched to intravenous trimethoprim-sulfamethoxazole (TMP/SMX) for 5 days, and then to meropenem until discharge. During hospitalization, the patient remained on bed rest. The patient was discharged home after 38 days of intravenous antibacterial treatment at which point his CRV was 1 mg/L, WBC 7.1 $\times$ 10^9/L and SR 18 mm/h. After discharge, he continued oral TMP/SMX 960 mg every 8 h for a duration of 4 weeks. At 2 months the follow-up MRI showed a resolution of the epidural compression, but residual contrast enhancement partially remained, as would be expected in the recovery phase after spondylodiscitis. A CT scan was performed at 9-months after surgery (Fig. 3).

Bilateral vestibular dysfunction was found on videonystagmography with caloric reflex testing. Patient received 2 courses of rehabilitation focused on ambulation, balance problems and backpain. At 6-month follow-up, he had recovered significantly from backpain. Most problematic complaint remained to be periodic imbalance. Patient continued with vestibular rehabilitation therapy. He received a hearing aid which had a positive effect.

3. Discussion

Listeriosis is a relatively rare and serious food-borne disease. Increasing numbers of listeriosis have been reported in the EU/EEA countries since 2009. In Estonia, an increasing rate of listeriosis has been observed since 2018 (2.05 cases per 100 000 population) (The European Union One Health, 2019). Listeriosis has a wide spectrum of clinical presentation. Therefore, clinicians should consider and recognize the uncommon manifestations of the disease.

Patients with back pain presenting to the emergency department require a comprehensive checkup for various conditions including blood analysis and MRI in cases of possible spinal infections. Delayed diagnosis of spondylodiscitis still remains common and leads to increased morbidity (Lener et al., 2018). Our patients case history is complicated by the preceding trauma. Spondydiscitis due to uncommon agents, including LM, might be underdiagnosed without microbiological confirmation. The patient's blood cultures remained negative throughout the case and a causative microorganism was confirmed only from tissues obtained during surgery.

We performed a literature review and found 5 cases of spondylodiscitis due to LM (Table 1). All patients described in the literature are male. In our case a predisposing factor for the infection was diabetes, which was reported in 2 other patients (Duarte et al., 2019; Chirgwin and Gleich, 1989). Diabetes remains a common risk factor for infection, as well as for failure of conservative treatment. Neurological deficit and failure of conservative treatment are the main indications for surgery (Lener et al., 2018). Early surgical debridement of infectious tissue in cases of pyogenic spondylodiscitis, with instrumentation when necessary, is associated with a better clinical outcome (Lener et al., 2018; Barber et al., 2022). There is currently no clear data on the use of instrumentation or the length of antibacterial therapy in LM spondylodiscitis. In our case no surgical instrumentation was used after partial debridement of the disk space and removal of the epidural abscess, and bony fusion was achieved upon recovery. The postoperative CT scan at 9-months showed no listhesis, angulation and no haloing around the screws. The patient had no axial symptoms and no neurological deficit, and no further studies have been performed.

Antibacterial treatment of LM spondylodiscitis varies in agents and duration as shown in a review of published cases (Table 1). Management of spondylodiscitis remains heterogenous, and it is determined by the causative microorganism, antibacterial susceptibility, and clinical picture. There have been no controlled trials directed at establishing a drug of choice or the duration of therapy for Listerial infection. Based on synergy in vitro and in animal models, most authorities suggest adding gentamicin to ampicillin for the treatment of invasive listeriosis (Lorber, 2010). In the MONALISA study, a nationwide prospective cohort study in France, that included patients with central nervous system, bloodstream, and pregnancy-associated Listeria infection, the use of an active beta-lactam or an aminoglycoside were each associated with reduced three-month mortality on multivariate analysis (odds ratio [OR] for active beta-lactam: 0.10, 95% CI 0.04–0.26; OR for aminoglycoside: 0.60, 95% CI 0.38–0.94) compared with regimens that did not include each of those options (Charlier et al., 2017). None of the authors have previously described complications related to treatment of LM spondylodiscitis. Unfortunately, our patient developed a side effect of gentamicin, despite daily dosing and careful monitoring of serum drug concentrations. Aminoglycosides are associated with ototoxicity in a substantial proportion of patients receiving the drug for prolonged periods of time and vestibular dysfunction is a common consequence. There are currently no recommendations for a truly safe gentamicin dose, regimen or serum levels (Rutka, 2019). Hearing loss is not a typical complication of gentamicin treatment (Hain et al., 2018). Ototoxic side effects are more common in patients with genetic predisposition (e.g. NOS3, GSTZ1 ja GSTP1 genotype) (Roth et al., 2008; Fischel-Ghodsian, 2005). Genetic screening of patients before aminoglycoside therapy could be a valuable method to prevent ototoxicity if rapid molecular tests

become widely available in the future.

4. Conclusion

Patients with spinal infections require a thorough workup. Microbiological cultures are essential in determining causative agents and antibacterial susceptibility due to possibility of rare pathogens.

Our case illustrates a spontaneous *Listeria monocytogenes* spondylodiscitis, in a patient with several comorbidities, treated with surgical debridement and prolonged antibiotic therapy. Gentamicin treatment requires care and attention to complications. Further studies are needed to establish a safe treatment protocol.

Declaration of competing interest

The authors of this article have no disclosures and do not have any conflict of interest.

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