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Case report

Sequential endogenous endophthalmitis, fungal keratitis, bacteremia and vertebral osteomyelitis in a person who injects drugs

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ABSTRACT

Purpose: To describe multiple ocular (and non-ocular) manifestations of disease that can present in a person who injects drugs (PWID). We report a case of a patient consecutively presenting across multiple visits to an ambulatory eye care clinic as the initial point of contact for endogenous endophthalmitis, fungal keratitis, bacteremia, and psoas abscess with vertebral osteomyelitis within a matter of weeks.

Observations: A 51-year-old male with past medical history of alcohol use disorder and injection drug use was initially seen in an eye clinic three days after suffering vision loss in the left eye associated with floaters, photophobia, and eye pain. After initial workup and treatment for panuveitis, endogenous endophthalmitis was suspected. A pars plana vitrectomy was performed, and intravitreal medications were given. A pathogen was never isolated from vitreous samples. Two weeks later, the patient presented with complaints of pain, blurry vision, and foreign body sensation in his opposite (right) eye. Examination revealed a corneal ulcer later identified as a *Paecliomyces* fungal infection. Two weeks after this, he developed fever, chills, and right-sided flank pain radiating to his testicles. Following evaluation by the emergency department and subsequent hospitalization after bacteremia was noted, he was found to have a right-sided psoas abscess with lumbar vertebral osteomyelitis. Fluid was drained, cultured, and grew methicillin-sensitive *Staphylococcus aureus* (MSSA). At his last visit, his best-corrected visual acuity was 20/20 OS and 20/30 OD despite central corneal scarring. It was only after hospitalization that he affirmed recent injection drug use, despite being queried about it through the course of his infections.

Conclusions and importance: Injection drug use is an increasingly common concern for all healthcare providers as the opioid crisis in the United States remains widespread. This case highlights multiple potential infectious processes which may impact persons who inject drugs when seen by eye care providers. It also describes difficulties in caring for people who inject drugs who may not provide critical and timely information relating to their injection drug use and/or may delay care even when faced with potentially vision- and/or life-threatening conditions.

1. Introduction

The ongoing opioid crisis in the United States has created new hurdles for health care practitioners across every discipline. According to CDC data, between 1999 and 2018, nearly 450,000 deaths were attributed to opioid overdose.[1] In 2018, out of the 67,367 deaths due to drug overdose, 70% (46,802) involved opiates – an average of nearly 130 deaths per day.[2] In 2017, over 11 million Americans (aged 12 and older) were opiate misusers, with approximately 886,000 reporting heroin use within the previous year.[3] The economic burden placed on the U.S. through prescription opiate abuse-related medical costs, lost productivity, criminal justice efforts, and substance abuse treatment are estimated between 70 and 90 billion dollars annually.[4] Injection drug use (IDU) places patients at high risk of bacterial infection which can lead to skin abscess, sepsis, pneumonia, and infective endocarditis.[5] Acute Hepatitis C cases also more than doubled in the U.S. between 2004 and 2014, in direct correlation with the widespread increase of intravenous opiate use.[6]

From an ophthalmic perspective, a major consequence of IDU is endogenous endophthalmitis (EE), and particularly endogenous fungal

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endophthalmitis (EFE). Multiple case series have reported IDU as a risk factor associated with EFE ranging from 23.1% in a 10-year study of 64 cases at a tertiary referral center in Australia, to as high as 70% in another study of 27 patients conducted between 2001 and 2007.[7–9] Both bacterial and fungal causative agents have been identified in EE, but multiple studies have shown that fungal organisms (most commonly *Candida* sp.) account for the majority of cases.[8,10] Through hematogenous spread, microbes can travel to the eye and cause an infectious posterior uveitis. This can present as vitritis, chorioretinal lesions, or can develop into the classic "string-of-pearls" sign due to fungal colonization of the vitreous.[11]

An additional sight-threatening complication of IDU and other forms of substance abuse is bacterial or fungal infection of the cornea.[12] Timely access to care may be a complicating factor to consider in persons who inject drugs (PWID). Many have experienced and/or perceive discrimination and mistreatment when interacting with healthcare professionals and may subsequently avoid the potential stigmatization associated with accessing health care services.[13] Any delay in care can be consequential since both endophthalmitis and corneal ulcers need to be treated in a timely manner for best visual prognosis.[14,15]

2. Case report

We present a 51-year-old male with previous history of alcohol use disorder and IDU who reported a three-day history of left eye vision loss associated with new floaters, photophobia, and eye pain. The patient noted that a corneal metallic foreign body was removed from his left eye three months prior. He also reported a recent history of fever, lip blisters, and cellulitis for which he received a 10-day course of cephalexin. He had prior history of LASIK surgery in both eyes and was an active soft contact lens wearer. There was no history of recent hospitalization, intraocular procedures, diabetes mellitus, surgery, catheterization, or recent dental work. The patient did report history of IDU within six months prior to his presentation, but he denied current injection drug use.

At initial presentation, best corrected visual acuity (BCVA) in his right eye was 20/20 and left eye was 20/70. Slit lamp examination of the right eye showed 1+ conjunctival injection with an otherwise normal exam. Exam of the left eye revealed 3+ conjunctival injection, an old corneal stromal scar without epithelial defect, pigmented endothelial keratic precipitates, and an anterior chamber reaction of 3+ cells, 2+ flare, and posterior synechiae. Fundus exam of the right eye was normal. The left eye revealed a hazy view secondary to 2+ vitritis with inflammatory snowballs and a yellow chorioretinal lesion superotemporal to the fovea (Fig. 1). Labs including ESR, HIV, syphilis IgG/IgM, ACE, Lyme, toxoplasmosis IgG/IgM, QuantiFERON-TB Gold, HLA-B27, and RF were sent as part of a uveitis work-up. Due to the yellow chorioretinal lesion and clinical suspicion for toxoplasmosis-related posterior uveitis, he was also started on SMX-TMP 800 mg/160 mg PO twice daily, prednisolone acetate 1% every 2 h, and atropine 1% twice daily.

The next day, his ESR, HIV, RF, and syphilis IgG/IgM results returned negative. He was asked to return to the clinic over the following week, but did not demonstrate an expected response to antibiotic therapy. Due to concern for endogenous endophthalmitis, blood cultures were drawn and the patient underwent pars plana vitrectomy with vitreous biopsy and intravitreal injection of 100 mcg voriconazole, 1 mg vancomycin, 2.25 mg ceftazidime, and 400 mcg dexamethasone. Vitreous samples were sent for quantitative PCR for toxoplasmosis, HSV 1 and 2, VZV, and CMV. Vitreous cultures were placed in thioglycolate and brain heart infusion (BHI) broths as well as plated on blood agar, chocolate agar, Columbia nalidixic acid (CNA) agar, Sabouraud dextrose agar (SDA), and inhibitory mold agar (IMA). Blood cultures were plated on blood agar and chocolate agar.

During the following two weeks of post-op visits, ACE, Lyme, HLA-B27, QuantiFERON-TB Gold, fungal and bacterial vitreous cultures with Gram/fungal stain, qPCR for toxoplasmosis, HSV 1 and 2, VZV, CMV, and blood cultures all returned negative. The patient improved clinically with resolution of the intraocular inflammation and left eye

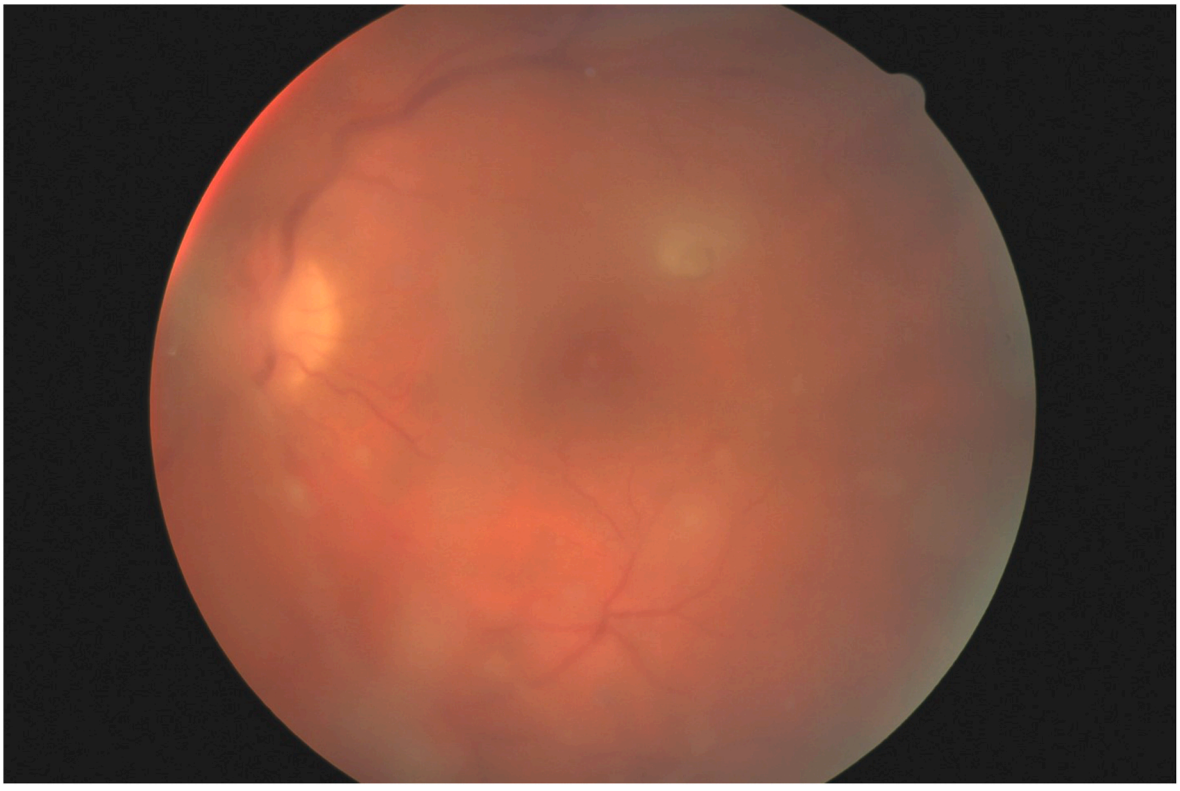

Fig. 1. Fundus photo of left eye showing vitritis and yellow chorioretinal lesion superotemporal to the fovea. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

visual acuity recovered to 20/30. Due to the clinical improvement associated with vitrectomy and intraocular antibiotics, endogenous endophthalmitis was suspected despite negative culture results.

Two weeks later, the patient returned reporting symptoms of pain in his opposite (right) eye, blurry vision, and a foreign body sensation. Best-corrected distance vision in his right eye was count fingers at 1' and his left eye was 20/40. Slit lamp examination revealed a central, oval corneal ulcer measuring 3 mm vertically by 2 mm horizontally with infiltrate, and an anterior chamber reaction of 3+ cells without hypopyon (Fig. 2). Slit lamp exam of the left eye was normal. Dilated fundus examination of both eyes was normal. Corneal culture was taken from the right eye and he was started on polymyxin B sulfate 10,000 units/mL with trimethoprim sulfate equivalent to 1 mg/mL (Polytrim) ophthalmic suspension four times daily and valaciclovir 1000 mg PO three times daily.

Worsening corneal inflammation and ciliary flush was noted one week later and the patient was referred to a corneal specialist. Visual acuity was CF OD and 20/40 OS. Polytrim was discontinued and 0.5% moxifloxacin ophthalmic suspension 1 drop every hour was started for broader antimicrobial coverage. Over the next 4 days, clinical and symptomatic improvement was noted. Corneal culture revealed *Paecilomyces* sp., thus 5% natamycin ophthalmic suspension was initiated every 2 h. Susceptibility testing performed at the UT Health San Antonio Fungus Testing Laboratory reported that specimen growth was not inhibited at a natamycin concentration of 32 μg/mL. There are no established breakpoints for interpretation and no other antifungals were assessed. At one-month follow-up, the corneal surface had healed with residual central scarring and his best-corrected distance visual acuity was 20/40 OD.

Approximately two weeks into treatment for his corneal ulcer, the patient came to the eye clinic for follow-up appearing ill and reporting one week of fever, chills, and right-sided flank pain radiating to his testicles. He was promptly referred to the emergency department where labs revealed an elevated WBC of 11.4 and CRP of 209. At this time, he again denied current recreational drug use. However, his urine toxicology returned positive for fentanyl, buprenorphine, tricyclics, and amphetamines. He left against medical advice but returned to the ED the following day after blood cultures grew methicillin-sensitive *Staphylococcus aureus* (MSSA). He was started on IV cefazolin and admitted to internal medicine for inpatient treatment.

During his stay, MRI revealed a right-sided, multilocular psoas abscess as well as osteomyelitis of the L1 and L2 vertebral bodies (Figs. 3 and 4). Abscess fluid was drained and cultured and also grew MSSA. He was discharged on oral levofloxacin 750 mg daily and rifampin 600 mg daily after a one-week hospitalization, and he was followed in the eye clinic for an additional six weeks. At his last visit, his left eye's visual acuity was 20/30 and showed complete resolution of his uveitis and vitritis. Visual acuity in the right eye was 20/20, and his corneal ulcer showed improvement with some residual scarring.

3. Discussion

We have presented a case of a person who injects drugs (PWID) who presented with sequential endophthalmitis, keratitis, bacteremia, and vertebral osteomyelitis within a short period of time. Though he achieved good vision following treatment of his endophthalmitis and keratitis, both infections were vision threatening. His bacteremia, psoas abscess and vertebral osteomyelitis were potentially life-threatening infections and he risked significant morbidity if permanent damage to his spinal cord had occurred. This case points to the importance of considering injection drug use (IDU) as a factor in ocular infections as well as a risk for non-ocular infections.

Paecilomyces is a ubiquitous filamentous fungus found in soil, decaying plants, and food products. *Paecilomyces* sp. are common laboratory contaminants and have been known to damage canned foods. Notably, they thrive in harsh environmental conditions and are resistant to all methods of sterilization.[16,17] *P. variotii* and *P. lilacinus* are the most commonly identified pathogens within the species, with *P. variotii* being known to cause pneumonia, pulmonary mycetoma, peritonitis, and endophthalmitis.[17]

Endogenous fungal endophthalmitis (EFE) is rare and is usually only seen in patients with compromised immune systems, patients with chronic intravascular access, or PWID. The mode of ocular infection is usually related to transient or chronic sepsis with vascular seeding of the eye leading to endophthalmitis. Major fungal pathogens include *Candida* sp., *Aspergillus* sp., *Fusarium* sp., and, to a lesser extent, *Scedosporium* sp.[7,18] Although we did not culture a pathogen from his vitreous, it is possible that it may have been *Paecilomyces* which responded to the intravitreal voriconazole he received. However, vancomycin and ceftazidime were also injected, and at least one case series has described an

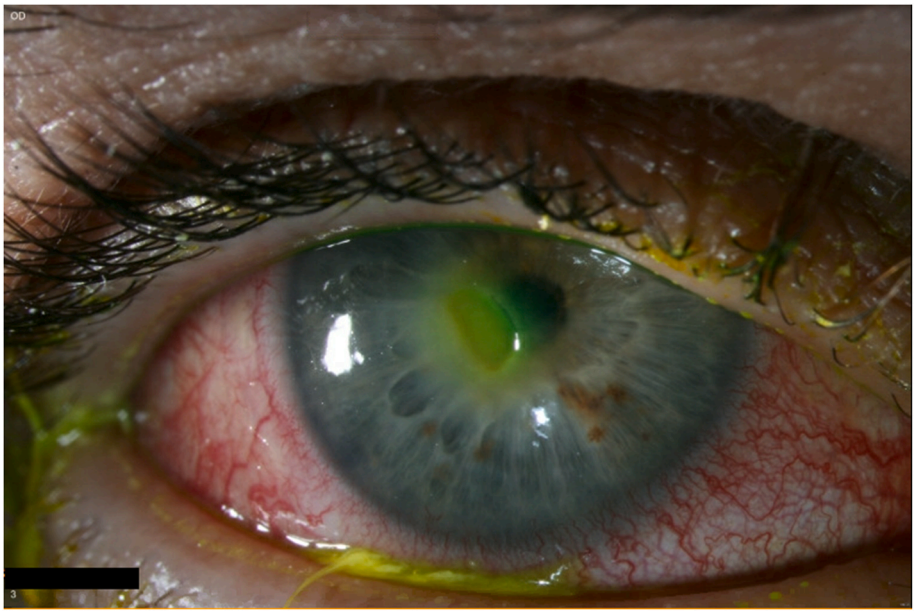

Fig. 2. Slit lamp photograph of the right eye taken 2 weeks after initial presentation. There is a paracentral oval corneal ulcer with fluorescein staining and conjunctival injection. The surrounding cornea is clear and no hypopyon is present.

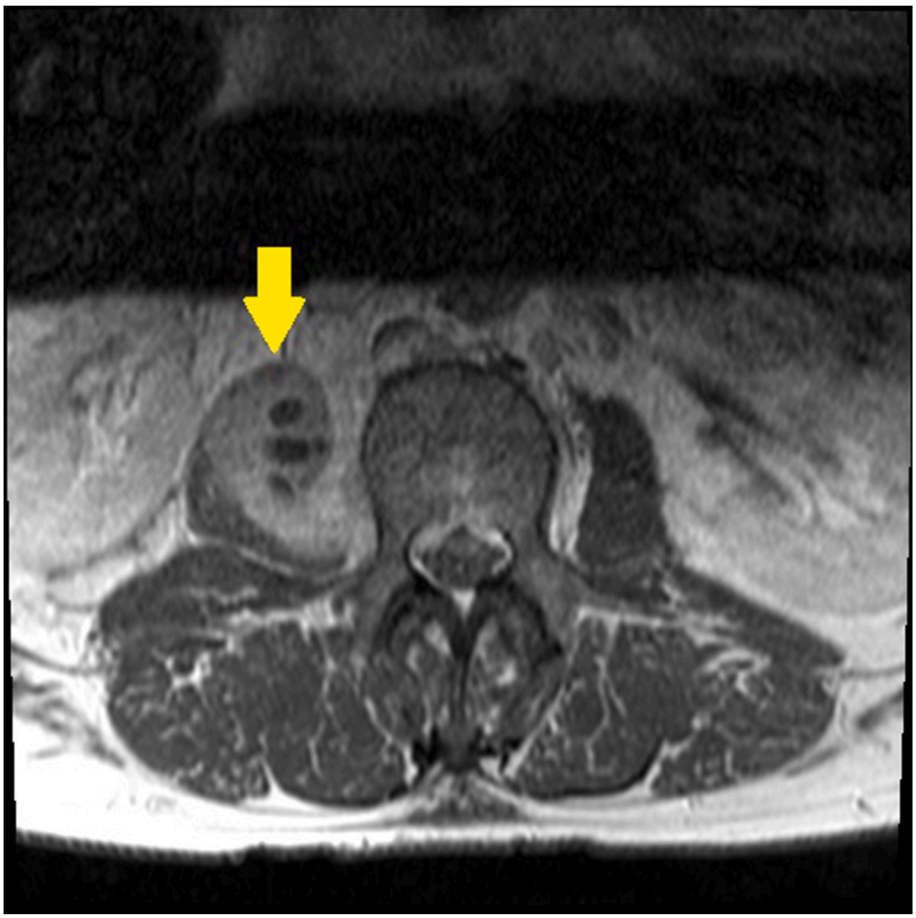

Fig. 3. Axial T1-weighted MRI shows multiloculated rim-enhancing abscess in the psoas muscle at the level of L1-2.

association between *Staphylococcal* endogenous endophthalmitis and pyogenic vertebral osteomyelitis.[19] Given that MSSA was cultured from both his blood and psoas abscess, this seems quite possible.

There are a handful of case reports of *Paecilomyces* keratitis in the literature associated with chronic keratopathy, corneal trauma, ocular surgery, extended soft contact lens wear, and prolonged use of corticosteroids.[20,21] Typically, microbial keratitis occurs following corneal trauma or chronic contact lens use causing damage to the corneal epithelial barrier leading to inoculation of the cornea and progression to corneal stromal infection. The patient in our case was a soft contact lens wearer without history of extended wear and had no other known risk factors. However, his keratitis involved the anterior stroma suggesting that his keratitis likely developed from inoculation of the anterior cornea. Another aspect to consider is our patient's history of alcohol use disorder, which was uncontrolled at the time of presentation. During his hospitalization, he stated that he regularly consumed between 8 and 24 beers daily. Nutritional co-morbidities associated with alcohol misuse such as vitamin A deficiency have been shown to lead to corneal ulceration and/or perforation.[22–24]

4. Conclusions

This case highlights several possible ocular (and non-ocular) manifestations of IDU. A complication of the evolving opioid epidemic is that PWID may sometimes minimize injection-related morbidity and do not pursue medical care until their condition has reached an emergent status.[25] The opioid epidemic needs to be met with an effort to encourage PWID to immediately seek medical care for injection-related harm instead of delaying treatment. This case demonstrates a patient who in three instances, delayed medical care for injection-related medical issues. To best triage these patients, medical providers should be aware of the vision threatening complications that can arise when PWID undermine traditional self-care and delay seeking medical attention. Eye care providers should also consider the possibility of non-ocular infections in PWID and alert their medical colleagues when they suspect these patients may have other infections related to transient (or sustained) bacteremia as was the case in our patient.

Patient consent

Consent to publish the case report was not obtained. This report does not contain personal information that could lead to the identification of the patient. An IRB determined that this activity is not research involving human subjects as defined by DHHS and FDA regulations, and as such, IRB review and approval was not required.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

CRediT authorship contribution statement

Chad Y. Lewis: Writing – review & editing, Project administration. **Michael E. Zegans:** Writing – review & editing, Supervision, Funding

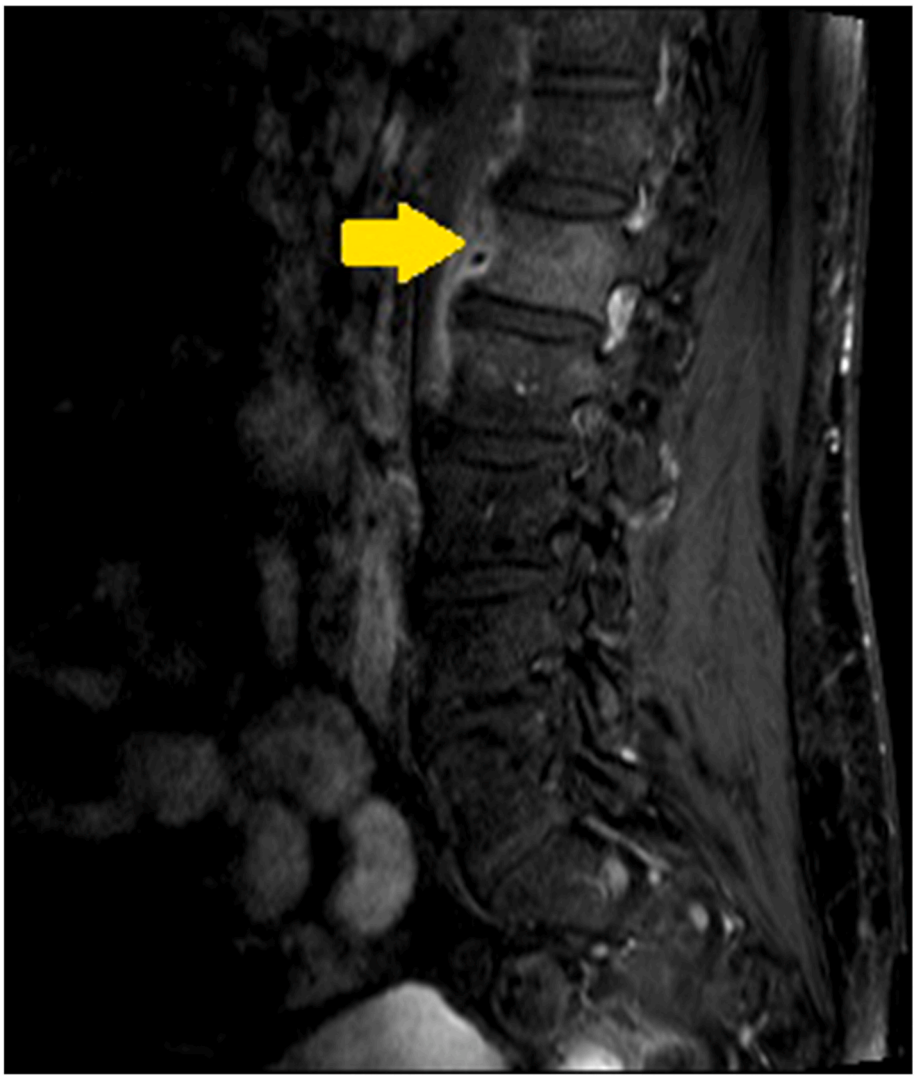

Fig. 4. Sagittal T1-weighted MRI shows abnormal enhancement in the L1 and L2 vertebral bodies, suggestive of osteomyelitis.

acquisition. **Nikhil N. Batra:** Writing – review & editing. **Kelsey L. Jordan:** Conceptualization, Writing – original draft.

Declaration of competing interest

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