CASE REPORT

Navigating the Uncharted: A Case Report of *Ignatzschineria spp.* Infection in Tissue Independently of Maggots Infestation

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ABSTRACT

Ignatzschineria spp. are a rare cause of human infection, typically associated with fly larvae infestations in open wounds. Most cases in the literature have reported that *Ignatzschineria spp.* are usually isolated from blood, urine, and abscess cultures, but not from tissue cultures. We report an interesting case of *Ignatzschineria spp.* detected in a tissue culture from a 62-year-old woman with diabetes, who had presented with gangrenous toes. She underwent debridement and ray amputation of the toes, before being treated with oral ciprofloxacin for three weeks based on the culture and sensitivity reports.
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INTRODUCTION

Ignatzschineria is a genus of Gram-negative, aerobic, and non-spore-forming bacilli. It belongs to the class of Gammaproteobacteria. It was first identified in 2001 by T*ó*th et al., who isolated bacterial strains from the larvae of the *Wohlfahrtia magnifica* fly. Initially named *Schineria*, it was later renamed *Ignatzschineria* by the same author in 2007. (1) This organism is typically found in Europe, Asia, and North Africa. (2) There are four known species within the *Ignatzschineria* genus: *Ignatzschineria indica, Ignatzschineria larvae, Ignatzschineria ureiclastica*, and *Ignatzschineria cameli*, with the latter being identified as recently as 2018. (1,3-4) *Ignatzschineria* infection might be unheard of in Malaysia, where patients with gangrenous diabetic foot are frequent visitors to the hospitals. Therefore, it is essential to discuss its clinical manifestations, methods for identifying, and treatments for this organism.

CASE REPORT

A 62-year-old woman, with underlying hypertension and type 2 diabetes mellitus, presented with gangrene of the left fourth and fifth toes. Physical examination revealed erythematous skin changes on the fourth toe and blackish discoloration on the fifth toe. There was slough present in the web space between the fourth and fifth toes, but there was no pus discharge. Laboratory studies showed a haemoglobin level of 14.5g/dL, a white blood cell count of 10.1×10^9/L, and a platelet count of 279×10^9/L. Ray amputation was performed on the affected toes, and tissue samples were sent for culture and sensitivity. After 24 hours of incubation, the isolated tissue sample grew a non-lactose fermenter colony on MacConkey agar, while the colonies on blood agar appeared greyish. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) identified the organism as *Ignatzschineria spp*.

Initially, the patient was empirically treated with oral cefazolin and metronidazole. Subsequently, upon review by the infectious disease team, the treatment was switched to oral ciprofloxacin 250mg twice daily, based on the antibiotic sensitivity result. The patient was discharged with oral ciprofloxacin 500mg twice daily, and the total duration of antibiotic treatment provided was three weeks following surgical intervention. Unfortunately, the patient was admitted again one month later with wet gangrene of the left third toe. She was counselled by the primary team for transtibial amputation to avoid any further complications, to which she agreed. The patient is recovering well and currently

she is still under follow up while awaiting for prosthesis fitting.

DISCUSSION

Ignatzschineria spp infections are often linked to maggots, which can cause myiasis. These bacteria are commonly detected in the digestive systems of flies. Patients who are infected with these bacteria present with various clinical manifestations, ranging from simple wound infection to bacteraemia culminating in septic shock and death. (4) Unfortunately, specific virulence factors among *Ignatzschineria spp* clinical isolates that may contribute to their pathogenicity have not been well-defined. (3) Transmission occurs once the bacteria are carried from larvae to the mucosal surfaces and damaged skin. Almost all reports of human infection involved the presence of open wounds and the host's poor hygiene. (1,4-5) Other risk factors include proximity to livestock, alcoholism, peripheral vascular disease, low socioeconomic status, and increasing age. (1)

Wounds infested with maggots, especially in the host with poor hygiene, are strongly associated with invasive *Ignatzschineria spp.* infection. In the cases of Ignatzschineria spp. infection, the absence of maggot infestation has been rarely observed. In our case, the patient may have had an unrecognised maggot infestation of her gangrenous foot. However, although maggots were not apparent or found during the examination of the gangrenous toes, *Ignatzschineria spp.* were still being isolated from the tissue culture taken intra-operatively. This emphasises the significance of recognising *Ignatzschineria spp.* as a potential pathogen in wound infections, irrespective of maggot presence, especially in individuals with predisposing risk factors such as diabetes mellitus and peripheral vascular disease. Mejias et al reported a case of breast abscess caused by *Ignatzschineria indica* without the presence of maggots or fly larvae in the abscess culture. Interestingly, the patient presented without fever, similar to our patient in this case. (5)

Ignatzschineria spp. are usually isolated from blood, urine, and abscess cultures in the existing literature, but none from tissue cultures. (1) In our case, the organism was isolated from a tissue culture obtained during the ray amputation procedure. The tissue was cultured on blood agar, Mac Conkey agar, and thioglycollate broth. All three were incubated at 37°C, under aerobic condition for 24 hours. We also incubate the tissue under anaerobic condition for 48 hours on blood agar. These gram-negative organisms on gram stain (Figure 1) display a smooth, grey convex colony (Figure 2) and non-lactose fermenter on Mac Conkey agar (Figure 3) after 24 hours incubation, while there was no growth in anaerobic condition.

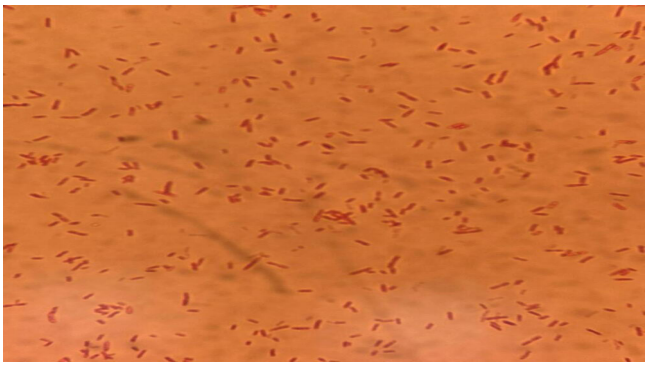

Figure 1: Gram stain (1000x) of Ignatzschineria spp. showing gram negative rod.

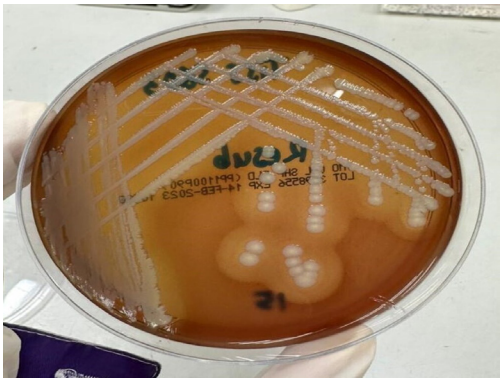

Figure 2: Smooth, grey convex colonies growing on Columbia agar with 5% sheep's blood.

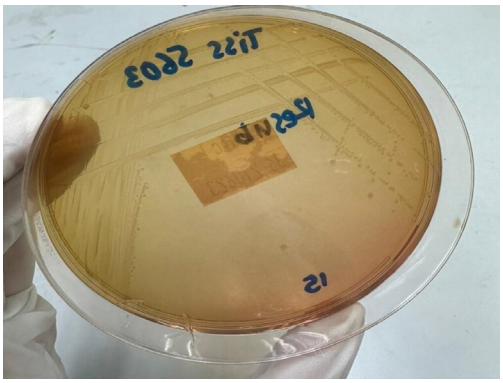

Figure 3: Non lactose fermenter colonies on Mac Conkey agar.

Ignatzschineria spp. have been proven to be challenging to identify, even using the standard identification techniques commonly used in clinical microbiology. In some of the cases reported in the literature, the organism was failed to be identified using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) alone, and 16S rRNA gene amplification and sequencing were required to confirm its presence. (1,5) Maniam et al in their report mentioned that although 16S rRNA was successful in narrowing down the identification to the *Ignatzschineria* genus, it was unable to determine the species level of the organism. This is most likely due to the limited database on genomic sequencing for this organism. However, in another case report, *Ignatzschineria indica*

were able to be identified from a blood sample by using MALDI-TOF MS alone. (5) In our case, we were able to identify *Ignatzschineria spp.* from tissue culture by using MALDI-TOF MS, with a score 2.06. Even though it did not detect up to the species level, identification of this organism enabled the attending clinicians to commence the appropriate treatment early, and disseminated myiasis can be prevented.

Due to the rarity of *Ignatzschineria spp.* infection, there is no current guideline for its antibiotic interpretation in the Clinical and Laboratory Standard Institute (CLSI). As Fear et al. have been using minimum inhibitory concentrations (MICs) for antimicrobial interpretation based on the CLSI non-Enterobacteriaceae breakpoints, we have also adopted the same approach. (3) The organism was tested against cefepime, ceftazidime, ciprofloxacin, imipenem, meropenem, piperacillin-tazobactam, and trimethoprim-sulfamethoxazole. All these antibiotics are found to be susceptible to this organism. (Table I) In all the reported cases, combination antibiotics were used to treat *Ignatzschineria spp.*; for example, vancomycin plus ciprofloxacin or piperacillin-tazobactam plus clindamycin were given separately. (1) In other cases, good outcomes were achieved when treated with a single combination of antibiotics such as amoxicillin/clavulanic acid or ampicillin/sulbactam. (1) There is a case which reported a carbapenem-resistant *Ignatzschineria spp.* from blood culture. The organism was found to be resistant against aztreonam, cefepime, meropenem, and piperacillin-tazobactam suggestive of beta-lactamase and carbapenemase production. However, it was sensitive to amikacin, gentamicin, levofloxacin, and tobramycin. The patient was therefore treated with parenteral vancomycin and cefepime for 11 days, before being changed to oral levofloxacin for another 7 days. (1) This situation is alarming, as this organism is considered to be an emerging pathogen for humans, and thus more studies need to be conducted to formulate a proper therapeutic antimicrobial guideline.

On the other hand, eradication of the source of infection by surgical debridement plays an important role in managing *Ignatzschineria* infection. In the reported cases, besides antimicrobials, the patients also underwent complete removal of the larvae and surgical debridement. (1-3,5) Amputation may also be required in some cases when myiasis is severe. (4). In our case, ray amputation was performed on the affected toes, which probably helped in treating the infection effectively. Surgical debridement is not only essential in reducing the bacterial load but also facilitates better penetration of antimicrobial agents, thus enhancing their efficacy in eradicating the infection.

Table I: Sensitivity profile of *Ignatzschineria spp.* isolate.

Antibiotic agent	Mic Value (ug/ml)	Interpretation
Cefepime	0.094	Susceptible
Ceftazidime	0.016	Susceptible
Ciprofloxacin	0.064	Susceptible
Imipenem	0.125	Susceptible
Meropenem	0.004	Susceptible
Piperacillin-tazobactam	0.047	Susceptible
Trimethoprim-sulfamethoxazole	0.0047	Susceptible

CONCLUSION

Ignatzschineria spp. infections are uncommon, but when present they pose significant pathogenicity in humans and are often associated with wounds and poor hygiene. Although typically associated with maggot infestations, it is important to consider that infections caused by *Ignatzschineria spp.* can occur even in the absence of maggots. Nevertheless, future studies will need to delve into the significance of this finding. Identifying *Ignatzschineria spp.* poses challenges due to the limitations of the conventional detection techniques; nevertheless, the MALDI-TOF MS has been shown to be beneficial, although other additional methods might be required for species-level discrimination.

Standardised treatment guideline for *Ignatzschineria spp.* infections do not exist yet, therefore more researches are needed to reach a consensus on this issue. In cases where the patient is compromised while culture and sensitivity results are yet to be conclusively obtained, empirical antimicrobial commencement may encompass broad-spectrum antibiotics. This should also take into consideration the beta-lactamase or carbapenemase production for the resistant strains.

Despite the challenges, successful outcomes have been reported with various antibiotics. However, vigilance is warranted due to the emerging reports of resistance, which highlight the evolving nature of *Ignatzschineria spp.* infections and the importance of ongoing surveillance and research efforts.

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