MEGA JOURNAL OF CASE REPORTS

OPEN ACCESS

Case Presentation

Compiled Date: October 30, 2024

Foot Osteomyelitis Caused by Lasiodiplodia Theobromae Infection: An Extremely Rare Case Report - The First Case Report in China

Enyou Jin[1#], Yusheng Yang[2#], Huimin Zhang[3#], Zhifan Yang[2], Yuxuan Zhang[2], Hongchao Wang[2], Wenchang Xu[2], Bin Yu[2*], Qingrong Lin[2*] and Yanjun Hu[2*]

[1]Zhuhai Hospital Affiliated to Southern Medical University, China

[2]Division of Orthopedics and Traumatology, Department of Orthopedics, Nanfang Hospital, Southern Medical University, China

[3]Department of Radiation Medicine, Guangdong Provincial Key Laboratory of Tropical Disease Research, School of Public Health, Southern Medical University, China

[*]**Corresponding author**: Bin Yu, Division of Orthopedics and Traumatology, Department of Orthopedics, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong Province, China, 510515, E-mail: yubinol@163.com

Qingrong Lin, Division of Orthopedics and Traumatology, Department of Orthopedics, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong Province, China, 510515, E-mail: titi1626@126.com

Yanjun Hu, Division of Orthopedics and Traumatology, Department of Orthopedics, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong Province, China, 510515, Tel: +86-13889904750; E-mail: huyanjun4750@smu.edu.cn

[#]Authors contributed equally to this work.

Abstract

Chronic osteomyelitis is often caused by bacteria, of which *Staphylococcus aureus* is the most common. Chronic osteomyelitis caused by Lasiodiplodia theobromae, a soil-borne subtropical fungus, has not been previously reported in China and is rare among infectious diseases worldwide, which are associated mainly with sinusitis and keratitis infection. In this study, we report the first case of chronic osteomyelitis caused by Lasiodiplodia theobromae in China. The pathogen was identified by imaging, pathology and genome-wide testing, and the disease was effectively cured by aggressive surgery and antifungal therapy. The purpose of this study was

to provide a reference for the subsequent treatment of osteomyelitis caused by Lasiodiplodia theobromae.

Keywords: Lasiodiplodia theobromae; Fungal infection; Foot osteomyelitis

Introduction

The dematiaceous fungus Lasiodiplodia theobromae belongs to the Ascomycota subphylum Pezizomycotina. It is primarily a plant pathogen that causes rot and dieback in fruits and plants in tropical and subtropical regions [1]. In China, Lasiodiplodia theobromae is present only in regions with a subtropical monsoon climate [2]. Human infections are uncommon and can have wide-ranging presentations. In global studies, only a few cases have been reported. Most of these cases are from tropical or subtropical climate regions. Rarely, the fungus has been linked to sinusitis, onychomycosis, corneal ulcers, osteomyelitis and phaeohyphomycosis. Despite the fact that the fungus thrives on common media quickly, sporulation is challenging and time-consuming; the detection of pathogenic metagenomics may be a better approach for rapid identification. We report the first Chinese case of foot osteomyelitis caused by Lasiodiplodia theobromae infection.

Case Presentation

A 46-year-old female in China visited our Division of Orthopedics and Traumatology, Department of Orthopedics, with left foot pain. The diagnosis and treatment of patients at other hospitals are not good, so these patients are referred to our hospital for treatment. Apart from left foot pain, he did not seem to have any specific symptoms. Upon admission, upon physical examination, her left foot swelling deformity, local pigmentation, scarring and sinus formation were observed, and her left foot compression pain and left foot joint activity were limited **(Figure 1)**. Digital radiography and CT examination revealed postoperative changes in patients with osteomyelitis **(Figure 2)**. The laboratory examination revealed a CRP level of 17.74 mg/ml, ESR of 30 mm/h, U_WBC of 380.90/μL, BACT of 6069.00/μL, HBsAg > 250.000 IU/ml, HBeAb > 4.5000 PEIU/ml, and HBcAb> 45.000 PEIU/ml.

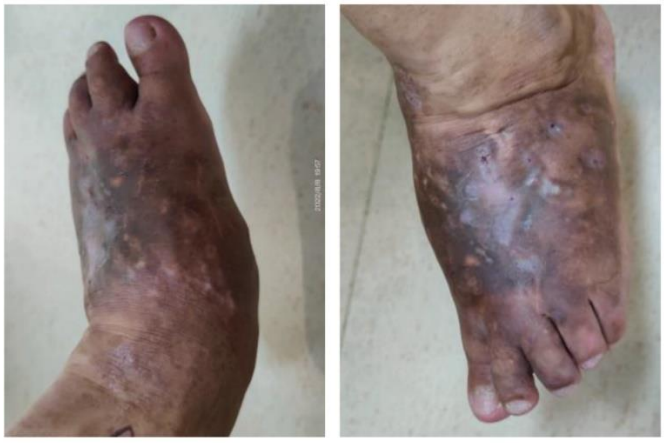

Figure 1: Left foot swelling deformity, local pigmentation, visible scarring and sinus formation were observed.

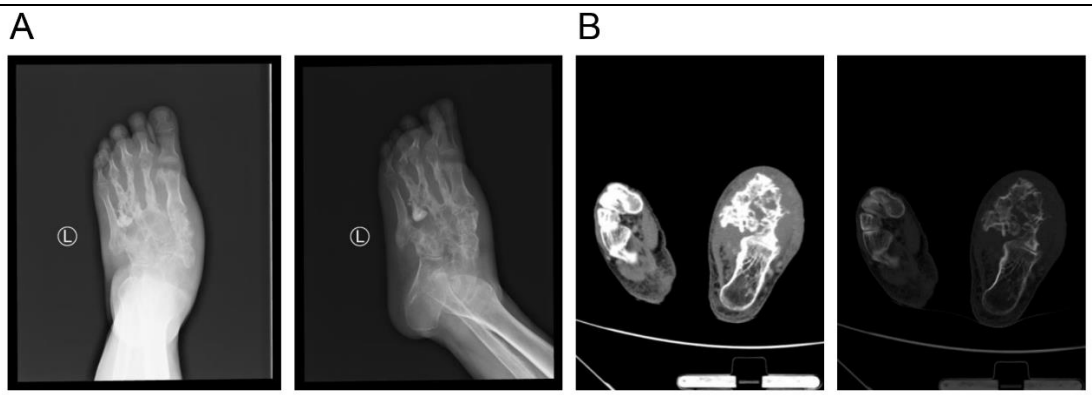

Figure 2: Digital radiography (A) and CT (B) examinations revealed postoperative changes in patients with osteomyelitis.

Therefore, we initially diagnosed the patient with osteomyelitis. We traced the patient's medical history and found that she lived in the countryside. At the time of the initial infection, she had a wound on her foot, and the wound was exposed to contaminated water. We speculate that her living environment and polluted water are the main reasons for her infection with Lasiodiplodia theobromae.

Before her operation at our hospital, she had already undergone surgery at two other hospitals. All the patients healed poorly. On the second and third days after admission to our hospital, the CT and MRI findings improved. She underwent surgery on the sixth day after admission. On the sixth day after admission, she underwent debridement of the bone and soft tissue infection, antibiotic bone powder implantation, and scar release **(Figure 3)**. After the operation, the patients were treated with antibiotics, pain relief and other symptomatic treatments. The intraoperative secretions and diseased tissues were sent to the laboratory for pathological examination, bacterial culture and identification, and fungal culture and identification. Before surgery, we suspected that the patient may have had *Mycobacterium tuberculosis*. However, the *Mycobacterium tuberculosis* complex nucleic acid test **(Figure 4)** and pathological examination **(Figure 5)** revealed that the patient was not infected with *Mycobacterium tuberculosis* but was infected with Aspergillus. [AAS (-), GMS (+), GRAM (-), PAS (+)]. Therefore, we invited an infectious disease doctor for consultation. Moreover, the intraoperative secretions were subjected to pathogenic metagenomics detection. Interestingly, the patient's pathogenic bacteria are not Aspergillus but rather Lasiodiplodia theobromae. The results revealed that the specific sequence number of Lasiodiplodia theobromae was 5727, and the relative abundance was 99.85% **(Figure 6)**. Therefore, we diagnosed foot osteomyelitis caused by Lasiodiplodia theobromae infection. The infectious physicians also agreed with our diagnosis. We subsequently treated the patient with voriconazole at a dosage of 200 mg twice a day. After treatment, the patient's condition improved, and the patient was discharged on the sixth day after surgery. The outpatient follow-up after discharge suggested that the patient’s infection foci disappeared and that the quality of life was good **(Figure 7)**.

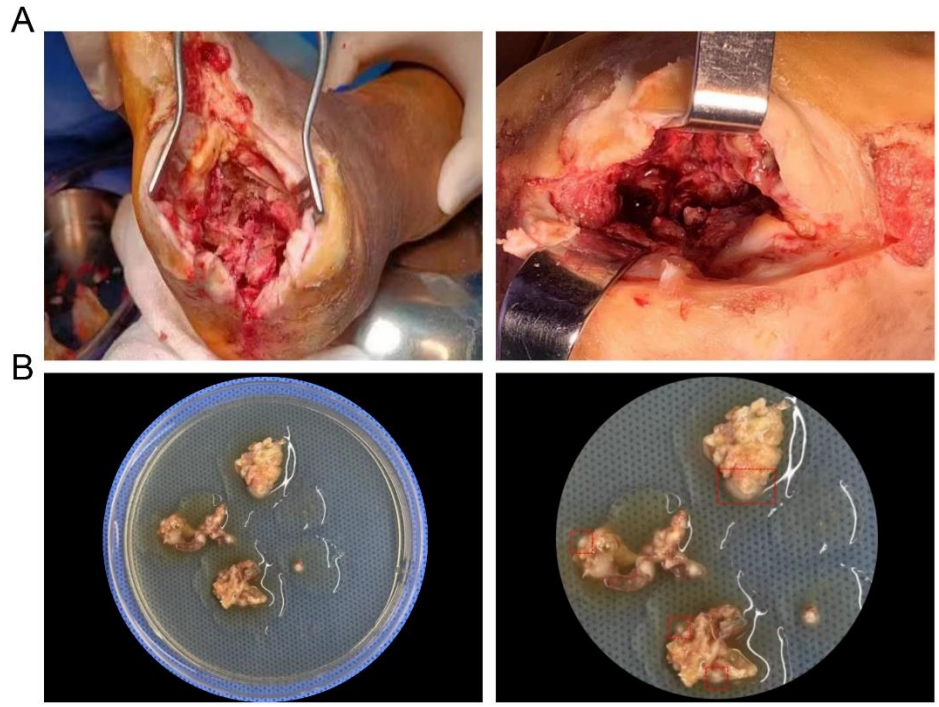

Figure 3: (A) Debridement of bone and soft tissue infection, antibiotic bone powder implantation, and scar release. (B) Surgical removal of the infected tissue revealed surface fungal mycelia-like material.

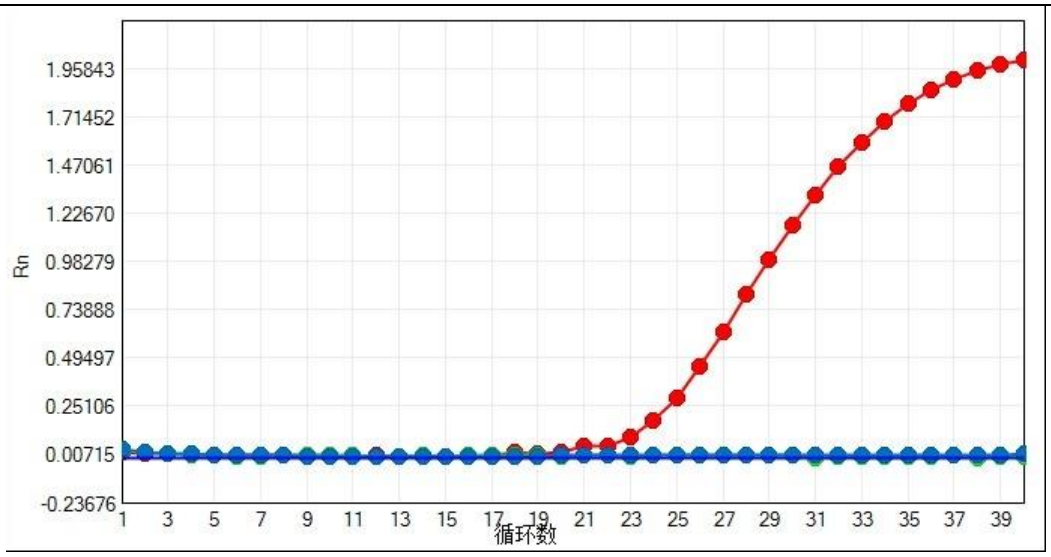

Figure 4: Nested polymerase chain reaction was negative for Mycobacterium tuberculosis.

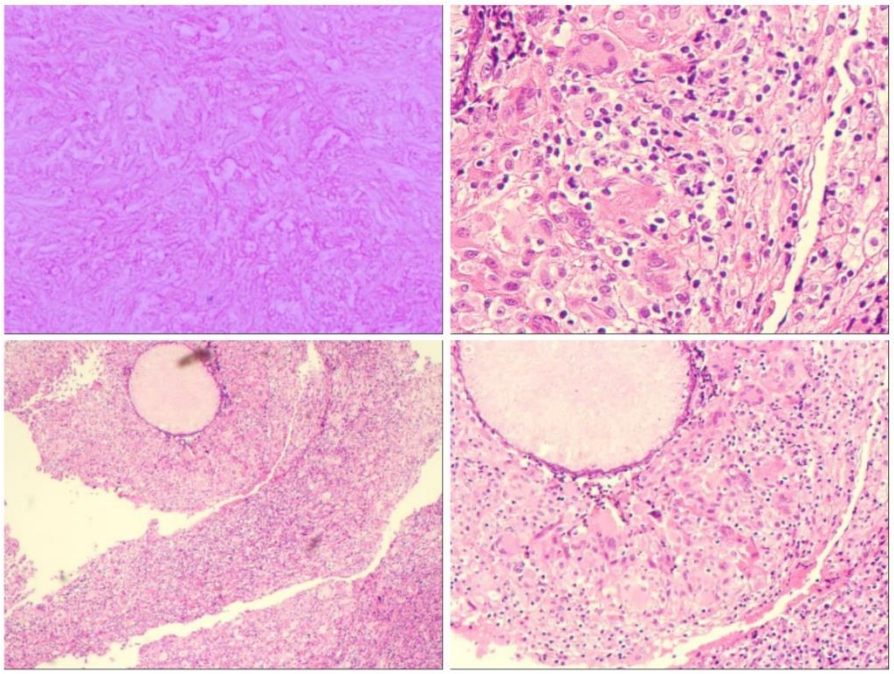

Figure 5: Pathology revealed chronic osteomyelitis, chronic suppurative inflammation of surrounding soft tissue with inflammatory fibrous tissue hyperplasia, and local fungal hyphae with peripheral granulomatous inflammation, and the morphology was consistent with that of Aspergillus.

Genus		Species			
Generic name	Sequence number	Species name	Confidence	Specific sequences	Relative abundance
Lasiodiplodia	5727	Lasiodiplodia theobromae	High	5727	99.85%

Figure 6: Metagenomic examination of infected tissues revealed that Lasiodiplodia theobromae was highly specific.

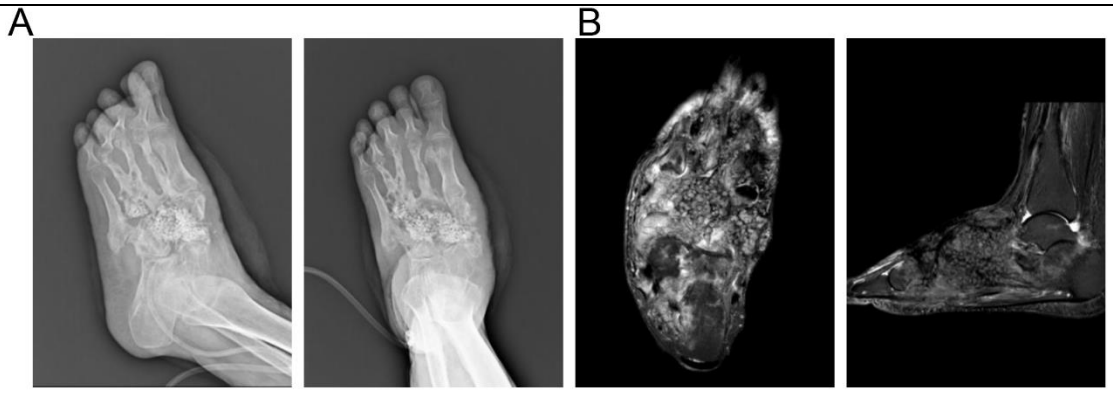

Figure 7: X-ray (A) and MRI (B) were performed after debridement of the infected tissue.

Discussion

Lasiodiplodia theobromae, also known as B. theobromae, is a member of the Sphaeropsic and a common saprophyte or secondary parasite of plants. Lasiodiplodia theobromae infection is not common in humans, and existing cases of Lasiodiplodia theobromae infection have been reported in patients with normal immune function and low immune function in different geographical regions of the world **[1,3-15] (Table 1)**. These infections mainly occur in tropical or subtropical regions of the world and involve ocular skin and nail infections caused by trauma or contact. It usually occurs because of hematogenous spread or via direct inoculation secondary to trauma **[11]**. Risk factors include intravenous drug abuse and an immunocompromised system **[11]**. Our patient works in the field with a foot wound and has low immunity, putting him at high risk of invasive fungal infections. To our knowledge, this is the second known case in the world. China is the first known case of Lasiodiplodia osteomyelitis.

Table 1: Clinical and demographic information of published cases of infections due to L. theobromae.

NO.	Age, years/sex	Predisposing condition	Clinical presentation	Diagnosis	Treatment	prognosis results	Origin
1	32/F	None	toe nail lesions	Phenotypic identification	Excision of nail	Cured	India, (First case, 1967)
2	40/F	None	Subcutaneous abscess	Phenotypic identification	Surgical debridement	Cured	Australia, 1996
3	50/F	None	Leg ulcer	Phenotypic identification	Excision and debridement of ulcer	Cured	Canada, 2004
4	45/M	Cadaveric liver Transplant recipient	Pneumonia	Phenotypic identification and DNA sequencing	Caspofungin IV	Died	Hong Kong, 2008
5	30/F	None	Fungal sinusitis	Phenotypic identification	Debridement surgery, Itraconazole 100 mgorally bd (2 months)	Cured	India, 2010
6	59/M	Traumatic inoculation	Subcutaneous	DNA sequencing	Excisional biopsy and oral voriconazole 200 mg bid for 3 months	Cured	Kenya,

			phaeohypho mycosis				2015
7	47/ F	3rd degree burns	Cutaneous infection involving necrotic burn site	DNA sequencing	Excision of necrotic tissue	Die d	Franc e, 2016
8	66/ M	Aplastic mia due to Mushroom Toxicity	Invasive fungal sinusitis	18 s r DNA sequencing	Surgical excision and amphotericin B IV and oral voriconazole for2 weeks	Cur ed	Korea , 2016
9	69/ M	Refractory multiple Myeloma with recent Autologous HCT	Osteomyelit is	28S rRNA fungal PCR	Amputation and amphotericin B IV for14 days followed by oral voriconazole for8 weeks	Die d	USA, 2016
1 0	75/ M	Diabetes type II	Invasive fungal sinusitis	ITS rDNA sequencing	Corneal transplantation with Keratoplasty followed by intracameral and intravitreal injections for 5 days, Amphotericin B and Voriconazole (0.1%) for 10 days.	Cur ed	Brazil , 2018
1 1	59/ M	Allogeneic hematopoieti c cell transplant recipient	Rhino sinusitis	Phenoytypic and DNA sequencing	Surgical debridement and oral antifungals for 20 weeks	Cur ed	Iran, 2018
1 2	50/ M	Traumatic inoculation	Keratitis	Phenotypic identificatio n	2% voriconazole without keratoplasty	Cur ed	India, 2019
1 3	56/ M	Diabetes	Rhino sinusitis	Phenoytypic and DNA sequencing	Debridement surgery, amphotericin B,(6 weeks, 5 mg/kg/day liposomal AmB)	Cur ed	India, 2023
1 4	46/ F	Foot ulcer	Osteomyelit is	PACE sequencing	Surgical debridement and voriconazole 200 mg bid for 1 month	Cur ed	China , prese

							nt case

Fungal osteomyelitis is rarely encountered, especially osteomyelitis caused by Lasiodiplodia theobromae. Mohan, M et al. [11] described a patient with Multiple Myeloma (MM) with no recent travel history who was diagnosed with Lasiodiplodia osteomyelitis. The patient was successfully treated with surgical debridement and antifungal medication. Clinicians should consider this to be one of the more unusual causes of osteomyelitis.

In this case, the source of infection was not identified but was suspected to be secondary to an indolent cutaneous infection. Due to poor wound healing, the patient's immune function is low. Lasiodiplodia is not a human commensal organism, and it is unlikely that infection was a result of hematogenous spread. In our case, the phenotypic identification of Lasiodiplodia theobromae was inconclusive. The isolates were sent to Guangzhou HUGO Biotech for PACE sequencing. The results revealed Lasiodiplodia theobromae infection. Its identification is a challenging task, in which PACE sequencing can aid in the accurate and speedy identification of the species. Very limited data are available for the formulation of specific treatment guidelines for such rare human pathogens. Therefore, management is often difficult. The reported cases include keratitis, endophthalmitis, cutaneous and subcutaneous infections, onychomycosis, pneumonia in a liver transplant recipient, and osteomyelitis and sinusitis [1,3-15]. Most of these cases are caused by low immune function or wound infection. Surgical, external or internal use of voriconazole is used for treatment, and the treatment effect is good. The treatment of infectious fungal osteomyelitis includes active surgical debridement and antifungal therapy. The best antifungal regimen for the treatment of osteomyelitis caused by Lasiodiplodia theobromae infection has not yet been determined. Among the cases described here, surgical debridement and oral voriconazole are better treatment options. This disease is difficult to address, almost always requires surgical intervention, and a long duration of antifungal treatment is needed for a better clinical outcome.

Conclusion

Our case highlights the importance of PACE sequencing to determine which fungal infection is most accurate. Rare fungi are increasingly observed in patients with low immunity or chronic wounds. For clinicians who treat such cases, multimodal treatments, such as surgical debridement, appropriate antifungal agents and systemic administration, are necessary.

Funding

The present study was supported by the National Natural Science Foundation of China (grant no. 82372421) and the Natural Science Foundation of Guangdong Province (grant no. 2024A1515013165).

References

1. Maurya, Anand Kumar, et al. “Rhino sinusitis caused by Lasiodiplodia theobromae in a diabetic patient.” Med Mycol Case Rep. 2023:40:22-24.
2. Yan JY, Xie Y, Zhang W, et al. Species of Botryosphaeriaceae involved in grapevine dieback in China. Fungal Diversity.

2013;61:221-36.

3. Restrepo A, Arango M, Velez H, Uribe L. The isolation of Botryodiplodia theobromae from a nail lesion. Sabouraudia. 1976;14(1):1-4.
4. Maslen MM, Collis T, Stuart R. Lasiodiplodia theobromae isolated from a subcutaneous abscess in a Cambodian immigrant to Australia. J Med Vet Mycol. 1996;34(4):279-83.
5. Summerbell RC, Krajden S, Levine R, Fuksa M. Subcutaneous phaeohyphomycosis caused by Lasiodiplodia theobromae and successfully treated surgically. Med Mycol. 2004;42(6):543-7.
6. Woo PC, Lau SK, Ngan AH, Tse H, Tung ET, Yuen KY. Lasiodiplodia theobromae pneumonia in a liver transplant recipient. J Clin Microbiol. 2008;46(1):380-4.
7. Kindo AJ, Pramod C, Anita S, Mohanty S. Maxillary sinusitis caused by Lasiodiplodia theobromae. Indian J Med Microbiol. 2010;28(2):167-9.
8. Papacostas LJ, Henderson A, Choong K, Sowden D. An nusual skin lesion caused by Lasiodiplodia theobromae. Med Mycol Case Rep. 2015:8:44-6.
9. Guégan S, Garcia-Hermoso D, Sitbon K, Ahmed S, Moguelet P, Dromer F, et al. Ten-Year Experience of Cutaneous and/or Subcutaneous Infections Due to Coelomycetes in France. Open Forum Infect Dis. 2016;3(2):ofw106.
10. Gu HJ, Kim YJ, Lee HJ, Dong SH, Kim SW, Huh HJ, et al. Invasive Fungal Sinusitis by Lasiodiplodia theobromae in a Patient with Aplastic Anemia: An Extremely Rare Case Report and Literature Review. Mycopathologia. 2016;181(11-12):901-908.
11. Mohan M, Shalin SC, Kothari A, Rico JC, Caradine K, Burgess M. Lasiodiplodia species fungal osteomyelitis in a multiple myeloma patient. Transpl Infect Dis. 2016;18(5):761-64.
12. Da Rosa PD, Locatelli C, Scheid K, Marinho D, Kliemann L, Fuentefria A, et al. Antifungal Susceptibility, Morphological and Molecular Characterization of Lasiodiplodia theobromae Isolated from a Patient with Keratitis. Mycopathologia. 2018;183(3):565-71.
13. Rodriguez A, Anjan S, Martinez OV, Lekakis LJ, Beitinjaneh A, Camargo JF, et al. Invasive Rhinosinusitis Caused by Lasiodiplodia theobromae in an Allogeneic Hematopoietic Cell Transplant Recipient Case Report and Review of Literature. Mycopathologia. 2018;183(5):841-5.
14. Vanam HP, Ather M, Madhura KS, Rudramurthy SM. First report of Lasiodiplodia pseudotheobromae keratitis susceptible to voriconazole in an Indian mango grower. Access Microbiol. 2019;1(6):e000055.
15. Maurya AK, Kumari S, Behera G, Bhadade A, Tadepalli K. Rhino sinusitis caused by Lasiodiplodia theobromae in a diabetic patient. Med Mycol Case Rep. 2023:40:22-24.

Citation of this Article

Jin E, Yang Y, Zhang H, Yang Z, Zhang Y, Wang H, Xu W, Yu B, Lin Q and Hu Y. Foot Osteomyelitis Caused by Lasiodiplodia Theobromae Infection: An Extremely Rare Case Report - The First Case Report in China. Mega J Case Rep. 2024;7(10):2001-2010.

Copyright