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Scedosporium apiospermum subcutaneous soft tissue infection in post renal transplant recipient: Case report

Sukanya Verma*; Ekta Patil; Vivekanandan Ramlingam; Rishit Harbada; Ramaswami Sethuraman; Chakravarthy Thirumalvalavan; Balakrishna Kalyansundaram

***Corresponding Author: Sukanya Verma**

Microbiologist SRL Diagnostic LTD, Prime Square Building, Plot No.1, Gaiwadi Industrial Estate, S V Road, Goregaon, West Mumbai - 400104, India.

Email: drvermasukanya@gmail.com

Abstract

Scedosporium species are ubiquitous fungi found in the sewage, polluted water. Scedosporium apiospermum and Scedosporium prolificans are two common species implicated in causing human infections. They are increasingly being recognized as pathogens in immunocompromised as well as immunocompetent individuals. There is increase in incidence of infection caused by these organism in patients on immunosuppressive therapy post solid Organ transplant. Spectrum of infection ranges from localized skin and subcutaneous infections to deep seated invasive infection. These organism are known to be resistant to Amphotericin B. Voriconazole is the Drug of choice. Other drug that can be used for therapy is Terbinafine. Hence the early species specific identification plays a important role in patient management.

Routinely available modalities for diagnosis of fungal infection include-Histopathological examination of tissue, fungal stain like KOH mount, Calcoflour White stain, fungal cultures and Fungal PCR. These provide clue to the preliminary diagnosis of fungal infection. Specific species identification is done based on the growth characteristics and biochemical reactions. Newer modalities available for Identification include MALDI TOF and DNA sequencing.

MALDI TOF is increasingly being used for faster diagnosis with good specificity.

Here we report a case of Sub cutaneous Scedosporium infection developing post renal transplant in young male. Early identification of the species was possible because of culture and identification by MALDI TOF and successfully treated using Oral Terbinafine.

Keywords

Scedosporium species; Sub cutaneous infection; Maldi TOF; Amphotericin resistant; Voriconazole; Terbinafine.

Background

Scedosporium species are filamentous fungi found ubiquitously in the environment in soil, sewage and polluted water. *Scedosporium apiospermum and Scedosporium prolificans (Lomentospora prolificans*) are the two species that are commonly isolated from human infections. The spectrum of infections ranges from transient colonization to invasive infections. Scedosporium infections are common cause of mycetoma and infections following penetrating trauma in immunocompetent individuals. In immunocompromised individuals it can cause lung infections, bone, soft tissue and CNS infections [1,2]. It is also responsible for causing fatal disseminated infection in Solid organ transplant patients on suppressive immunotherapy. The clinical presentations of these infections are non-specific leading to a delayed diagnosis [3]. Early diagnosis of fungal is essential so that appropriate therapy can be initiated on time and fatal disseminated infections can be prevented. Diagnosis requires high index of clinical suspicion supported by appropriate laboratory evidence. Laboratory diagnosis of fungal infections relies on visualization of fungal elements in the tissue on 20% Potassium Hydroxide mount or Calcoflour white stain and Histopathological analysis. Further identification requires growth on Culture. Various identification modalities available include identification based on the morphological structures on nutritionally deficient agar, Biochemical reaction, MALDI TOF/MS or DNA sequencing [4].

Scedosporium species are known to be resistant to multiple antifungal agents including Amphotericin B, posing a challenge for treatment [2,5]. Voriconazole is considered as the first line therapy for treatment of these infections. Choice of appropriate antifungal is very essential in management of fungal infection in immunocompromised hosts. Other drugs available as choice for treatment but less commonly used include Itraconazole and Terbinafine [6,7].

Here we report a case of subcutaneous skin infection in young male, post renal transplant successfully treated with Terbinafine.

Case Report

A 38 years old male, presented to Nephrology OPD with complaints of hypertension, pedal edema and signs of mild renal failure. He was diagnosed with chronic glomerulonephritis and subjected to native kidney biopsy that showed chronic IgA nephropathy with M1E0S1T1-C1 score.

He was started on treatment with injectable Methyl Prednisolone bolus and was followed up with monthly bolus doses of Injection Cyclophosphamide. However he progressed to develop ESRD in 12 months requiring renal replacement therapy which was initiated through temporary double lumen catheter. He did not improve on renal replacement ultimately requiring a renal transplant.

He underwent living donor renal transplant with mother as donor but from a different blood group. His initial anti body titer was 1: 512. He required blood group specific immunoadsorption followed by cascade plasmapharesis to reach a nadir antibody titer of 1: 8. Post - transplant he went into DIC, requiring plasmapheresis. He gradually recovered to reach baseline creatinine of 1.2 mg/d and was maintained on Rituximab 100mg Single Dose. He was kept on triple immunosuppression of Prednisolone, Tacrolimus and Mycophenolate Mofetil.

After 6 months during the follow-up visit in outpatient department the patient complained of swelling in the left post occipital region. On examination, the swelling wastender, discrete, firm with limited mobility. He was afebrile and did not show any signs of systemic infection. Enlarged lymph nodes could not be related to any local infection in the adjoining draining areas.

A fine needle aspiration was performed and the aspirate was sent for Fungal culture, Bacterial culture, Mycobacterial culture and Histopathological examination.

Histopathology report was suggestive of Non caseating granulomatous inflammation and granulation tissue, with no evidence of fungal organism/atypical cells.

There was no Mycobacterial or Bacterial growth on cultures. 20% Potassium Hydroxide mount and Periodic acid Schiff stain demonstrated Septate Fungal Hyphae (Figure 1). The biopsy sample was inoculated on Sabouraud's dextrose Agar and Brain Heart Infusion agar at 30°C and 37°C which grew black to gray colonies with cottony aerial mycelia within 7 days (Figure 2 and Figure 3).

Slide culture was performed on Corn meal Agar which showed septate hyphae with long to short conidiophores bearing oval shaped conidia in singles (Figure 4) Based on the morphology the isolate was preliminarily identified as Scedosporium species.

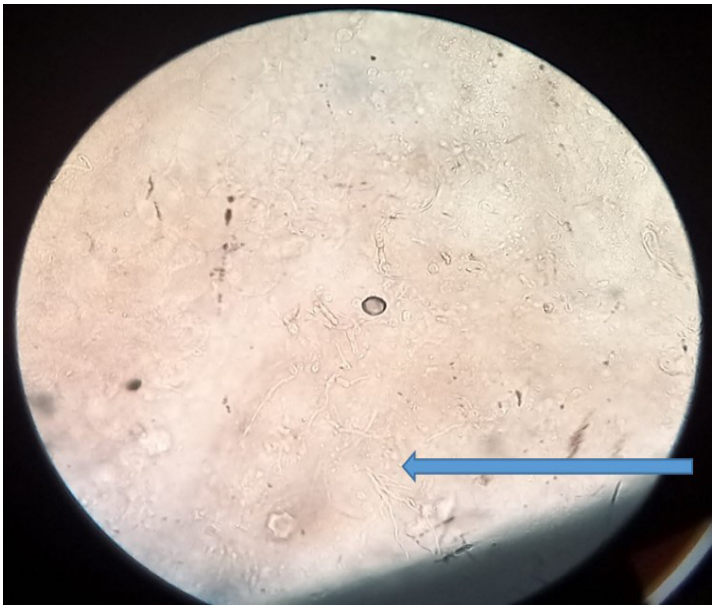

Figure 1: KOH mount showing presence of Septate fungal Hypahe.

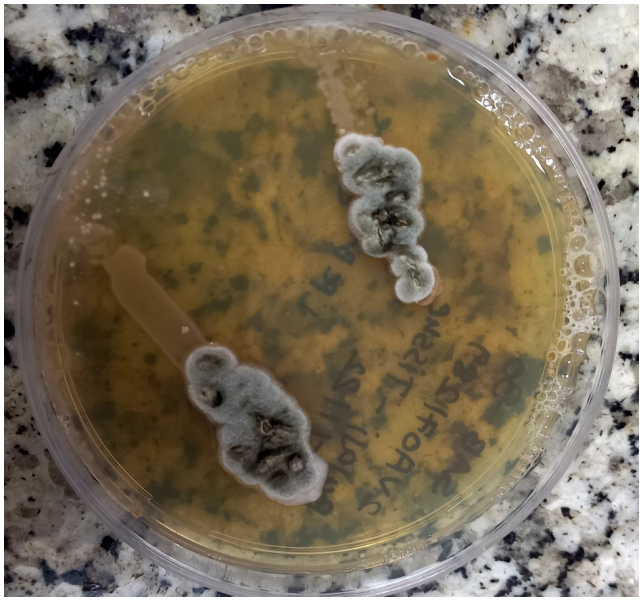

Figure 2:

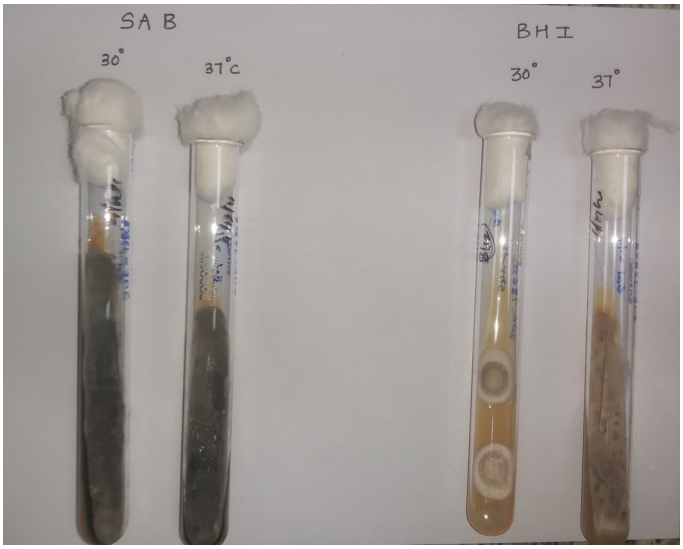

Figure 3:

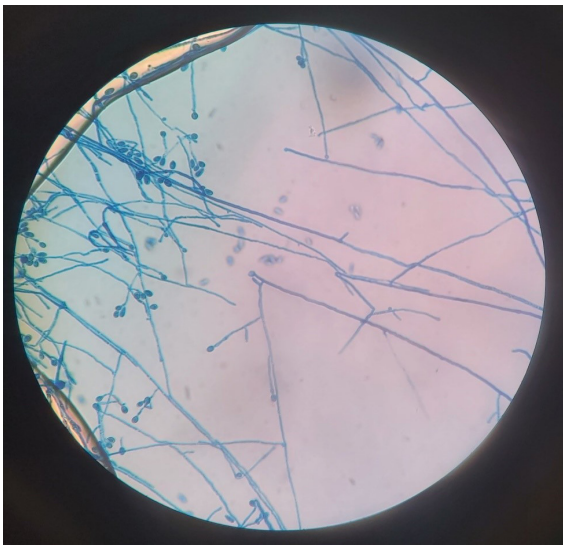

Figure 4:

The node was completely excised and biopsy was sent again for fungal culture. Repeat culture also yielded the same growth and was identified using MALDI-TOF as Scedopsorium apiospermum.

Post-surgical excision of the node the patient was started on Oral Terbinafine 250 mg OD for 8 weeks and continuously followed up. He responded well to the treatment with no residual lesion.

Discussion

Scedosporium species are environmental fungi found in soil, water, sewage, plant, chicken, manure and other animal excreta [8]. They are increasingly being recognized as potential pathogen in immunosuppressed as well as immunocompetent hosts. Infections can manifest in form of localized skin and subcutaneous infection resembling Mycetoma to deep seated invasive infection involving lungs, brain, tendon and joints. Mortality in certain susceptible population can be as high as 50% [4].

Scedosporium species are emerging cause of infections in solid organ transplant recipients and haematopetic stem cell transplant recipients. They account for 25% cases of all Non - Aspergillus fungal infections in these group of patients and for 3% of all fungal infections in post renal transplant recipients with a mortality rate of 70% mortality [8,9].

Ours was also a young male, post renal transplant on Immunosuppressive agents post renal transplant, who developed Scedosporium apiospermum subcutaneous infection after 6 months.

High index of suspicion along with prompt diagnosis is required in identifying these cases. Various modalities are available for diagnosis of fungal infections. Histopathology plays a role in confirming invasive infections; however it does not provide a definite fungal identification. In our case too Histopathology analysis did not aid in the diagnosis. There was discrepancy in the histopathology finding and culture finding this could be due to alteration of fungal morphology because of fragmentation during tissue proces-

sing or alteration of fungal characteristics due to host immune response [10].

Fungal KOH mount is pivotal in early diagnosis of fungal infection. In our case the preliminary diagnosis of fungal infection was based on finding of septate hyphae on KOH mount and Periodic acid Schiff stain. Potassium hydroxide mount does not provide any clue to specific identification apart from septate fungal hyphae which can also be a differential for other fungi like Aspergillus species, Fusarium species, Penicillium species etc.

Culture is the only gold standard available for providing the definite identification [1]. MALDI TOF is increasingly being used for rapid identification of fungal isolates. Literature provides evidence that MALDI TOF can identify Scedosporium species upto the genus level with 100% specificity [8]. In our case early diagnosis was possible because of fungal culture and provisional identification by morphological analysis, followed by MALDI TOF.

These species are known to be inherently resistant to Amphotercin B. Voriconazole remains the drug of choice for treatment of Scedosporium infections. Surgical resection along with antifungal therapy provides a complete resolution to treatment. Combination anti-fungal therapy i.e voriconazole along with Terbinafine or Eichnocandins play a better role in reducing mortality [8]. Because of resistant nature of these species it is essential that species level identification is performed.

In our case we could not perform the antifungal susceptibility and the patient was empirically started on Oral Terbinafine mono therapy in a dose of 250 mg OD for 8 weeks. On subsequent follow up the patient responded well to surgical excision and oral Terbinafine therapy. There were no residual lesions observed.

Voriconazole could not be used in our patient because of the pharmacokinetic interaction with Tacrolimus. Though Terbinafine has not been widely used for therapy, there is one case report from Hungary where the authors successfully used Terbinafine for treatment of skin infection caused by Scedosporium. Despite the high MIC value of Terbinafine, the patient responded well.

Conclusion

Scedosporium infections are increasingly becoming common in immunosuppressed individuals. Early diagnosis using microbiological examination is essential to establish the diagnosis of Scedosporium infections. In view of the varied susceptibility profile of this organism, it is essential that susceptibility testing of Scedosporium is performed.

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Authors Information: Sukanya Verma[1]*; Ekta Patil[2]; Vivekanandan Ramlingam[3]; Rishit Harbada[4]; Ramaswami Sethuraman[5]; Chakravarthy Thirumalvalavan[5]; Balakrishna Kalyansundaram[6]

[1]Microbiologist, SRL Diagnostic Limited, Mumbai, India.

[2]Senior Microbiologist, SRL Diagnostic Limited, Mumbai, India.

[3]Consultant Microbiologist, K G Hospital and Post Graduate Medical Institute, India.

[4]Consultant Nephrologist, Mumbai, India.

[5]Consultant Nephrologist, K G Hospital and Post Graduate Medical Institute, Mumbai, India.

[6]Consultant E.N.T Surgeon, K G Hospital and Post Graduate Medical Institute, Mumbai, India.

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