International Journal of Research in Medical Sciences
Chandrasekaran J et al. Int J Res Med Sci. 2023 Mar;11(3):1031-1034
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20230594

Case Report

A rare cutaneous infection in a chronic intra-muscular drug abuser

Jagadeesh Chandrasekaran*, Sri Lasya Karjala, Jayashri Vijayaragavelu

Department of Internal Medicine, Apollo Hospital, Greams Lane, Chennai, Tamil Nadu, India

Received: 14 January 2023
Accepted: 03 February 2023

***Correspondence:**
Dr. Jagadeesh Chandrasekaran,
E-mail: lasyakarjala@gmail.com

ABSTRACT

After rhinocerebral and pulmonary, mucormycosis affecting the skin is considered to be the third most common type of mucormycosis. It has varied presenting features and hence it is important to make a diagnosis early to achieve better outcomes. Although a large proportion of published cases have no underlying disease, it is most commonly associated with diabetes and blood malignancies. The mode of infection is usually due to cutaneous trauma, while the rest of the cases are health-care associated. *Apophysomyces spp* are usually seen in Asia, while Rhizopus is the most common genus in Europe, North America and South America. It is usually treated with antifungals like amphotericin B and/or surgery. In this article, we presented a case of a middle aged immune-competent female with a history of recurrent intramuscular and intravenous drug usage presenting with cutaneous mucormycosis.

Keywords: Cutaneous mucormycosis, Health care associated cutaneous infection, Opportunistic infection

INTRODUCTION

Mucormycosis is an opportunistic and invasive fungus belonging to the division Glomerulomycota and subphylum Mucormycotina. They are ubiquitously found in nature in decaying organic matter, soil, and animal excreta.

It is most commonly associated with diabetes mellitus, while other risk factors include blood malignancies, transplantation, corticosteroid usage, prolonged neutropenia, trauma, iron overload, burns, illicit IV drug use or neonatal pre-maturity.

Cutaneous Mucormycosis is the third most common type of mucormycosis. It is usually post traumatic. However, in a significant proportion of individuals, it is seen to be associated with sub-optimal health care. It is often difficult to diagnose due to the rarity of the illness and vague clinical presentation. It is associated with higher mortality and morbidity and hence it is important to make the diagnosis as early as possible to achieve a better outcome.

CASE REPORT

A 46 year old female, with known history of type 2 diabetes mellitus, hypertension, hypothyroidism and osteoarthritis in bilateral knees, presented with altered sensorium and breathlessness for three days. She also had complaints of low grade fever for two days. She had a history of recurrent intravenous and intramuscular drug (tramadol, lignocaine, paracetamol) usage (site: bilateral upper limbs and lower limbs) for the past two years at a frequency of once in 1-2 weeks. She had an increased frequency of the same (once in 2-3 days) over four months and she had swelling in all four limbs over the past four months. She also developed ulceration over all four limbs over two months. Some of the ulcers progressed to black lesions over the past two months.

On examination, she had tachypnoea (RR-22/min), tachycardia (140/min) and hypoxia (78% in room air). She also had hypoglycemia (CBG-53 mg/dl). She was hence started on intravenous dextrose infusion and she was started on nasal prongs airway with 2 liters of oxygen. Her local examination revealed bilateral pitting type pedal

edema up to knees. She also had edema of bilateral upper limbs and multiple. She had multiple ulcerations over all four limbs. The ulcers were circular, indurated, pitting in the centre. Some lesions had black necrotic eschars. An arterial blood gas analysis was done and it revealed a pH of 7.32, lactates of 1.77 and creatinine of 2.45. Her urine dip was positive for nitrates. She was started on IV antibiotics.

Table 1: Showing the baseline laboratory parameters of the patient.

Parameters	Patient's value	Lab reference range
Hb (g/dl)	8.9	11.5-16.5
Total count ($\times10^3$/mm^3)	13.94	4-11
Platelet count ($\times10^3$/mm^3)	90	150-450
Blood urea (mg/dl)	66	13-43
Serum creatinine (mg/dl)	2.1	0.6-1.1
Total bilirubin (mg/dl)	3.4	Upto 1.3
Direct bilirubin (mg/dl)	1.7	0.0-0.4
Indirect bilirubin (mg/dl)	1.7	0.0-1.2
Alkaline phosphatase (U/l)	321	<104
Aspartate transaminase (U/l)	37	<31
Alanine transaminase	51	<34
Gamma glutamyl transpeptidase (U/l)	65	<36
Total protein (g/dl)	5.5	6.0-8.0
Serum albumin (g/dl)	3	3.5-5.2
Serum globulin (g/dl)	2.5	2.0-3.5
PT (sec)	17/11	10-14
INR	1.59	
aPTT (sec)	35/27	24- 32
Procalcitonin (ng/ml)	9.05	<0.15
NTPROBNP (pg/ml)	35,000	<249

Her baseline investigations revealed elevated HbA1C, anemia, leukocytosis and thrombocytopenia. She developed acute kidney injury. Her total bilirubin was 3.4 mg/dl with direct bilirubin of 1.7 mg/dl and indirect bilirubin of 1.7 mg/dl. Her liver enzymes revealed elevated ALP (321 U/l). She also had deranged coagulation profile. Her procalcitonin level was elevated (9.05 ng/ml) and NTPROBNP was more than 35000 pg/ml. Her urine routine showed 3+ proteinuria. She developed sudden hypotension and hence she was started on ionotrope support. She continued to have elevated blood urea and serum creatinine. On day 2, she developed a sudden drop and low platelet count. Her blood and urine cultures came back positive for E. coli. She was continued on IV antibiotics.

A tissue culture was sent from the left thigh and it was suggestive of mucormycosis. Histopathological examination of the samples revealed thick, aseptate hyphae with right angled branching suggestive of mucormycosis. IV antifungals were initiated. She underwent wound debridement at 16 areas and biopsies showed features of zygomycosis and candida in a few places. She was on VAC dressing for the same. On post-operative day-4, she developed 50-80 ml of bleeding from the sacral dressing and compression dressing was applied.

Repeat wound cultures were sent. The tissue samples showed growth of *Acinetobacter, Pseudomonas* and *Klebsiella.* She underwent a repeat wound debridement and skin grafting. She was on multiple IV antibiotics which included polymixin B, colistin, targocid and tigecycline based on sensitivity profile over different durations during her hospital stay. The patient developed metabolic acidosis and worsening lactate level (>20). She developed new onset hypotension and hypokalemia secondary to antifungal therapy. Supportive measures were given.

In spite of therapy and regular dressing, the patient continued to worsen. She developed deranged coagulation parameters with PT 20/11, aPTT 48/27 and INR 1.9. She was given multiple blood transfusions for anemia and worsening coagulation profile. A repeat ECHO was done and it revealed grade III diastolic dysfunction. On day 35, she had an episode of cardiac arrest and was revived. There was another episode of cardiac arrest the next day from which she could not be revived and was declared dead.

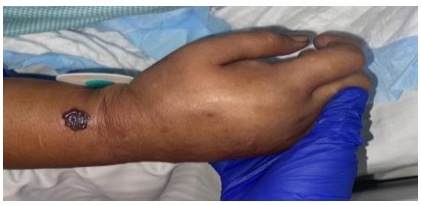

Figure 1: Oval shaped black necrotic lesion noted on the right distal part of forearm.

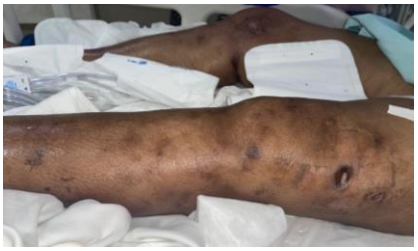

Figure 2: Shows multiple pigmented lesions over the left leg and a depressed oval shaped lesion with central depression and peripheral necrosis on the lateral part of left thigh.

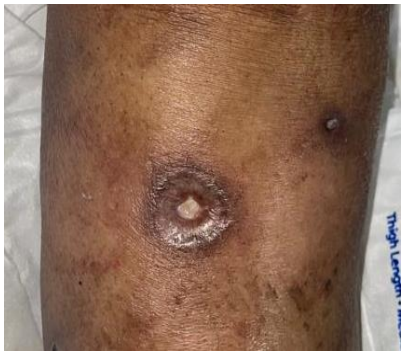

Figure 3: Shows circular lesion with central depression, similar to bull's eye lesion described in literature.

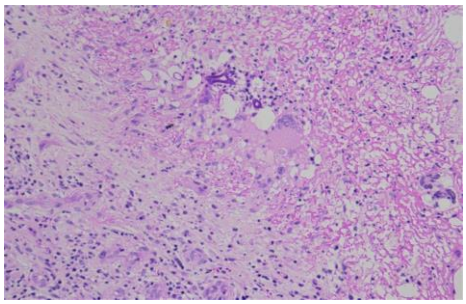

Figure 4: Shows 40X magnification of the fungus. It shows the characteristic thick, aseptate hyphae.

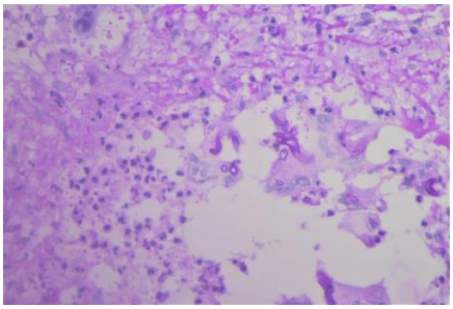

Figure 5: Shows aseptate hyphae with right angled branching and surrounding giant cell reaction of the cells.

DISCUSSION

Apophysomyces and *Saksenaea* species are usually isolated from cutaneous mucormycosis. Unlike other fungal infections, 43-67% of cases of cutaneous mucormycosis can be seen in immunocompetent host. 10-15% of the cases are associated with diabetes mellitus and 5-16% of the cutaneous mucormycosis cases are associated with solid organ transplant recipients. Penetrating trauma is considered to be the most common predisposing factor and is seen in 23-88% of the cases. The next most important risk factor is intra-muscular injection in sub-optimal health-care facility and it is seen in 42% of the reported cases. Other risk factors include open wound trauma (21%), motor vehicle accident (3-33%), surgery (8-30%), contaminated dressings (8-15%), burns (5-11%), natural disasters (5%), animal bites and scratches (9%).

Based on the extent of the invasion, it is classified as localized infection, deep extension, or as a part of the disseminated infection. 32-56% of the cases have localised infection, 24-52% of the cases have deep extension and 16-20% of the patients present with disseminated infection. Primary cutaneous mucormycosis occurs if the skin is infected by direct inoculation and secondary form occurs due to dissemination from other locations, more commonly from a rhinocerebral infection.[1]

The classical clinical sign of mucormycosis is a black eschar. The lesions in cutaneous mucormycosis show significant variability ranging from full blown eschar or cellulitis or abscess. The lesions usually start as small nodules which can be erythematous or ulcerative nodular wounds or as vesicles grouped in a circular fashion. Some authors described mold like growth, tender purupuric macules with peripheral erythema or a cottony growth. Occasionally, the lesions may be woody hard and indurated swellings or 1 cm hard papules or vesicular eruptions. In some cases, the patients presented as a 'purple bull's-eye lesion' or 'bull's-eye infarct'. Few cases of mucormycosis had lesions described as ecthyma gangrenosum, 'erythema nodosum-like rash', or 'pyoderma gangrenosum - like'. The pain severity in the lesions varied significantly, ranging from completely painless in some cases to painful or very painful in others. Sepsis may or may not be associated with the lesions and it varies depending upon the underlying disease and extent of infection.[2]

It is however important to recognise cutaneous mucormycosis in the early stage of the illness as it can progress rapidly leading to gangrene and hematogenous dissemination. *M. irregularis*, *Saksenaea vasiformis*, *Mucor hiemalis*, *Syncephalastrum* sp, and *Rhizopus microsporus* are usually associated with slowly progressing lesions. As per Anna et al the most common site of involvement of cutaneous mucormycosis was lower limbs followed by upper limbs, abdomen, face and other areas.[2] Early detection can be achieved by direct KOH microscopic examination, observing the presence of non-septated, hyaline, hyphae, 5 µm wide and 20 to 50 µm long, with irregular branching at right angles, which are mainly seen at the periphery of the lesion. There is an increase in culture positivity in recent years. Cultures must be performed in sabouraud and potato dextrose agar media and antibiotics which inhibit fungal growth should be avoided.[1]

A biopsy and molecular diagnostic tests should be performed to establish a diagnosis. The biopsy should be taken from the center of the lesion, including subcutaneous fat. Edema, thrombosis, infarctions, necrosis and an inflammatory reaction which includes polymorphonuclear cells, plasma cells, and eosinophils are usually seen in the histopathology picture of primary cutaneous

mucormycosis. Hematoxylin and eosin stain reveals thick, hyaline, non-septated and bifurcated hyphae. But they are best visualized with periodic acid-Schiff and Grocott. As most of the microscopic features are nonspecific and a differential diagnosis with other filamentous fungi must be entertained.

A multimodality approach is essential to improve survival in cutaneous mucormycosis. Extensive surgical debridement forms the core part of treatment of cutaneous mucormycosis. It should be supported with antifungal therapy, correction of the underlying metabolic or impaired immunological status, and control of other concomitant infections. Complete resection of necrotic tissues should be followed by a careful re-evaluation of the wound, in order to diagnose the remaining infection. Considering the invasive nature of the infection, most patients require multiple debridements, or a final amputation. The antifungal of choice is deoxycholate amphotericin B (d-AmB); it can be substituted by lipid formulations because of their better safety profile. The duration of therapy is not clear. A few authors recommend continuing amphotericin B until clinical and radiological resolution, while others recommend it for 6 to 8 weeks. The recommended duration of the therapy may not be feasible in some patients due to intolerance, often secondary to renal failure. Some azole derivatives like posaconazole and isavuconazole have exhibited variable activity against mucorales in susceptibility *in vitro* essays.[3]

Apart from pulmonary and rhinocerebral sites, other sites of mucormycosis are increasingly reported as described by Madhumitha et al and Mathi et al.[4,5] In an older publication by Adam et al disease-related mortality among patients with involvement of only an extremity was 15.5%, while the combined mortality associated with disease of the other locations was 32%.[6] In a systematic review by Anna et al the crude mortality of patients with mucormycosis of extremities and other locations was found to be 26% and 43%, respectively.[2]

CONCLUSION

Cutaneous mucormycosis is an invasive fungal infection usually affecting immunocompromised. Many cases are also reported in immunocompetent patients. Uncontrolled diabetes is considered as an important risk factor. Trauma to skin is considered as the common mode of inoculation. It can be rapidly progressive in most of the cases. Hence, it warrants an early diagnosis and treatment as it can be fatal in the long run in most cases. Diagnosis can be arrived at with demonstration of the fungal elements or by newer diagnostic modalities. This case describes the importance of aseptic precautions during intramuscular and IV drug usage, and the need for strict glycemic control. In this case, it is difficult to point out the source of infection. The most likely source of infection may be the contaminants in the intramuscular or intravenous medicine or lack of aseptic precautions during parenteral drug administration. This case also throws light on the high risk of recurrent infections in the post debridement stage of the illness. The readers must note that cutaneous mucormycosis is a disease which warrants a low threshold for suspicion in the right settings and intensive treatment at an early stage due to associated high mortality.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Prakash H, Chakrabarti A. Global Epidemiology of Mucormycosis. J Fungi. 2019;5(1):26.
2. Skiada A, Drogari-Apiranthitou M, Pavleas I, Daikou E, Petrikkos G. Global Cutaneous Mucormycosis: A Systematic Review. J Fungi (Basel). 2022;8(2):194.
3. Pérez AD, Welsh EC, Miranda I, Ocampo-Candiani J, Welsh O. Cutaneous mucormycosis. An Bras Dermatol. 2017;92(3):304-11.
4. Madhumitha R, Jagadeesh C, Sharma AN, Nambi P, Gopalakrishnan R. Isolated renal mucormycosis in an apparently healthy immune competent adult. Int J Med Health Sci. 2017;6(2).
5. Kumar MMR, Jagadeesh C, Madhumitha R, Gopalkrishnan R. Ileal mucormycosis in an immunocompetent individual presenting as septic shock: One of its kind presentations. JMSCR. 2018;6(8).
6. Adam RD, Hunter G, DiTomasso J, Comerci G. Mucormycosis: emerging prominence of cutaneous infections. Clin Infect Dis. 1994;19(1):67-76.

Cite this article as: Chandrasekaran J, Karjala SL, Vijayaragavelu J. A rare cutaneous infection in a chronic intra-muscular drug abuser. Int J Res Med Sci 2023;11:1031-4.