Case report

Invasive fungal infection in immunocompetent trauma patients – A case series

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ABSTRACT

Zygomycosis is the third leading cause of invasive fungal infection after candidiasis and aspergillosis. Although zygomycosis mostly affects immunocompromised individuals trauma may potentiate infection in immunocompetent individuals. The mortality rate of Zygomycosis is around 50% due to angioinvasion. Here we report a series of 5 cases of angio invasive fungal infection in immunocompetent individuals who sustained trauma in urban areas, out of which only one patient survived following high above knee amputation.

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1. Introduction

Zygomycosis also known as mucormycosis is an aggressive fungal infection commonly found in patients with traumatic injury. Although Zygomycosis is found in immunocompromised individuals, it has also been reported in immunocompetent patients.^{1–3} The predisposing factors may include systemic immunosuppressive therapy, hematological malignancies, uncontrolled diabetes mellitus and prolonged neutropenia.⁴ Once the infection is established the mortality rate is greater than 50%.² Successful treatment depends on adequate debridement and antifungal therapy. In this paper we report a series of 5 cases of zygomycosis, out of which only one case survived after high above knee amputation.

2. Materials and methods

All the five cases presented to us with open fractures following road traffic accidents in urban areas. One case initially went to an outside hospital where above knee slab was given and regular wound dressings were done and presented to us two days after the injury. Blood investigations showed elevated total count, ESR, CRP and their serology was negative for HIV, one case had low Hb of 8.2. Blood and urine cultures were negative in all the cases. All the cases were taken up for emergency wound debridement and external fixator application. They were started on broad spectrum

antibiotics. One developed pseudomonas infection in culture and was started on meropenam. Cultures were also done to rule out anaerobic infection using chocolate, macconkey, blood agars and incubated in an anaerobic jar, some times Robertson cook media was used as transport media. Also x-rays did not show any soft tissue gas suggestive of anaerobic infection. All of the cases developed rapid tissue necrosis, four of the cases developed blackened necrotic areas with foul smelling discharge on the second day post debridement and one case on the 4th day post debridement and were suspected to have necrotizing fasciitis. They were taken for second debridement and the histological finding of non-suppurative necrosis of subcutaneous fat raised the suspicion of fungal infection. The debrided tissues were sent for fungal culture. Culture on Sabaroud's agar showed a white colony of growth and 10% KOH mount showed broad aseptate hyphae. Lactophenol cotton blue test of the culture showed broad aseptate hyphae with champagne glass appearance of sporangial sack consistent with Zygomycosis. All the patients were started on Amphotericin B. Due to progressive necrosis they were taken for repeated debridements (4 debridements in one case, 3 debridements in 3 cases and two debridements in one case) at an interval of 2 days each. When further debridement was not possible they were taken up for high above knee amputation. One case immediately after amputation developed severe hypokalemia and died due to cardiac arrest in the ICU. Post amputation two cases developed atelectasis of the lung and severe hypoxemia along with stump infection. The patients were put on ventilator support and bronchoalveolar lavage was done to relieve hypoxemia and the bronchial washings were sent for culture which came

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Fig. 1. CASE1: A 14 years old female with open injury to the right femur-showing wound at initial presentation.

positive for zygomycosis. Despite of antibiotic therapy the patient general condition deteriorated and died from septic shock. One post amputation patient developed stump infection on third post op day and also bilateral pneumonia and pulmonary edema following myocardial ischemia and died. Post operatively the patient was kept in the ICU and she was hemodynamically stable. The one patient which survived went in for hypokalemia twice in the ICU following amputation and correction was given but she was hemodynamically stable. Following amputation the stump

was put on vacuum assisted closure dressing. Wound size gradually reduced and secondary closure was done 3 weeks post amputation and sutures removed two weeks later. Amphotericin B was continued for 3 weeks followed by oral posaconazole for 3 months duration. Wound was completely healed after 3 months. Chest x rays taken at 6 months and 1 year interval were normal. After that there was no recurrence of infection in a time period of 3 years follow (Fig. 1).

3. Results

A total of 5 cases of invasive fungal infection were evaluated in our hospital. The age of the cases ranged from 14 to 55 (mean 38 years). None of our patients were immunosuppressed. All of them sustained motor vehicle road-side accidents and 4 of them had Gustilo Anderson Grade III B injury and one of them had Grade II. Four of our cases had femur fractures and one had foot involvement. Out of the five cases taken up for high above knee amputation three developed stump infection inspite of vacuum assisted closure dressing and wound care. Two cases developed hypokalemia out of which one case recovered with correction and the other went in for cardiac arrest. Two cases went in for severe stump infection and subsequently septic shock and one case went in for bilateral pneumonia and pulmonary edema following myocardial ischemia. Only one case survived after high above knee amputation and vacuum assisted closure application (Tables 1 and 2).

4. Discussion

The fungal class Zygomycetes is divided into two orders: Mucorales and Entomophthorales. The order Mucorales are capable of causing a fulminant angioinvasive infection with high rates of morbidity and mortality and this type of infection is termed either mucormycosis or zygomycosis (Fig. 2).

Zygomycosis is the third leading cause of invasive fungal infection after candidiasis and aspergillosis.⁶ Zygomycosis clinically presents as either superficial or deep infection. Superficial

Table 1
Case details.

Si no	Age/sex	Site	Grade of compound fracture	Immune status	Time to initial debridement	Number of debridements	Complications	Survival
1	14/F	Rt Thigh (Femur #)	Grade III B	Immunocompetent	2 days	4	Hypokalemia	Survived
2	45/M	Rt Thigh (Femur #)	Grade III B	Immunocompetent	7 h	3	Septic shock	Died
3	40/M	Rt Foot	Grade III B	Immunocompetent	18 h	2	Hypokalemia Cardiac arrest	Died
4	36/M	Lt Thigh (Femur #)	Grade II	Immunocompetent	9 h	3	Septic shock	Died
5	55/M	Rt Thigh (Femur #)	Grade III B	Immunocompetent	11 h	3	Pneumonia Pulmonary edema	Died

Table 2
Microbiological details.

SL NO	AGE/SEX	SITE	Anaerobic culture	KOH mount (Hyphae)	Fungal Culture
1	14/F	Rt Thigh (Femur #)	No growth	Aseptate	<i>A. elegans</i>
2	45/M	Rt Thigh (Femur #)	No growth	Aseptate	Mucor
3	40/M	Rt Foot	No growth	Aseptate	Mucor
4	36/M	Lt Thigh (Femur #)	No growth	Aseptate	Mucor
5	55/M	Rt Thigh (Femur #)	No growth	Aseptate	<i>A. elegans</i>

A. elegans–*Apophysomyces elegans*.

Fig 2. CASE1: A 14 years old female with open injury to the right femur-after wound debridement and external fixator application.

infection is rare. Deep infection manifests as gangrene. Our patients developed large zones of blackened and necrotic foul smelling tissue. Surgical debridement remains the mainstay of treatment. Repeated removal of necrotic tissue may be required to prevent dissemination. Current literature recommends radical debridement of the lesion till bleeding tissue is encountered and the margins are free of fungal growth. Although radical debridement was done in all our cases and edges showing free of growth,

Fig. 3. CASE1: A 14 years old female with open injury to the right femur-showing post amputation and VAC dressing wound.

Fig. 4. CASE 2: A 55 years old male with RTA and injury to right thigh-showing wound at presentation.

Fig 5. CASE 2: A 55 years old male with RTA and injury to right thigh-showing picture after wound debridement.

Fig. 6. CASE 2: A 55 years old male with RTA and injury to right thigh-showing recurrence of infection after high above knee amputation.

Fig. 7. 10% KOH mount showed broad aseptate hyphae.

the patients developed progressive myonecrosis and only one patient survived after high knee amputation (Fig. 3).

Deepali Jain et al. in 2006¹² reported 18 cases of zygomycotic necrotizing fasciitis out of which fifteen were immunocompetent and they concluded that zygomycosis must be concluded as a differential diagnosis not only in immunocompromised patients but also in the absence of any underlying disorder (Fig. 4).

Kantogiorgi et al. in 2007³ reported a case of rapidly progressive cutaneous zygomycosis in a young otherwise healthy farmer, with multiple bone fractures, wounds and soft tissue injuries after an accident with an agricultural machine, who inspite of supportive care, surgical debridements and antifungal therapy, died from refractory septic shock (Fig. 5).

Ryan et al. in 2009¹¹ reported an immunocompetent poly-trauma patient who died 24 days after an open femur fracture that was complicated by necrotizing lower extremity zygomycosis infection. In our study all the cases were immunocompetent and sustained road side motor vehicle accidents and their clinical condition deteriorated inspite of aggressive surgical and medical therapy.

In our study all the cases were immunocompetent and sustained road side motor vehicle accidents and their clinical condition deteriorated inspite of aggressive surgical and medical

Fig. 8. Lactophenol cotton blue mount of culture, broad aseptate hyphae showed champagne glass appearance of sporangial sac. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 9. Culture grown on Sabouraud's agar showed white cottony growth.

therapy. Although these fungi are found readily in vegetations, soil and decaying matter, all our cases acquired zygomycosis infection following a road traffic accident in Urban areas which has not been previously reported (Fig. 6).

Diagnosis of zygomycosis is by tissue culture and microscopic examination. The 10% KOH of sample showed broad aseptate hyphae. Culture grown on Sabouraud's agar showed a white cottony growth almost filling the tube. Lactophenol cotton blue mount of the culture (magnification 400 $\times$) indicated that broad aseptate hyphae showed champagne glass appearance of the sporangial sac.¹⁰ In our study all of the cases showed aseptate hyphae, three of them showed culture positive for mucor and two of them for *A. elegans* (Fig. 7).

Complete or serial radical wound debridement of all the necrotic tissue is the single most effective management. Since zygomycosis rapidly disseminates through the vasculature, a wide zone of excision is required. With extensive deep tissue involvement of vital structures, partial or total amputation of the limb should be strongly considered. All of our cases were taken up for high above knee amputation due to extensive infection, inspite of which only one case survived (Fig. 8).

Medical management of zygomycosis comes secondary to extensive surgical debridement. The commonly used anti fungal agents do not have any effect on zygomycosis. High dose amphotericin B is the drug of choice. The adverse effects of amphotericin included hypokalemia, renal impairment and infusion related intolerance reactions. In our cases liposomal amphotericin B was started in one case and in rest of the cases non liposomal was used due to its high cost effectiveness. It complements surgical debridement by slowing the progression of mucormycosis by controlling infection in areas where vital structures cannot be completely resected (Fig. 9).

Several others authors have reported on invasive zygomycosis in immunocompetent patients. Patino et al.¹³ reported 8 patients with severe necrotizing fasciitis due to zygomycosis following volcanic eruptions. Andresen et al.¹⁴ reported a case of zygomycosis in a previously healthy patient, who developed extensive muscle necrosis after a traumatic injury following Tsunami. The important cause described by various authors is soil contamination and extensive soft tissue injury along with breakage of cutaneous barrier. In our study all our cases had severe soil contamination and soft tissue loss.

5. Conclusion

(A) Angio invasive fungal infection can occur even in immunocompetent individuals with road-side motor vehicle accidents even in Urban areas.

- (B) Mainstay of treatment in these cases is aggressive wound debridement and antifungal therapy, inspite of aggressive treatment mortality is high in these patients.
- (C) The progression of the infection is very rapid and there must be no hesitation in taking up the patient for early amputation.

Conflict of interest

None.

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