Case Report

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Mucormycosis of the Breast in a Patient With Breast Carcinoma After COVID-19 Pneumonia

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ABSTRACT

Mucormycosis is a rare, but potentially fatal, fungal infection which is caused by mucormyctes. These forms of fungi are typically known to infect immunocompromised individuals but are rare in immunocompetent individuals. Herein, we report the case of a 52 year-old female who was diagnosed with right breast carcinoma in Manipal Hospital, a tertiary cancer care center. The patient was a known diabetic and hypertensive and who had recently recovered from coronavirus disease-2019 (COVID-19) pneumonia. In the due course of management, she developed mucormycosis infection at the operative site in her right breast where she had a radiation therapy-induced wound. This patient was successfully treated with an aggressive regimen of early surgical debridement along with administration of systemic amphotericin B.

Keywords: Axillary dissection, breast carcinoma, chemotherapy, COVID-19, mucormycosis, neoadjuvant chemotherapy

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Key Points

- Mucormycosis is an uncommon but potentially fatal fungal infection that usually affects patients with altered immunity, such as in diabetes, post COVID-19 pneumonia and in those with a history of corticosteroid intake.
- Tissue necrosis, is a hallmark of mucormycosis and is often a late sign.
- In this case aggressive treatment with early surgical debridement with the administration of systemic amphotericin B oral antifungal treatment led to a favorable response.

Introduction

Mucormycosis is a rare, but potentially fatal, invasive fungal infection which is caused by mucormyctes. It typically affects patients with immune-compromising conditions, such as hematologic malignancy, stem cell or solid organ transplantation, or uncontrolled diabetes. (1). The prevalence of mucormycosis varies from 0.005 to 1.7 per million population but in India its prevalence is nearly 80 times higher (0.14 per 1000) owing to the high number of coronavirus disease-2019 (COVID-19) cases, as reported in a recent estimate for the year 2019–2020 (2). Globally, the highest number of cases are reported from India (2).

In a recent systematic review, it was stated that the predominant sufferers of mucormycosis were hyperglycemic (83.3%). Furthermore, carcinoma (3%) was indicated as the second leading co-morbidity in these patients. A history of corticosteroid intake for the treatment of COVID-19 was present in a striking 76.3% of cases of mucormycosis. The authors declared diabetes mellitus (DM) as an independent risk factor for both severe COVID-19 and as well as mucormycosis (3). In recent times, COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has gained global attention due to its high rates of infectivity and mortality. Furthermore, these COVID-19 infected patients are frequently noted to be pre-disposed to a wide range of opportunistic bacterial and fungal infections (4). A large majority of the accounted

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cases of fungal co-infection have been reported to be due to two groups of fungal pathogens, *Aspergillus* and *Candida* (5). To date, no case of breast mucormycosis in a case of breast carcinoma after COVID-19 pneumonia has been published. Therefore, we believe our case is unprecedented and will contribute by providing an effective strategy for management in such patients.

Case Presentation

A 52 year-old, Indian, post-menopausal female presented to the department of surgical oncology, in Manipal Hospitals comprehensive cancer centre, with a suspicious lump in the upper outer quadrant of her right breast. She had a pre-exisiting diagnosis of DM and hypertension. Moreover, she had recently recovered from COVID-19 pneumonia. Histopathology reported an infiltrating ductal carcinoma (IDC) of the right breast, cT2N3bM0, Stage III C, grade 2, Luminal B with Ki-67 of 70%.

Thereafter, following a metastatic work-up, the patient was planned for neoadjuvant chemotherapy (NACT) to downsize the tumour. Post NACT, she underwent right breast conservation surgery with axillary lymph node clearance with local oncoplasty after giving written informed consent. Following surgery, she had an uneventful recovery.

The histopathological report documented a complete pathological response at the primary tumor site and 2/10 lymph nodes were reported to be positive. Therefore, as per protocol, she received adjuvant radiation therapy, following which she developed a radiation-induced wound at the operative site that developed into a chronic nonhealing ulcer (Figures 1 and 2).

So, a multidisciplinary team meeting was held and it was thought to be a non-healing wound secondary to ischemia, and the decision was taken to proceed with hyperbaric oxygen therapy (HBOT). Regular dressings were done and she was subjected to two weeks of HBOT. Regrettably, the wound did not show signs of healing, and consequently she developed a high-grade fever. In her best interest, she was admitted and managed conservatively with intravenous medications.

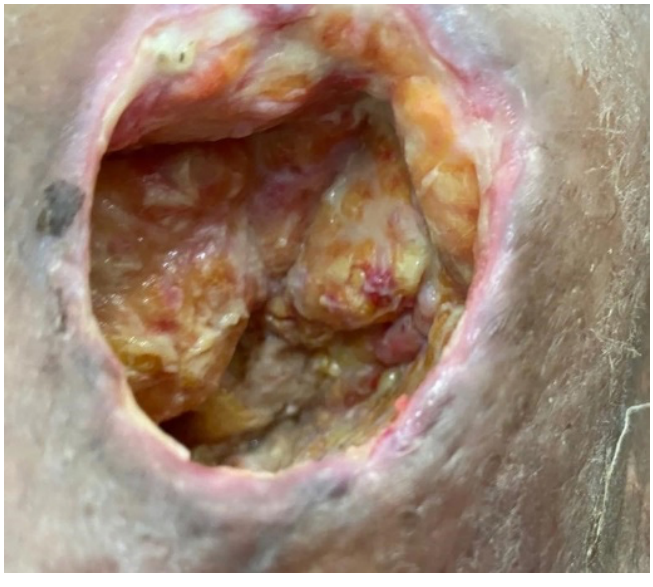

Figure 1. Infected breast wound

Following this, the decision was taken for wound debridement and wound tissue was sent for histopathological examination, to accurately identify the cause of the non-healing nature of her wound. The histopathological examination demonstrated an extensive necrosis of the breast parenchyma with polymorphonuclear infiltration, hemorrhage, and thrombosed blood vessels, and many broad aseptate hyaline fungal hyphae branching at 90° suggestive of mucormycosis (Figures 3 and 4). Subsequently, an aggressive approach was adopted for her treatment, consisting of wound debridement and excision of necrotic tissue, succeeded by the initiation of intravenous liposomal Amphotericin B (1 mg/kg/day in the form of infusion in 5% dextrose) for 15 days. Thereafter, she was given one month of oral fluconazole. The wound healed satisfactorily with regular dressings, antifungal treatment, and high protein nutrition over a period of 45 days (Figure 5).

Discussion and Conclusion

Aggressive treatment with early surgical debridement together with the administration of systemic amphotericin B led to a favorable response in our patient (Figure 5). In this case, many high-risk comorbidities were present, such as uncontrolled blood sugar levels, post COVID-19 pneumonia status, and an immune-compromised condition following standard chemotherapy and radiation therapy for breast carcinoma. All of these factors were addressed promptly and effectively, leading to the patient's complete recovery.

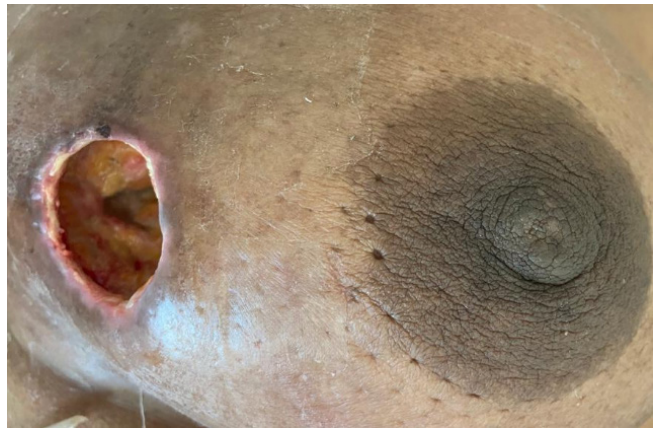

Figure 2. Infected breast wound in right breast

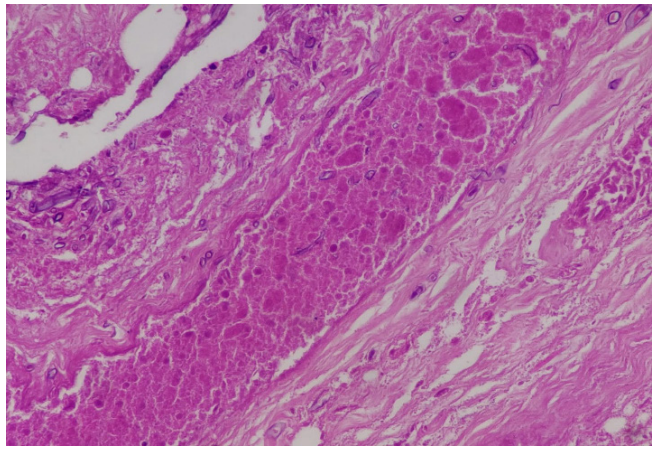

Figure 3. Histopathology showing broad aseptate hyaline fungal hyphae and angioinvasion. (Periodic acid-Schiff-diastase stain)

Available literature says that mucormycosis is an uncommon, but potentially fatal fungal infection, that usually affects patients with altered immunity. It is an angioinvasive disease caused by mold fungi of the genus *Rhizopus*, *Mucor*, *Rhizomucor*, *Cunninghamella*, and *Absidia*, of the order *Mucorales* and class *Zygomycetes* (6). *Rhizopus oryzae* is the most common type and responsible for nearly 60% of mucormycosis cases in humans (7). *Rhizopus* organisms produce an enzyme, ketone reductase, which allows them to thrive in high glucose, acidic conditions. Serum from healthy individuals inhibits the growth of *Rhizopus*, whereas serum from individuals experiencing diabetic ketoacidosis stimulates growth (8).

Tissue necrosis, a hallmark of mucormycosis, is often a late sign (9). Mucormycosis is difficult to diagnose which affects outcomes and results in a poor prognosis. The pressing priority should be the timely initiation of antifungal therapy which is proven to improve the outcome of the infection with mucormycosis. This was illustrated in a retrospective study of 70 patients with hematologic malignancy who had mucormycosis in which delayed amphotericin B therapy (starting treatment ≥6 days after diagnosis) resulted in an almost twofold increase in mortality at 12 weeks after diagnosis (83% vs. 49%) (10). It has been noted that the delay of just a week often doubles the 30-day mortality from 35% to 66%. The conundrum revolves around the poor prognosis of mucormycosis, despite accurate and aggressive treatment protocols (9). Therefore, early diagnosis and treatment are pivotal in avoiding a high risk of fatal outcome.

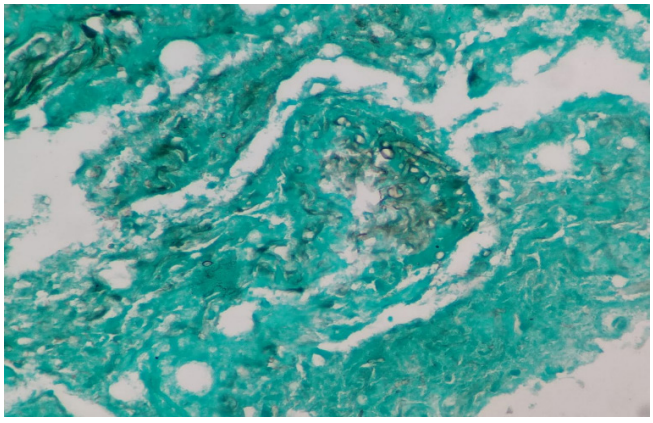

Figure 4. Histopathology showing broad aseptate hyaline fungal hyphae and angioinvasion. (Grocott Methamine silver stain)

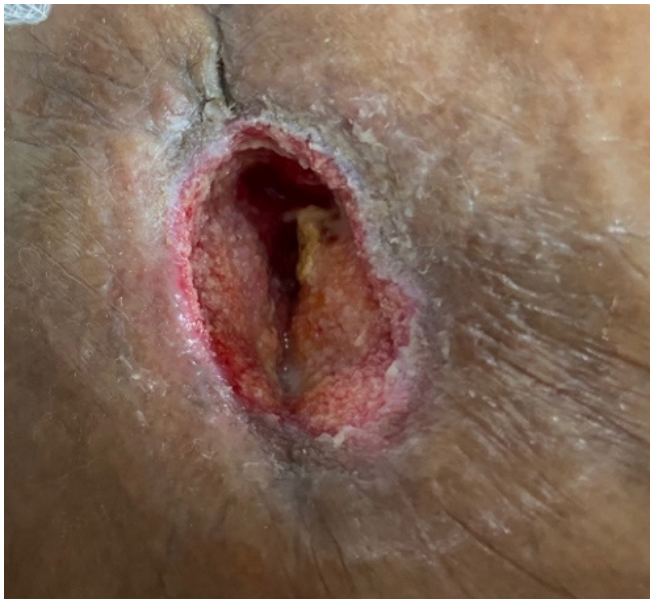

Figure 5. Wound healing post debridement and antifungals

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.P.S., R.J., B.C.A., K.R.A., R.K., A.R., S.R.; Concept: S.P.S., R.J., K.R.A., E.S.; Design: S.P.S., R.J., K.R.A., R.K., H.I.; Data Collection and/or Processing: S.P.S., R.J., H.K.K., A.P., A.F.; Analysis and/or Interpretation: S.P.S., R.J., R.K., K.R.A., S.R.; Literature Searching: S.P.S., R.J., A.P., E.S.; Writing: S.P.S., R.J., R.K., K.R.A., H.I., H.K.K.

Conflict of Interest: No conflict of interest declared by the authors.

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