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ORIGINAL ARTICLE PAEDIATRIC

Paediatric mucormycosis: a retrospective review of manifestations, diagnosis and treatment at a major tertiary paediatric hospital

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Abstract

Background: Cutaneous mucormycosis is a rare yet severe fungal infection that affects immunocompromised paediatric patients. Although prompt diagnosis is essential, excisional tissue biopsy often necessitates general anaesthesia in the paediatric population, which presents risks in the unwell and immunocompromised patient. This study assessed the diagnostic value of the biopsy and associated outcomes in paediatric cutaneous mucormycosis.

Methods: We retrospectively analysed 38 paediatric patients (aged 0–18 years) with suspected or confirmed mucormycosis at a tertiary hospital. Data on demographics, underlying conditions, clinical presentation, diagnostics, treatments and outcomes were collected.

Results: Out of the 38 patients included, mucormycosis was confirmed in 10 cases. Most patients were immunocompromised, with 60.5 per cent having haematological malignancies and 47.4 per cent experiencing neutropenia. Cutaneous involvement was the exclusive manifestation in 90 per cent of confirmed cases. Biopsies were conducted in 73.7 per cent of patients; however, only 28.6 per cent yielded positive results. General anaesthesia is frequently required. Antifungal therapy was initiated in 89.5 per cent of cases, whereas surgical debridement was only required in 28.9 per cent of cases. The mortality rate was 20 per cent in confirmed cases and 39.3 per cent in suspected cases.

Conclusion: Excisional biopsy plays a diagnostic role in suspected paediatric cutaneous mucormycosis but is associated with low yield and procedural risks. The development of improved non-invasive diagnostic alternatives may mitigate unnecessary procedural risks in this patient population.

Updated September 10, 2026: An earlier version mispelt the word retrospective in the article title. It is 'retrospective' not 'restrospective'.

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Introduction

Mucormycosis, also referred to as zygomycosis, is a rare yet life-threatening infection caused by fungi belonging to the order *Mucorales*. It predominantly affects immunocompromised individuals, including patients undergoing chemotherapy and those with haematological malignancies, uncontrolled diabetes or severe neutropenia.[1–3] This infection can manifest in various forms, including rhino-orbital-cerebral, pulmonary, gastrointestinal, disseminated and cutaneous infections. Among these, cutaneous mucormycosis, although less frequently reported, remains a significant and potentially underdiagnosed manifestation, particularly in paediatric populations.[4]

Cutaneous mucormycosis frequently arises from the direct introduction of fungal spores into compromised skin or wounds. This can occur through trauma, surgical sites, burns or catheter insertion. Clinical manifestations may vary from non-specific erythema or swelling to rapidly progressing necrosis and eschar formation.[5–7] In paediatric patients, particularly those who are immunocompromised, these dermatological changes may be misdiagnosed as more common conditions, potentially delaying the consideration of invasive fungal infections.

Timely diagnosis is essential because the systemic spread of mucormycosis is associated with high mortality and morbidity if not promptly addressed with antifungal treatment and surgical debridement. However, diagnosing cutaneous mucormycosis typically necessitates a tissue biopsy for histopathological examination, which often requires general anaesthesia in the paediatric population, and fungal culture.[8–11] A biopsy not only involves inherent risks, but also has cosmetic implications when lesions are located in visible areas such as the face or neck. Furthermore, the diagnostic yield of biopsy and culture remains uncertain, potentially subjecting children to invasive procedures that may not contribute to clinical decision-making.[9–11] It is important to note that special stains are required to identify *Mucor*, including Gomori methenamine silver and periodic acid-Schiff.

There is a paucity of data regarding the paediatric population with cutaneous mucormycosis, and even less information is available on the utility of excisional biopsy in suspected cases within this demographic. This study aims to first delineate the clinical presentation of children with suspected cutaneous mucormycosis and subsequently assess the diagnostic efficacy of excisional biopsy in this group. Through this investigation, we seek to explore the risks and benefits associated with performing invasive diagnostic procedures in this context.

Methods

Ethics

This project was reviewed by the Royal Children's Hospital Melbourne Research Ethics and Governance Office and was deemed exempt from formal Human Research Ethics Committee review. Organisational approval was granted through the clinical audit/quality assurance pathway (Ref: QA/97780/RCHM-2023). Individual patient consent was not sought because this was a retrospective quality assurance review of existing medical records using deidentified data.

Study design and data collection

This descriptive retrospective cohort study analysed data from paediatric patients with suspected or confirmed mucormycosis at the Royal Children's Hospital in Melbourne, Australia, from 2018 to 2023. The study population included patients aged 0–18 years who underwent diagnostic testing for cutaneous mucormycosis. Patients were identified through electronic searches using terms such as 'mucor' or 'mucormycosis'. The data collected included patient demographics, underlying medical conditions, clinical manifestations, diagnostic methods, causative pathogens, treatment approaches and patient outcomes. Variables such as age, sex, predisposing factors (eg, haematological malignancies, solid organ transplantation, diabetes mellitus and other immunocompromising conditions) and clinical presentation (eg, disseminated disease, rhino-orbito-cerebral, pulmonary, cutaneous and gastrointestinal involvement) were recorded. The diagnostic modalities reviewed included histopathological examination, microbiological culture, polymerase chain reaction (PCR) and frozen section analysis. The treatment data included antifungal therapy, surgical intervention and patient prognosis. The primary outcome was the rate of positive biopsies and the frequency of biopsies performed among the suspected cases.

Patients were classified as confirmed mucormycosis if histopathology, microbiological culture or PCR identified *Mucorales* organisms. Suspected mucormycosis referred to patients in whom clinical concern for cutaneous mucormycosis

prompted diagnostic investigation and/or empiric antifungal treatment, but microbiological and histopathological confirmation was not obtained. Management decisions were undertaken through multidisciplinary team discussions involving infectious diseases, microbiology, pathology, dermatology, radiology and surgical teams, including plastic surgery where appropriate, to reach consensus regarding diagnosis and treatment.

Results

Patient demographics and underlying conditions

The study included 38 paediatric patients, consisting of 10 (26.3%) confirmed cases of cutaneous mucormycosis and 28 (73.7%) suspected cases with negative diagnostic results. Most patients were immunocompromised, with haematological malignancies being the most prevalent (60.5%), followed by neutropenia (47.4%), corticosteroid use (28.9%), and haematopoietic stem cell transplantation (HSCT) (26.3%). Notably, a subset of patients (7.9%) had no documented predisposing factors, highlighting the potential for mucormycosis to occur even in immunocompetent individuals (**Table 1**).

Clinical manifestations

The clinical manifestations exhibit significant variability in patients with suspected cutaneous mucormycosis. The most frequently observed features included pulmonary complications (13.2%), such as pneumonia, lung necrosis or haemoptysis, and rhino-orbito-cerebral involvement (13.2%), consistent with previously reported patterns in immunocompromised populations. Disseminated disease was uncommon, identified in only 2.6 per cent of cases. Notably, among the confirmed cases, 90 per cent presented exclusively with cutaneous manifestations, without rhino-orbital, gastrointestinal or systemic dissemination (**Table 2**).

Diagnostic methods

Biopsy of the skin or soft tissue lesions was the primary diagnostic method used in 73.7 per cent of patients. Histopathological confirmation was obtained in 28.6 per cent of samples. Despite strong clinical suspicion in numerous instances, microbiological culture did not yield fungal growth in 73 per cent of patients. Culture was attempted in 97.4 per cent of patients and PCR analysis was conducted in 71.1 per cent, aiding pathogen identification in several cases (**Table 3**). The most frequently isolated fungal species in confirmed cutaneous mucormycosis cases were *Mucor* (40%), *Rhizopus* (20%), *Lichtheimia* (20%), and *Cunninghamella* (10%). Mixed infections involving *Aspergillus* species were also observed, particularly in immunocompromised hosts, indicating that cutaneous lesions may reflect a more complex or polymicrobial fungal involvement (**Table 4**).

Table 1. Underlying conditions

Condition	Number (%)
Haematological malignancy	23 (60.5)
Neutropenia	18 (47.4)
Corticosteroid use	11 (28.9)
Haematopoietic stem cell transplantation (HSCT)	10 (26.3)
Malnutrition	6 (15.8)
Other malignancy (eg, lung, brain, renal, etc)	4 (10.5)
Aplastic anaemia	3 (7.9)
Trauma burn	3 (7.9)
Iron overload/deferoxamine therapy	2 (5.3)
Renal failure	2 (5.3)
Cirrhosis	2 (5.3)
Solid organ transplant	1 (2.6)
Diabetes mellitus	1 (2.6)
Premature birth	0 (0)
Human immunodeficiency virus	0 (0)
Primary immunodeficiency	0 (0)
No underlying conditions	3 (7.9)

Note: Patients may have more than one underlying condition; therefore categories are not mutually exclusive and percentages may total more than 100%

Table 2. Clinical manifestations

Clinical form and features	Number (%)
Cutaneous (inflammation, necrotic eschar)	38 (100)
Pulmonary (pneumonia, lung necrosis, haemoptysis)	5 (13.2)
Rhino-orbito-cerebral (sinusitis, fever, headache, nasal discharge, nasal mucosa/palatal eschar)	5 (13.2)
Gastrointestinal (necrotising enterocolitis)	1 (2.6)
Disseminated disease (> 1 non-contiguous location of *Mucorales* infection)	1 (2.6)

Thus, among patients who underwent biopsy under general anaesthesia, the majority of whom presented with facial or other visible skin lesions, only 28.6 per cent demonstrated positive histopathological findings and 27.0 per cent yielded positive cultures. This raises concerns regarding the diagnostic yield of these invasive procedures in cases of cutaneous presentations (**Table 3**).

Table 3. Diagnostic methods performed

Test	Total tests conducted: n (%)	Positive tests: n (%)
Histopathology†	28 (73.7)	8 (28.6)
Microbiological culture	37 (97.4)	10 (27.0)
Polymerase chain reaction (PCR) analysis	27 (71.1)	8 (28.6)
Frozen section	2 (5.3)	0 (0)

† *Histopathology required excisional biopsy*

Table 4. Causative pathogen

Fungal species	Number (%)
Mucor spp	4 (40)
Rhizopus spp	2 (20)
– *R microspores*	1
– Unspeciated	1
Lichtheima spp	2 (20)
– *L corymbifera*	1
– *L ramose*	1
Cunninghamella spp	1 (10)
– *C bertholletiae*	1
Unidentified *Mucorales*	1

Treatment approaches

Antifungal therapy was administered to 34 out of 38 patients (89.5%), including all confirmed mucormycosis cases and the majority of suspected cases, with amphotericin B and posaconazole being the most commonly used agents. In the suspected cases, empiric antifungal treatment was commonly initiated because many patients were highly immunocompromised and untreated mucormycosis carries substantial mortality risk. Surgical debridement, including the excision of cutaneous lesions, was performed in 11 out of 38 patients (28.9%) including 9 out of 10 (90%) confirmed cases, highlighting its important role when mucormycosis was confirmed or strongly suspected (**Table 5**).

One patient with confirmed mucormycosis did not undergo surgical intervention and was managed with antifungal therapy alone. This patient was an extremely premature infant with progressive respiratory failure over the first months of life, who was deemed too clinically unstable to undergo surgery. The treating team considered surgical debridement futile, as the patient's deterioration and subsequent death were attributed to underlying respiratory failure rather than mucormycosis.

Combination therapy, involving both antifungal agents and surgical procedures, was implemented in 10 out of 38 patients (26.3%), consistent with current practices, particularly when diagnostic certainty was higher (**Table 5**). Other non-surgical management approaches included supportive wound care, antimicrobial optimisation and close clinical observation.

Table 5. Treatment modalities and outcomes

Treatment modality	Total cases: n (%)	Mucor positive: n (%)	Cured, no long-term morbidity: n (%)	Cured, long-term morbidity: n (%)	Died: n (%)
Surgery	11 (28.9)	9 (81.8)	7 (63.6)	3 (27.3)	1 (9.1)
Antifungal medication	34 (89.5)	10 (29.4)	18 (52.9)	3 (8.8)	13 (38.2)
Surgery + antifungal medication	10 (26.3)	9 (90)	6 (60.0)	3 (30.0)	1 (10.0)
Surgery only	1 (2.6)	0 (0)	1 (100)	0 (0)	(0)
Antifungal only	24 (63.2)	1 (4.2)	12 (50)	0 (0)	12 (50)
Other treatment	3 (7.9)	0	2 (66.7)	0 (0)	1 (33.3)
No treatment	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Patient outcomes

Among the confirmed cutaneous mucormycosis cases, 50 per cent achieved complete recovery without long-term morbidity, while 30 per cent survived with residual morbidity. The mortality rate in this cohort was 20 per cent, which is in line with previously reported survival outcomes in paediatric mucormycosis. In the suspected cases, the cure rate without long-term morbidity was 60.7 per cent, while the mortality rate was higher at 39.3 per cent. This likely reflects the severity of underlying comorbid conditions and critical illness in this high-risk population rather than mortality attributable to mucormycosis itself (**Table 6**).

A notable finding was the high rate of invasive procedures, particularly biopsy under general anaesthesia, among suspected cutaneous cases. Despite this, only 28.6 per cent of biopsies yielded positive diagnostic results, highlighting the limited utility of biopsy in certain contexts and raising concerns about procedural risk, especially in paediatric patients with lesions in cosmetically sensitive areas, such as the face (**Table 3**). This emphasised the need to develop or validate less invasive diagnostic tools to guide treatment decisions for suspected cutaneous mucormycosis while potentially reducing exposure to unnecessary invasive procedures.

Outcomes according to treatment modality are summarised in **Table 5**. Patients undergoing combined surgical and antifungal management generally demonstrated favourable outcomes compared with those managed with antifungal therapy alone. However, surgical intervention was predominantly performed in patients who were ultimately confirmed to have mucormycosis, with 90 per cent of patients receiving combined management later confirmed to be mucormycosis-positive. In contrast, antifungal therapy was administered more broadly across clinically suspicious cases, despite only 29.4 per cent of these patients ultimately having confirmed mucormycosis. These findings suggest that surgical intervention was relatively selective toward higher-probability cases of invasive fungal disease and support the importance of careful patient selection before proceeding to invasive procedures and general anaesthesia in this vulnerable paediatric population.

Discussion

This study provides a comprehensive overview of the current diagnostic and management strategies for paediatric cutaneous mucormycosis at a tertiary paediatric hospital, with a particular focus on the diagnostic yield of excisional biopsy. A notable proportion of negative results from excisional biopsy were observed among patients with suspected cutaneous mucormycosis (71.4%). Although excisional biopsy remains the definitive diagnostic modality, particularly given the high stakes of missed diagnoses, our findings indicate that only 28.6 per cent of biopsies in suspected cases resulted in a confirmed diagnosis. This relatively low diagnostic yield likely reflects the exhaustive investigation of this patient population due to prevailing concerns. Nevertheless, despite these limitations, biopsy remains indispensable in cases where mucormycosis is suspected because of the serious consequences of diagnostic delay or misdiagnosis.

Clinicians responsible for the care of immunocompromised children frequently encounter significant diagnostic uncertainties. The initial dermatological manifestations of mucormycosis are often non-specific and may resemble a variety of benign or more prevalent infectious and non-infectious dermatoses. Consequently, the clinical threshold for performing a biopsy is understandably low, contributing to a high incidence of negative results. This cautious approach is endorsed by international guidelines and aligns with the risk tolerance observed in paediatric oncology, transplantation, and critical care settings.[11,12] In many instances, clinicians are obliged to conduct biopsies to exclude infection, particularly in immunocompromised children, despite the low diagnostic yield and procedural risks such as general anaesthesia and potential cosmetic consequences. A comprehensive multi-

Table 6. Outcome of illness

Treatment modality	Total cases: n (%)	Mucor positive: n (%)	Suspected cases: n (%)
Cured (no long-term morbidity)	22 (57.9)	5 (50)	17 (60.7)
Cured (long-term morbidity)	3 (7.9)	3 (30)	0 (0)
Death	13 (34.2)	2 (20)	11 (39.3)

centre prospective study conducted in 2017 (the APRICOT study) involving over 31,000 anaesthetic procedures in children across Europe reported an overall rate of 5.2 per cent for severe perioperative critical events (respiratory or cardiac complications that could result in major disability or death).[13] This underscores the increasing need for alternative, less-invasive diagnostic modalities, especially in children with elevated surgical risk profiles.

This diagnostic uncertainty also influences management decisions. Both confirmed and many suspected cases received empiric treatment, including antifungal therapy and surgical intervention where indicated, because delayed treatment of mucormycosis carries substantial mortality risk in profoundly immunocompromised patients. Patients undergoing combined surgical and antifungal management generally demonstrated favourable outcomes; however, 90 per cent of these patients were ultimately confirmed to have mucormycosis, suggesting that invasive intervention was relatively selective toward higher-probability cases. In contrast, antifungal therapy was administered more broadly across clinically suspicious cases, despite only 29.4 per cent of these patients ultimately having confirmed mucormycosis. These findings highlight the challenge of balancing timely treatment of invasive fungal disease against the risks of potentially unnecessary intervention, including procedural morbidity associated with general anaesthesia.

Traditional histopathological and micro-biological diagnostic methods continue to pose challenges, particularly owing to the limited culture sensitivity associated with the fastidious nature of *Mucorales* fungi. This aligns with the existing literature, which indicates that culture positivity ranges between 50–60 per cent, even in confirmed cases.[14,15] In our cohort, despite microbiological culture being conducted in 97.4 per cent of cases, only a minority yielded positive results. To address these limitations, molecular techniques, such as PCR, have demonstrated potential for enhancing diagnostic accuracy.[16] The implementation of PCR, which can be performed on swabs or skin scrapings and was used in 71.1 per cent of our cases, could be further expanded to complement conventional diagnostics and potentially reduce the reliance on more invasive procedures. Furthermore, the development of non-invasive serological markers, such as *Mucorales*-specific cell-free DNA detection in plasma, represents an emerging diagnostic modality. Studies have shown that serum-based PCR for *Mucorales* DNA may provide early and accurate infection detection, thereby circumventing the need for tissue biopsies.[17] Additionally, point-of-care diagnostic technologies, such as lateral flow assays, have proven successful in diagnosing invasive aspergillosis and may hold promise for adaptation to mucormycosis. If developed for *Mucorales* detection, these assays could facilitate bedside diagnosis.[18] However, further validation of these alternative diagnostic methods in paediatric populations is essential to confirm their utility before their application in real-world clinical settings.

While excisional biopsy remains the definitive method for diagnosing cutaneous mucormycosis, the low positive rate observed in this cohort highlights the need for a more sensitive and selective approach for determining which patients should undergo biopsy. Our findings suggest that diagnostic sensitivity may be significantly enhanced by incorporating clinical risk factors, lesion characteristics and non-invasive fungal diagnostics prior to proceeding with general anaesthesia. Based on the demographic and clinical patterns observed in this study, three domains appear particularly informative in identifying patients with the highest likelihood of mucormycosis: host risk factors (eg, profound neutropenia, HSCT, high-dose corticosteroids, haematological malignancy); lesion phenotype suggestive of angioinvasion and rapidly progressive lesions unresponsive to broad-spectrum antimicrobial therapy.

We propose that children exhibiting both high-risk host factors and a high-risk lesion phenotype, or any child with positive non-invasive PCR findings, constitute a population in which diagnostic biopsy is more likely to yield positive and clinically informative results. This approach may enhance the diagnostic sensitivity while minimising the number of invasive procedures performed in low-yield scenarios.

Clinical implications

Excisional biopsy remains an important diagnostic tool in suspected cases of paediatric cutaneous mucormycosis; however, its low diagnostic yield and frequent requirement for general anaesthesia highlight the need for careful patient selection. Incorporating clinical risk factors and non-invasive diagnostic modalities may reduce unnecessary invasive procedures while maintaining diagnostic accuracy in this high-risk population.

Limitations

This study has several limitations. First, its retrospective design introduced inherent biases, including potential inconsistencies in documentation and diagnostic procedures. Second, as this was a single-centre study conducted at a tertiary paediatric hospital, the generalisability of the findings to other centres with varying diagnostic resources and patient populations may be limited. Third, the relatively small number of confirmed cutaneous mucormycosis cases restricts the statistical power of subgroup analyses and the ability to draw definitive conclusions regarding diagnostic and treatment outcomes. Additionally, while long-term morbidity related to surgical management was recorded, immediate biopsy or general anaesthesia-related complications were not consistently documented in the medical records, limiting assessment of the procedural morbidity. Larger multicentre prospective studies incorporating standardised protocols for the diagnosis and management of cutaneous mucormycosis are necessary to validate our findings and support the development of clinical practice guidelines.

Conclusion

This study highlights the challenges inherent in diagnosing paediatric cutaneous mucormycosis. Excisional biopsy remains an essential diagnostic tool because of the potentially severe consequences of missed diagnosis. However, our findings revealed a relatively low diagnostic yield of excisional biopsy in this context. These results reflect current practice and underscore the importance of evaluating diagnostic accuracy to inform clinical decisions. Future research into less invasive diagnostic methods could complement existing approaches, potentially reducing children's exposure to the risks associated with general anaesthesia and procedural complications while maintaining appropriate clinical investigation.

Data sharing statement

The authors confirm that the data supporting the findings of this study are available within the article.

Author contributions

All authors contributed to the conception and design of the study. AE and JC collected and analysed the data and drafted the manuscript. SS, DW and DK contributed to the data interpretation and critically revised the manuscript for important intellectual content. All authors contributed to data interpretation and subsequent revision, and approved the final version of the manuscript.

Conflict of interest

The authors have no conflicts of interest to disclose.

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