ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2019 January 26; 7(2): 122-259

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

Contents

Semimonthly Volume 7 Number 2 January 26, 2019

ORIGINAL ARTICLE

Case Control Study

Retrospective Cohort Study

Retrospective Study

SYSTEMATIC REVIEW

CASE REPORT

Contents

World Journal of Clinical Cases

Volume 7 Number 2 January 26, 2019

ABOUT COVER

Associate Editor of *World Journal of Clinical Cases*, Shuhei Yoshida, MD, PhD, Assistant Professor, Division of Gastroenterology, Yachiyo Medical Center, Tokyo Women's Medical University, Chiba 276-8542, Japan

AIMS AND SCOPE

World Journal of Clinical Cases (*World J Clin Cases*, *WJCC*, online ISSN 2307-8960, DOI: 10.12998) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

The primary task of *WJCC* is to rapidly publish high-quality Autobiography, Case Report, Clinical Case Conference (Clinicopathological Conference), Clinical Management, Diagnostic Advances, Editorial, Field of Vision, Frontier, Medical Ethics, Original Articles, Clinical Practice, Meta-Analysis, Minireviews, Review, Therapeutics Advances, and Topic Highlight, in the fields of allergy, anesthesiology, cardiac medicine, clinical genetics, clinical neurology, critical care, dentistry, dermatology, emergency medicine, endocrinology, family medicine, gastroenterology and hepatology, geriatrics and gerontology, hematology, immunology, *etc*.

INDEXING/ABSTRACTING

World Journal of Clinical Cases (*WJCC*)is now indexed in PubMed, PubMed Central, Science Citation Index Expanded (also known as SciSearch®), and Journal Citation Reports/Science Edition. The 2018 Edition of Journal Citation Reports cites the 2017 impact factor for WJCC as 1.931 (5-year impact factor: N/A), ranking WJCC as 60 among 154 journals in Medicine, General and Internal (quartile in category Q2).

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Yun-Xiaojian Wu* **Proofing Editorial Office Director:** *Jin-Lei Wang*

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Semimonthly

EDITORS-IN-CHIEF
Dennis A Bloomfield, Sandro Vento

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2307-8960/editorialboard.htm

EDITORIAL OFFICE
Jin-Lei Wang, Director

PUBLICATION DATE
January 26, 2019

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2019 January 26; 7(2): 228-235

DOI: 10.12998/wjcc.v7.i2.228

ISSN 2307-8960 (online)

CASE REPORT

Successful treatment of invasive fungal rhinosinusitis caused by *Cunninghamella*: A case report and review of the literature

Yong-Cai Liu, Min-Li Zhou, Ke-Jia Cheng, Shui-Hong Zhou, Xue Wen, Cheng-Dong Chang

ORCID number: Yong-Cai Liu (0000-0003-3680-3975); Min-Li Zhou (0000-0001-9254-1389); Ke-Jia Cheng (0000-0001-5078-1448); Shui-Hong Zhou (0000-0002-7163-2289); Xue Wen (0000-0001-9190-2752); Cheng-Dong Chang (0000-0001-7452-8316).

Author contributions: Cheng KJ and Zhou SH designed the report; Zhou ML, Wen X, and Chang CD collected the patient's clinical data; Liu YC and Zhou ML analyzed the data and wrote the paper.

Supported by Zhejiang Province Public Welfare Fund, No. 2014C33203; and National Natural Science Foundation of China, No. 81770976.

Informed consent statement: Consent was obtained from relatives of the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Yong-Cai Liu, Min-Li Zhou, Ke-Jia Cheng, Shui-Hong Zhou, Department of Otolaryngology, the First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, Zhejiang Province, China

Xue Wen, Cheng-Dong Chang, Department of Pathology, the First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, Zhejiang Province, China

Corresponding author: Shui-Hong Zhou, PhD, Professor, Department of Otolaryngology, the First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Road, Shangcheng District, Hangzhou 310003, Zhejiang Province, China. 1190051@zju.edu.cn
Telephone: +86-571-87236894
Fax: +86-571-87236895

Abstract

BACKGROUND

Invasive fungal rhinosinusitis (IFR) caused by *Cunninghamella* is very rare but has an extremely high fatality rate. There have been only seven cases of IFR caused by *Cunninghamella* reported in English and, of these, only three patients survived. In this article, we present another case of IFR caused by *Cunninghamella*, in which the patient was initially treated successfully but then deteriorated due to a relapse of leukemia 2 mo later.

CASE SUMMARY

A 50-year-old woman presented with a 2-mo history of right ocular proptosis, blurred vision, rhinorrhea and nasal obstruction. Nasal endoscopic examination showed that the middle turbinate had become necrotic and fragile. Endoscopic sinus surgery and enucleation of the right orbital contents were performed successively. Additionally, the patient was treated with amphotericin B both systematically and topically. Secretion cultivation of the right eye canthus showed infection with *Cunninghamella*, while postoperative pathology also revealed fungal infection. The patient's condition gradually stabilized after surgery. However, the patient underwent chemotherapy again due to a relapse of leukemia 2 mo later. Unfortunately, her leukocyte count decreased dramatically, leading to a fatal lung infection and hemoptysis.

CONCLUSION

Aggressive surgical debridements, followed by antifungal drug treatment both systematically and topically, are the most important fundamental treatments for IFR.

Manuscript source: Unsolicited manuscript

Received: October 2, 2018
Peer-review started: October 2, 2018
First decision: November 1, 2018
Revised: November 12, 2018
Accepted: December 14, 2018
Article in press: December 15, 2018
Published online: January 26, 2019

Key words: Cunninghamella; Invasive fungal rhinosinusitis; Acute myeloid leukemia; Treatment; Prognosis; Case report

Core tip: Invasive fungal rhinosinusitis (IFR) caused by *Cunninghamella* is very rare but has an extremely high fatality rate. There have been only seven cases of IFR caused by *Cunninghamella* reported in English and, of these, only three patients survived. The middle turbinate has been found to be the most common site of invasion, followed by the maxillary and ethmoid sinuses. Antifungal drug treatment and/or surgical treatments are the most important fundamental treatments. In this article, we present another case of IFR caused by *Cunninghamella*, in which the patient was initially treated successfully but then deteriorated due to a relapse of leukemia 2 mo later.

Citation: Liu YC, Zhou ML, Cheng KJ, Zhou SH, Wen X, Chang CD. Successful treatment of invasive fungal rhinosinusitis caused by *Cunninghamella*: A case report and review of the literature. *World J Clin Cases* 2019; 7(2): 228-235
URL: https://www.wjgnet.com/2307-8960/full/v7/i2/228.htm
DOI: https://dx.doi.org/10.12998/wjcc.v7.i2.228

INTRODUCTION

Invasive fungal disease (IFD) usually occurs in immunocompromised populations, such as patients with leukemia or undergoing transplants of hematopoietic cells, the intestine, lung, or liver; it is rare in immunocompetent populations. IFD has been associated with many factors, such as prolonged immunosuppression, pulses of corticosteroids, chronic graft dysfunction, previous use of broad-spectrum antibiotics, neutropenia, cytomegalovirus infection, diabetes, and advanced age[1]. Among patients with hematologic disease, those with acute leukemia are at the highest risk of developing IFD[2]. The mortality rate of patients with IFD is significantly higher than that of patients without IFD[3].

In leukemia patients, many types of fungi can cause IFD, such as *Mucorales, Aspergillus, Candida, Fusarium, Alternaria, Penicillium, Acremonium*, and *Saccharomyces*. Invasive infection with *Cunninghamella* is uncommon. *Cunninghamella* species are fungi belonging to the class *Zygomycetes* and the order *Mucorales*[4]. In healthy hosts, this fungal organism has a low potential for virulence[4]. Leukemia may decrease host immunity and increase the risk of invasive infection with *Cunninghamella*[5]. *Cunninghamella* occurring in leukemia patients classically follows a pattern of pulmonary infection by inhalation of aerosolized spores and dissemination to other organs[6]. It can be divided into several types: rhinocerebral, pulmonary, cutaneous, gastrointestinal, or disseminated infections[7]. The prognosis of this disease is poor even with treatment, and the mortality rate is high[8]. In this article, we present another case of invasive fungal rhinosinusitis (IFR) caused by *Cunninghamella*, in which the patient was successfully treated at first but then deteriorated during subsequent chemotherapy, to illustrate this lethal disease.

CASE PRESENTATION

Chief complaints

A 50-year-old female patient presented to our otolaryngological ward complaining of right ocular proptosis, distending pain, blurred vision, epiphora, bilateral nasal obstruction, and rhinorrhea for about 2 mo.

History of present illness

Four months earlier, the patient was hospitalized in the hematology ward with a diagnosis of acute myeloid leukemia and treated with chemotherapy for three cycles. Two months earlier, the patient complained of right ocular proptosis, distending pain, blurred vision, epiphora, bilateral nasal obstruction, and rhinorrhea after the second cycle of chemotherapy, with a leukocyte count of 0.4×10^{-9}/L and neutrophils at 2.7%. The symptoms did not improve after treatment with an antibiotic and glucocorticoid;

the right ocular proptosis was aggravated and the eyesight in the right eye gradually decreased to the point of blindness.

Physical examination upon admission

Nasal examination showed slight edema of the nasal mucosa, slight hypertrophy of the bilateral inferior turbinates, and a partial defect of the mucous membrane of the right middle turbinate. Ocular examination showed right ocular proptosis, difficulty of eye opening, multi-direction activity limitation, chemosis, blindness, and blackening of the skin of the inner canthus.

Laboratory and imaging examinations

Routine blood tests indicated an elevation of the leukocyte count to 15.5×10^{-9}/L, and of neutrophils to 93.3%. A computed tomography (CT) scan of the sinuses revealed inflammation of the bilateral maxillary and ethmoid sinuses, and the right frontal and sphenoid sinuses. The bones of the sinus walls were not affected. The CT scan also revealed right ocular proptosis, blurring of intraorbital fat, and thickening of extraocular muscles. Magnetic resonance imaging revealed thickening of the right extraocular muscles with a high signal on T2-weighted images. The right eyeball was pressed and distorted, but there was no obvious abnormality within the left orbit (Figure 1).

FINAL DIAGNOSIS

Secretion cultivation of the right eye canthus showed infection with *Cunninghamella* (Figure 2), and postoperative pathology revealed a large quantity of fungus mycelia and spores within the necrotic tissue of the nasal cavity and paranasal sinus (Figure 3).

TREATMENT

We performed endoscopic sinus surgery and right orbit decompression surgery under general anesthesia (Figure 1). The nasal septum deviated slightly toward the right side and there was a partial mucous membrane defect of the right middle turbinate. We resected part of the right middle turbinate and opened the right maxillary and ethmoid sinus during the operation. We found abundant dark-red blood clots and necrotic tissue in the right maxillary sinus. The mucous membrane of the right ethmoid sinus showed partial avascular necrosis, and the mucous membrane of the posterior ethmoid sinus had partly blackened. We resected a large proportion of the right orbital lamina. The orbital fascia was distended toward the ethmoid sinus, and the orbital fascia was also resected. The right uniform process, a mass in the right maxillary sinus, the right middle turbinate, the mucous membrane of the posterior ethmoid sinus, and the intraorbital fat were inspected in a further pathological examination.

After the surgery, the patient was treated with amphotericin B, meropenem, metronidazole, tigecycline, and posaconazole. Secretion cultivation of the right eye canthus showed infection with *Cunninghamella*, and postoperative pathology revealed a large quantity of fungus mycelia and spores within the necrotic tissue of the nasal cavity and paranasal sinus. Then amphotericin B irrigation (amphotericin B 20 mg, NS 250 mL, bid) was applied in the nasal cavity, and amphotericin B eye drops (amphotericin B 25 mg, 5% GNS 16 mL, 2–5 drops/30 min) were also administered. Ten days after the nasal surgery, an extremely serious infection of the right orbit occurred and an ophthalmologist performed an enucleation of the right orbital contents. Postoperative pathology of the right eyeball also revealed fungal infection. After the second surgery, the patient was treated with amphotericin B, voriconazole, and piperacillin/tazobactam. Dressing changes of the right orbit and amphotericin B nasal irrigation were done every day.

OUTCOME AND FOLLOW-UP

The patient's condition was gradually stabilized. Endoscopic examination showed that the patient was recovering well after the nasal surgery. However, 2 mo after the second surgery, the patient's bone marrow examination showed leukemia relapse. She was treated with chemotherapy again and CT examination showed mycotic infection of the right lung. The patient was then treated with posaconazole,

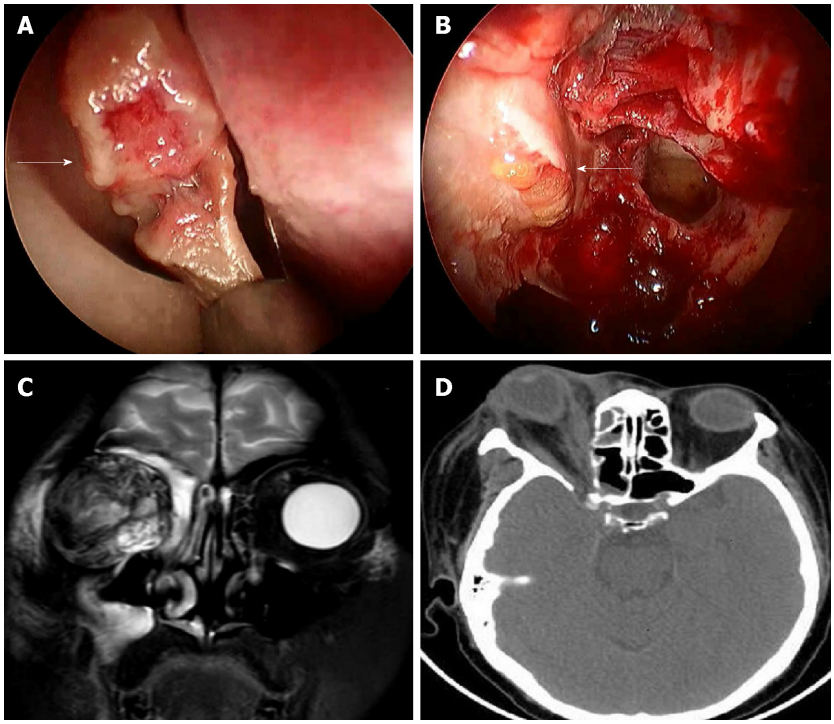

Figure 1 Nasal endoscopy, computed tomography, and magnetic resonance imaging images. A: Endoscopic sinus surgery showed that the middle turbinate turned to be necrotic and fragile; B: The orbital fat appeared dark yellow, losing its bright color; C: Magnetic resonance imaging T2-weighted coronal image; D: Axial computed tomography scan with soft tissue window revealed inflammatory changes in the orbital fat, right ocular proptosis, thickening of extraocular muscles, and the distorted eyeball.

amphotericin B, caspofungin, tigecycline, and sulperazone, but her condition deteriorated until finally hemoptysis led to her death.

DISCUSSION

The reported incidence of IFD in patients with leukemia ranges from 2% to 15%[9]. IFD remains a common cause of morbidity and mortality among patients with leukemia; it is mainly caused by *Candida* and *Aspergillus* species[10]. IFD caused by *Cunninghamella* in patients with acute leukemia is extremely rare. However, this kind of IFD usually appears as a disseminated type and has a very poor prognosis. Su *et al*[11] reported a disseminated *Cunninghamella* infection in a girl with acute lymphoblastic leukemia, who ultimately died of disseminated intravascular coagulopathy. Strasfeld *et al*[12] presented three cases of invasive *Cunninghamella* infection in allogeneic transplant recipients: two of the disseminated type and one pulmonary type. All patients died shortly after the confirmation of invasive *Cunninghamella* infection[12]. We searched the PubMed database for reports of IFD caused by *Cunninghamella*, presenting as the rhinocerebral type, for the period 1980 to 2017 and found cases in English-language articles that included clinical details.

To our knowledge, there have been only eight cases (including the present case) of IFD, caused by *Cunninghamella* and presenting as the rhinocerebral type, reported in English (Table 1)[13-19]. Among them, there were six males and two females. The male-to-female ratio was 3:1. The patients ranged in age from 15 to 70 years, with a mean age of 50.9 years. In this review, three patients lived in the United States, and the other five lived in Thailand, Bangladesh, Sri Lanka, Italy, and China, respectively. Seven (87.5%) patients had underlying conditions and only one (12.5%) patient had no accompanying disease. Among them, four (50%) patients had acute leukemia (two AML, one acute promyelocytic leukemia, and one mixed lineage T-cell and myeloid acute leukemia), three (37.5%) had diabetes mellitus, one (12.5%) had bone marrow transplantation, one (12.5%) had myelodysplasia, and one (12.5%) had sideroblastic anemia and hemochromatosis.

The most common symptoms in our review were facial pain/swelling (five patients, 62.5%) and fever (four patients, 50%), followed by nasal obstruction/rhinorrhea/epistaxis (three patients, 37.5%), epiphora (three patients,

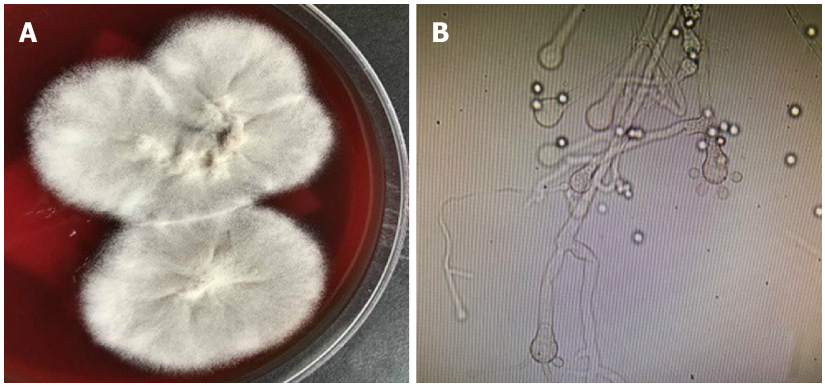

Figure 2 Culture results. A: Macroscopic appearance of C. *bertholletiae*; B: Microscopic morphology showing sporangiophore and sporangiola of C. *bertholletiae*. Lactophenol cotton blue staining. C. *bertholletiae*: *Cunninghamella bertholletiae*.

37.5%), and vision loss (two patients, 25%). Other symptoms included mental confusion (one patient, 12.5%), hearing loss (one patient, 12.5%), dyspnea (one patient, 12.5%), and purulent drainage in the oral cavity (one patient, 12.5%). In our review, the most commonly affected region was the paranasal sinuses (eight patients, 100%), followed by the orbit (three patients, 37.5%), brain (two patients, 25%), and lung (two patients, 25%). Payne *et al*[20] studied 41 cases of acute invasive fungal sinusitis and found that mucosal abnormalities of the middle turbinate and septum, specifically necrosis of the middle turbinate, could be important predictors of disease. Among eight patients, there were six with *Cunninghamella* infection confirmed by culture/biopsy from the nasal cavity, one with *Cunninghamella* infection confirmed by culture of the sputum, and one (our patient) with *Cunninghamella* infection confirmed by culture of the eye canthus secretions. It has been reported that middle turbinate biopsies have a sensitivity of 75% to 86% and a specificity of 100% for the diagnosis of acute invasive fungal sinusitis[21]. The middle turbinate has been found to be the most common site of invasion, followed by the maxillary and ethmoid sinuses. Our patient was found to have a necrotic and fragile middle turbinate during surgery, and postoperative pathology revealed mycotic infection.

In our review, four (50%) patients received drug and surgical treatments, while the other four (50%) received drug treatment only. Among the four patients receiving surgical treatment, all received nasal sinusectomy, two received orbit surgery, and one received jaw sinusotomy. In our review, all patients received antifungal drug treatment, such as amphotericin B (7/8, 87.5%), fluconazole (1/8, 12.5%), or posaconazole (1/8, 12.5%). Seven patients (all except Pt. 3) received amphotericin B treatment after culture/biopsy confirming *Cunninghamella* infection. Because the respiratory status of Patient 3 deteriorated quickly, he died before culture of his sputum confirmed *Cunninghamella* infection[15]. IFR is a lethal disease that has a very poor prognosis. In our opinion, confirmation by culture/biopsy and directed antifungal drug treatment are very important. Early empiric therapy must be started as soon as an invasive mold infection is suspected, and after confirmation and/or isolation of the fungus the treatment should be modified to ensure the appropriate drug and dosage[22]. Topical use of amphotericin B combined with endoscopic surgical debridement, followed by intravenous amphotericin B treatment, may constitute acceptable management for aggressive fungal infection[23]. Chen *et al*[24] studied 46 patients with invasive fungal sinusitis and suggested that early introduction of an anti-fungal agent and aggressive surgical debridement potentially decrease morbidity and mortality in high-risk patients. Other accompanying treatments should include tight regulation of blood glucose, management of diabetic ketoacidosis, and reversal of the underlying immunocompromised state when possible[25].

In our review, only three (3/8, 37.5%) patients survived; one had diabetes mellitus, one had diabetes mellitus and myelodysplasia, and one had no underlying disease. The others (5/8, 62.5%) died; four of them had acute leukemia, and the fifth had diabetes mellitus, sideroblastic anemia, and hemochromatosis. Turner *et al*[26] performed a systematic review of 52 studies and found that diabetic patients appear to have a better overall survival rate than patients with other comorbidities, while patients who have intracranial involvement, or who do not receive surgery as part of their therapy, have a poor prognosis. Schwartz *et al*[27] studied 54 consecutive patients with acute myelogenous leukemia and reported that major factors associated with cases ultimately developing IFD included the duration of chemotherapy, the number

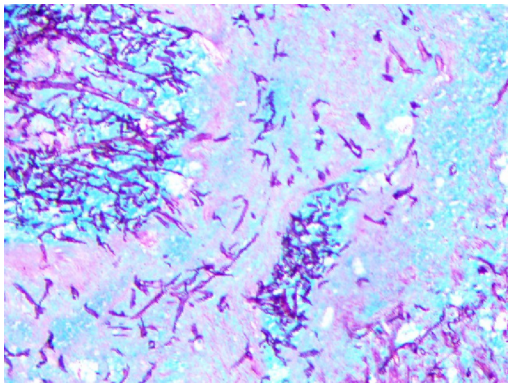

Figure 3 Histological findings. Histopathologic examination showed a large quantity of fungus mycelia and spores (gomori methenamine silver staining, × 200).

of sites colonized with fungi, and the number of fungal species isolated on certain surveillance cultures. According to the study of Dwyhalo *et al*[25], patients who are diagnosed and treated early, *i.e.*, when the fungal load is low, have the best outcomes. In our case, the patient's condition gradually stabilized after surgical debridement and antifungal drug treatment. However, she underwent chemotherapy again and her leukocyte count decreased, leading to fatal lung infection and hemoptysis.

CONCLUSION

IFR caused by *Cunninghamella* is very rare but has an extremely high fatality rate. The middle turbinate has been found to be the most common site of invasion, followed by the maxillary and ethmoid sinuses. Aggressive surgical debridements, followed by antifungal drug treatment both systematically and topically, are the most important fundamental treatments.

Table 1 Invasive fungal rhinosinusitis caused by *Cunninghamella* reported in English

Ref.	Sex/age	Region	Underlying conditions	Symptoms	Site(s) of involvement	Drug treatment	Surgery	Outcome
Brennan *et al*[13], 1983	M/70	United States	Diabetes mellitus, sideroblastic anemia, hemochromatosis	Facial pain and palsy, periorbital swelling, hearing loss, visual loss, fever, mental confusion	Nasal sinuses, orbit, brain	Amphotericin B	Orbital decompression, sinus surgery	Died
Chetchotisakd *et al*[14], 1991	F/68	Thailand	Diabetes mellitus	Headache, left eye pain	Nasal sinuses	Amphotericin B, 5-flucytosine	Sinus surgery	Survived
Kontoyiani *et al*[15], 1994	M/51	United States	Acute promyelocytic leukemia	Fever, nasal obstruction, dyspnea, fatigue,	Nasal sinuses, lung	Imipenem, vancomycin, trimethoprim-sulfamethoxazole, fluconazole, SCH 39304	No	Died
Ng *et al*[16], 1994	M/70	Bangladesh	Diabetes mellitus, myelodysplasia	Facial pain, fever, epistaxis	Maxillary sinus	Amphotericin B, rifampin	No	Survived
Jayasuriya *et al*[17], 2006	M/42	Sri Lanka	None	Periorbital oedema, epiphora	Nasal sinuses	Amphotericin B	No	Survived
Righi *et al*[18], 2008	M/41	Italy	Acute myeloid leukaemia	Facial swelling, palatal oedema, purulent drainage in the oral cavity	Nasal sinuses, orbit, brain	Amphotericin B	Sinus surgery, Bone marrow transplantation	Died
LeBlanc *et al*[19], 2013	M/15	United States	Mixed lineage T-cell and myeloid acute leukemia, bone marrow transplantation	Facial pain, fever, epiphora	Nasal sinuses	Amphotericin B	No	Died
Present case, 2017	F/50	China	Acute myeloid leukaemia	Ocular proptosis, pain, visual loss, epiphora, nasal obstruction and rhinorrhea	Nasal sinuses, orbit, lung	Amphotericin B, meropenem, metronidazole, tigecycline, posaconazole	Sinus surgery, orbital decompression, orbital content enucleation	Died due to leukemia relapse

REFERENCES

1 **Santos T**, Aguiar B, Santos L, Romaozinho C, Tome R, Macario F, Alves R, Campos M, Mota A. Invasive Fungal Infections After Kidney Transplantation: A Single-center Experience. *Transplant Proc* 2015; **47**: 971-975 [PMID: 26036497 DOI: 10.1016/j.transproceed.2015.03.040]

2 **Pagano L**, Caira M, Candoni A, Offidani M, Fianchi L, Martino B, Pastore D, Picardi M, Bonini A, Chierichini A, Fanci R, Caramatti C, Invernizzi R, Mattei D, Mitra ME, Melillo L, Aversa F, Van Lint MT, Falcucci P, Valentini CG, Girmenia C, Nosari A. The epidemiology of fungal infections in patients with hematologic malignancies: the SEIFEM-2004 study. *Haematologica* 2006; **91**: 1068-1075 [PMID: 16885047]

3 **Nicolato A**, Nouér SA, Garnica M, Portugal R, Maiolino A, Nucci M. Invasive fungal diseases in patients with acute lymphoid leukemia. *Leuk Lymphoma* 2016; **57**: 2084-2089 [PMID: 26949001 DOI: 10.3109/10428194.2016.1154957]

4 **Cohen-Abbo A**, Bozeman PM, Patrick CC. Cunninghamella infections: review and report of two cases of Cunninghamella pneumonia in immunocompromised children. *Clin Infect Dis* 1993; **17**: 173-177 [PMID: 8399862 DOI: 10.1093/clinids/17.2.173]

5 **Malkan AD**, Wahid FN, Rao BN, Sandoval JA. Aggressive Cunninghamella pneumonia in an adolescent. *J Pediatr Hematol Oncol* 2014; **36**: 581-582 [PMID: 25089609 DOI: 10.1097/MPH.0000000000000235]

6 **Zarei M**, Morris J, Aachi V, Gregory R, Meanock C, Brito-Babapulle F. Acute isolated cerebral mucormycosis in a patient with high grade non-Hodgkins lymphoma. *Eur J Neurol* 2000; **7**: 443-447 [PMID: 10971606]

7 **Ortín X**, Escoda L, Llorente A, Rodriguez R, Martínez S, Boixadera J, Cabezudo E, Ugarriza A. Cunninghamella bertholletiae infection (mucormycosis) in a patient with acute T-cell lymphoblastic leukemia. *Leuk Lymphoma* 2004; **45**: 617-620 [PMID: 15160928 DOI: 10.1080/1042819031000139693]

8 **Darrisaw L**, Hanson G, Vesole DH, Kehl SC. Cunninghamella infection post bone marrow transplant: case report and review of the literature. *Bone Marrow Transplant* 2000; **25**: 1213-1216 [PMID: 10849536 DOI: 10.1038/sj.bmt.1702395]

Cornely OA, Maertens J, Winston DJ, Perfect J, Ullmann AJ, Walsh TJ, Helfgott D, Holowiecki J,

9 Stockelberg D, Goh YT, Petrini M, Hardalo C, Suresh R, Angulo-Gonzalez D. Posaconazole vs. fluconazole or itraconazole prophylaxis in patients with neutropenia. *N Engl J Med* 2007; **356**: 348-359 [PMID: 17251531 DOI: 10.1056/NEJMoa061094]

10 **Hammond SP**, Marty FM, Bryar JM, DeAngelo DJ, Baden LR. Invasive fungal disease in patients treated for newly diagnosed acute leukemia. *Am J Hematol* 2010; **85**: 695-699 [PMID: 20652970 DOI: 10.1002/ajh.21776]

11 **Su YY**, Chang TY, Wang CJ, Jaing TH, Hsueh C, Chiu CH, Huang YC, Chen SH. Disseminated Cunninghamella bertholletiae Infection During Induction Chemotherapy in a Girl with High-Risk Acute Lymphoblastic Leukemia. *Pediatr Neonatol* 2016; **57**: 531-534 [PMID: 25440778 DOI: 10.1016/j.pedneo.2014.04.010]

12 **Strasfeld L**, Espinosa-Aguilar L, Gajewski JL, Stenzel P, Pimentel A, Mater E, Maziarz RT. Emergence of Cunninghamella as a pathogenic invasive mold infection in allogeneic transplant recipients. *Clin Lymphoma Myeloma Leuk* 2013; **13**: 622-628 [PMID: 23850285 DOI: 10.1016/j.clml.2013.05.002]

13 **Brennan RO**, Crain BJ, Proctor AM, Durack DT. Cunninghamella: a newly recognized cause of rhinocerebral mucormycosis. *Am J Clin Pathol* 1983; **80**: 98-102 [PMID: 6858971 DOI: 10.1093/ajcp/80.1.98]

14 **Chetchotisakd P**, Boonma P, Sookpranee M, Pairojkul C. Rhinocerebral mucormycosis: a report of eleven cases. *Southeast Asian J Trop Med Public Health* 1991; **22**: 268-273 [PMID: 1948290]

15 **Kontoyianis DP**, Vartivarian S, Anaissie EJ, Samonis G, Bodey GP, Rinaldi M. Infections due to Cunninghamella bertholletiae in patients with cancer: report of three cases and review. *Clin Infect Dis* 1994; **18**: 925-928 [PMID: 8086554 DOI: 10.1093/clinids/18.6.925]

16 **Ng TT**, Campbell CK, Rothera M, Houghton JB, Hughes D, Denning DW. Successful treatment of sinusitis caused by Cunninghamella bertholletiae. *Clin Infect Dis* 1994; **19**: 313-316 [PMID: 7986905 DOI: 10.1093/clinids/19.2.313]

17 **Jayasuriya NS**, Tilakaratne WM, Amaratunga EA, Ekanayake MK. An unusual presentation of rhinofacial zygomycosis due to Cunninghamella sp. in an immunocompetent patient: a case report and literature review. *Oral Dis* 2006; **12**: 67-69 [PMID: 16390472 DOI: 10.1111/j.1601-0825.2005.01154.x]

18 **Righi E**, Giacomazzi CG, Lindstrom V, Albarello A, Soro O, Miglino M, Perotti M, Varnier OE, Gobbi M, Viscoli C, Bassetti M. A case of Cunninghamella bertholettiae rhino-cerebral infection in a leukaemic patient and review of recent published studies. *Mycopathologia* 2008; **165**: 407-410 [PMID: 18340546 DOI: 10.1007/s11046-008-9098-z]

19 **LeBlanc RE**, Meriden Z, Sutton DA, Thompson EH, Neofytos D, Zhang SX. Cunninghamella echinulata causing fatally invasive fungal sinusitis. *Diagn Microbiol Infect Dis* 2013; **76**: 506-509 [PMID: 23602784 DOI: 10.1016/j.diagmicrobio.2013.03.009]

20 **Payne SJ**, Mitzner R, Kunchala S, Roland L, McGinn JD. Acute Invasive Fungal Rhinosinusitis: A 15-Year Experience with 41 Patients. *Otolaryngol Head Neck Surg* 2016; **154**: 759-764 [PMID: 26884367 DOI: 10.1177/0194599815627786]

21 **Middlebrooks EH**, Frost CJ, De Jesus RO, Massini TC, Schmalfuss IM, Mancuso AA. Acute Invasive Fungal Rhinosinusitis: A Comprehensive Update of CT Findings and Design of an Effective Diagnostic Imaging Model. *AJNR Am J Neuroradiol* 2015; **36**: 1529-1535 [PMID: 25882281 DOI: 10.3174/ajnr.A4298]

22 **Krcmery V**, Kunova E, Jesenska Z, Trupl J, Spanik S, Mardiak J, Studena M, Kukuckova E. Invasive mold infections in cancer patients: 5 years' experience with Aspergillus, Mucor, Fusarium and Acremonium infections. *Support Care Cancer* 1996; **4**: 39-45 [PMID: 8771293 DOI: 10.1007/BF01769874]

23 **Saedi B**, Sadeghi M, Seilani P. Endoscopic management of rhinocerebral mucormycosis with topical and intravenous amphotericin B. *J Laryngol Otol* 2011; **125**: 807-810 [PMID: 21729440 DOI: 10.1017/S0022215111001289]

24 **Chen CY**, Sheng WH, Cheng A, Chen YC, Tsay W, Tang JL, Huang SY, Chang SC, Tien HF. Invasive fungal sinusitis in patients with hematological malignancy: 15 years experience in a single university hospital in Taiwan. *BMC Infect Dis* 2011; **11**: 250 [PMID: 21939544 DOI: 10.1186/1471-2334-11-250]

25 **Dwyhalo KM**, Donald C, Mendez A, Hoxworth J. Managing acute invasive fungal sinusitis. *JAAPA* 2016; **29**: 48-53 [PMID: 26704655 DOI: 10.1097/01.JAA.0000473374.55372.8f]

26 **Turner JH**, Soudry E, Nayak JV, Hwang PH. Survival outcomes in acute invasive fungal sinusitis: a systematic review and quantitative synthesis of published evidence. *Laryngoscope* 2013; **123**: 1112-1118 [PMID: 23300010 DOI: 10.1002/lary.23912]

27 **Schwartz RS**, Mackintosh FR, Schrier SL, Greenberg PL. Multivariate analysis of factors associated with invasive fungal disease during remission induction therapy for acute myelogenous leukemia. *Cancer* 1984; **53**: 411-419 [PMID: 6581852 DOI: 10.1002/1097-0142(19840201)53:3<411::AID-CNCR2820530308>3.0.CO;2-E]

P- Reviewer: El-Shazly AE, Vento S

S- Editor: Ji FF **L- Editor:** Wang TQ **E- Editor:** Wu YXJ

Published By Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
Help Desk:https://www.f6publishing.com/helpdesk
https://www.wjgnet.com