

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Brain mucormycosis in a child with acute lymphoblastic leukemia ☆

Shahla Ansari Damavandi, MD^a, Shadi Adib, MD^b, Neda Ashayeri, MD^{c,*}

^a Professor of Pediatrics, Department of Hematology-Oncology, Ali Asghar Children's Hospital, Iran University of Medical Sciences, Tehran, IR

^b Resident of Pediatrics, Department of Hematology-Oncology, Ali Asghar Children's Hospital, Iran University of Medical Sciences, Tehran, IR

^c Fellowship of Hematology and Oncology, Department of Hematology-Oncology, Ali Asghar Children's Hospital, Iran University of Medical Sciences, Tehran, IR

ARTICLE INFO

Article history:

Received 9 May 2021

Revised 15 June 2021

Accepted 16 June 2021

Keywords:

Mucormycosis

Brain abscess

Acute lymphoblastic leukemia

ABSTRACT

This article reports a rare case of Brain Mucormycosis in a 12 year-old girl who presented with relapse Acute Lymphoblastic Leukemia (ALL). On the 12th day of chemotherapy, although there was no CNS symptoms, the second Lumbar Puncture (LP) revealed the CNS relapse which developed to brain abscess presenting with right side hemiparesis. The brain magnetic resonance imaging (MRI) and the brain biopsy revealed small, multifocal necrosis and acute inflammation with septal fungal hyphae branching, which was proven to be caused by Mucormycosis according to Polymerase Chain Reaction (PCR). The patient responded to treatment with intravenous liposomal Amphotericin B and Caspofungin after two months, suggesting that Brain Mucormycosis in ALL cases can be managed with sequential therapy by antifungals.

© 2021 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

Mucormycosis is a life-threatening fungal infection which is caused by opportunistic fungal species [1]. These infections are seen primarily in patients with diabetes mellitus, malignancy, and chronic immunosuppression patients, particularly in children receiving chemotherapy for hematological malignancies [2–4]. Mucormycosis can be associated with severe in-

fections, significant morbidity and mortality in immunosuppressed patients [2–4].

Isolated cerebral mucormycosis and brain abscess, without involving rhino-sinus areas, are uncommon central nervous system (CNS) complications and typically seen in patients with a history of intravenous drug abuse. These rare complications in immunosuppressed patients usually occur following fungal ascending from the nasal tracks to sinuses or orbital regions and then occasionally to the brain. [2] Brain

☆ Competing interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Correspondence author.

E-mail address: neda_ashayeri@yahoo.com (N. Ashayeri).

<https://doi.org/10.1016/j.radcr.2021.06.049>

1930-0433/© 2021 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

abscesses may cause mortality when the diagnosis is delayed. Recent studies have reported that the mortality rate caused by brain abscess in immunocompromised patients is 75%, but it is estimated to about 90% in fungal based infections [5]. Fungal infections of the CNS are hardly treated in immunocompromised patients. Severity of immunosuppression, history of fungal infections, and the ability of anti-fungal agent cross the blood-brain barrier are the most important factors affecting the outcome of the disease [6].

Case presentation

The patient was a 12 year-old girl with a history of B-cell ALL diagnosed at age of 5. She presented in Ali-Asghar Children's Hospital, Tehran, Iran, with chief complaint of enlargement of abdomen and bruising of the body. The patient had already completed a 2 year period of chemotherapy successfully at the time of the malignancy diagnosis, and she had been symptom free for 5 years.

Beside limited range of motion of the left knee and bone pain in both legs, general physical examination and neurological examination were normal. There was no sign of nasal inflammation, discharge and diplopia. In primary work-up, count blood cell (CBC), lumbar puncture (LP), renal and liver tests were normal, but bone biopsy from left leg came back positive for ALL. Chemotherapy was started instantly. On the 12th day of chemotherapy, although the patient did not have any CNS symptoms, the second LP showed lymphocytes of 2000. The CNS relapse was proven that time. After receiving one-year chemotherapy and 12 sessions radiotherapy, throughout maintenance chemotherapy, the patient experienced right side hemiparesis. The brain magnetic resonance imaging (MRI) ordered by neurology team revealed various small masses and lesions with abscess formation in the right frontal lobe and the right cerebellar hemisphere. Afterward, the abscess was surgically drained and open brain biopsy performed by neurosurgery team discovered extensive multifocal necrosis, acute inflammation and septal fungal hyphae branching. Mucormycosis was diagnosed based on positive result of polymerase chain reaction (PCR) for mucormycosis. The patient responded to treatment with intravenous liposomal amphotericin B (5 mg/kg/day) and caspofungin (70 mg/kg on the first day followed by 50mg/kg/day) after two months. The MRI following the treatment showed lesions' regression. Posaconazole (400 mg/day) was continued as the maintenance treatment along with the maintenance chemotherapy.

Discussion

Fungal infections are a major problem in children suffering from cancer. Mucormycosis is an invasive and rare fungal infectious disease that can be caused by any fungal species of the *Mucorales* order [5]. Mucormycosis is mainly limited to immunocompromised patients. Hematological malignancies, diabetes mellitus, transplantation, immunosuppressants in-

cluding antineoplastic chemotherapy and antirejection therapy are the main predisposing risk factors for mucormycosis [7]. Recent investigations have shown that mucormycosis is associated with high mortality rate in patients with the hematological malignancies or during induction chemotherapy [5,7].

Although mucormycosis in children is rare, it is associated more commonly with acute leukemia than with other conditions [9]. In a study, Bonifaz *et al.*, [8] considered 158 confirmed cases of mucormycosis, of which 14% were children. They also found that the major underlying predisposing factors were diabetes mellitus (68.18%) and hematologic diseases (27.7%) patients. A growing number of studies have shown mucormycosis in different organs of children with acute lymphoblastic leukemia. However, most published reports are single cases. For example, Dworsky *et al.*, [10] reported an invasive rhinocerebral mucormycosis in a 17 year-old female with ALL. Similarly, Samanta *et al.*, [11] detected rhinocerebral mucormycosis in a 8 year-old child having ALL, who was on prolonged chemotherapy and corticosteroid therapy. In another study, Irga *et al.*, [12] found a mucormycosis with thyroid involvement in a 11-year-old girl treated for ALL. Primary cutaneous [13], colonic and gastrointestinal mucormycosis [7] were reported previously in children with ALL. Several lines of studies have indicated that rhinocerebral mucormycosis is the most frequent and severe form, because of the spread of the fungi in facial and cerebral structures which may lead to early death or mutilating sequelae [14]. Roden *et al.*, [15] demonstrated that the incidence of rhinocerebral pattern in cases is 39%, while Bonifaz *et al.*, [8] reported the frequency of rhinocerebral pattern in 77.29% of cases.

In the current study, we report a rare case of ALL with brain mucormycosis. Hemiparesis and brain abscess were resulted as a severe consequence of the mucormycosis. CSF cultures throughout the period of hospital stay of the patient were negative, indicating absence of a disseminated infection. We identified mucormycosis using PCR method. Although culturing is a reliable method for the identification of the specific fungal species, cultures from infected tissue are usually negative, and the different zygomycetes may share similar morphology on histopathology [7]. Thus, molecular methods using PCR of fungal DNA from open biopsy samples provide accurate identification of zygomycetes species.

In this case combination therapy with liposomal amphotericin and caspofungin provided partial treatment; however, posaconazole administration resulted in good clinical condition and hemiparesis treatment after 4 months. Recent reports have considered liposomal liposomal amphotericin as a choice of antimycotic therapy in ALL patients [16-18].

Flair and T2 Images in Figure 1 show high signal intensity of bilateral centrum semiovale, white matter of frontal lobes (predominantly in Rt side) and cerebellar hemispheres that contain some low signal nodules.

After contrast administration some nodular and ring enhancing nodules at corticomedullary junction of bilateral centrum semiovale, frontal lobes and cerebellar hemispheres are found.

These findings are in favor of fungal abscess with peripheral edema.

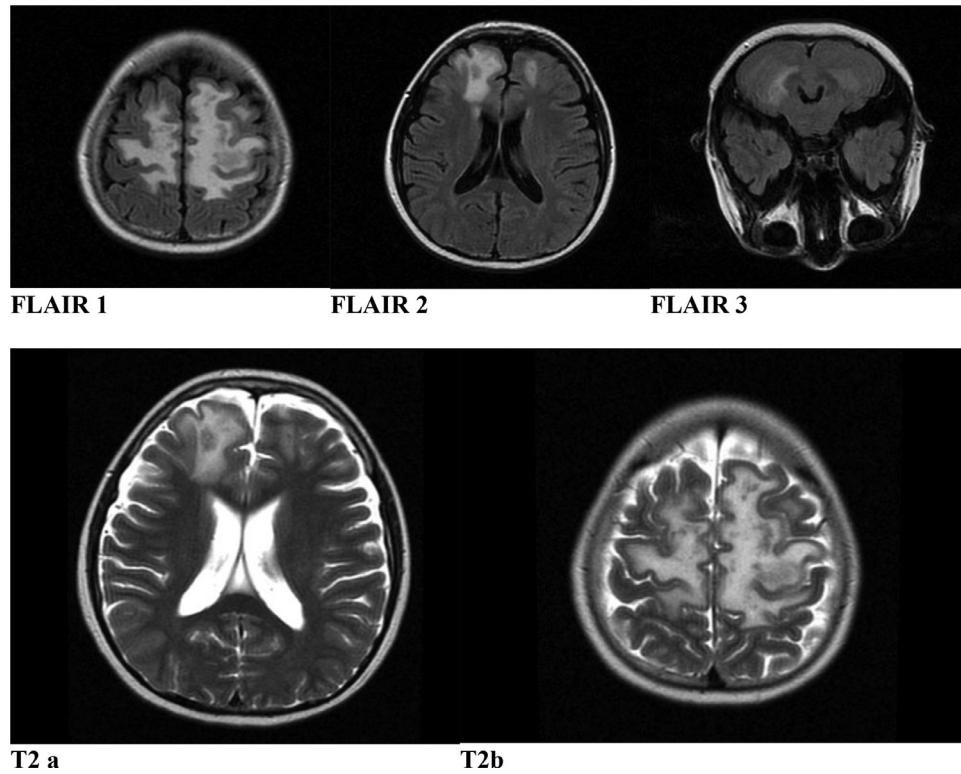


Fig. 1 – Magnetic resonance imaging (MRI) of the brain which revealed various small masses and lesions with abscess formation.

Conclusion

In conclusion, our report has revealed that brain abscesses and hemiparesis can be resulted as a complication of mucormycosis in children receiving chemotherapy and, therefore, physicians must be aware of this rare and life-threatening condition. Invasive diagnostic method of brain biopsy is essential to detect the causative organism and to start targeted antimicrobial therapy. Prolonged administration of antimycotic is necessary even in the setting of ongoing chemotherapy.

Patient consent

The authors obtained written informed consent from the patient for submission of this manuscript for publication.

REFERENCES

- [1] Epstein NE, Hollingsworth R, Black K, Farmer P. Fungal brain abscesses (aspergillosis/mucormycosis) in two immunosuppressed patients. *Surg Neurol* 1991;35:286–9.
- [2] Verma A, Brozman B, Petito CK. Isolated cerebral mucormycosis: report of a case and review of the literature. *J Neurol Sci* 2006;240(1-2):65–9.
- [3] Ito T, Mori H, Takeda A, Suzuki H, Sonoda K, Tanno K, et al. A case of childhood acute lymphoblastic leukemia associated with cutaneous mucormycosis. *Rinsho Ketsueki* 1982;23:511–18.
- [4] Sh Ansari, Shirzadi E, Elahi M. The Prevalence of fungal infections in children with hematologic malignancy in Ali-Asghar Children Hospital between 2005 and 2010. *Iran J Ped Hematol Oncol* 2015;5(1):1–10.
- [5] Gupta A, Jain S, Agrawal C, Kapoor G. Successful outcome of mucormycosis in two children on induction therapy for acute lymphoblastic leukemia. *Indian J Med Paediatr Oncol* 2013;34:313–16.
- [6] Levy V, Rio B, Bazarbachi A, Hunault M, Delmer A, Zittoun R, et al. Two cases of epidemic mucormycosis infection in patients with acute lymphoblastic leukemia. *Am J Hematol* 1996;52:64–5.
- [7] Lin WY, Chang TK, Chou CM, Shen CY, Wang JD. Intraabdominal mass as presentation of colonic mucormycosis in a child with acute lymphoblastic leukemia. *J Pediatr Hematol Oncol* 2011;33:e72–4.
- [8] Bonifaz A, Tirado-Sanchez A, Calderon L, Romero-Cabello R, Kassack J, Ponce RM, et al. Mucormycosis in children: a study of 22 cases in a Mexican hospital. *Mycoses* 2014;57(Suppl 3):79–84.
- [9] Pagano L, Offidani M, Fianchi L, Nosari A, Candoni A, Picardi M, et al. Mucormycosis in hematologic patients. *Haematologica* 2004;89:207–14.
- [10] Dworsky ZD, Bradley JS, Brigger MT, Pong AL, Kuo DJ. Multimodal Treatment of Rhinocerebral Mucormycosis in a Pediatric Patient With Relapsed Pre-B Acute Lymphoblastic Leukemia. *Pediatr Infect Dis J* 2018;37(6):555–8.
- [11] Samanta DR, Senapati SN, Sharma PK, Shruthi BS, Paty PB, Sarangi G. Hard palate perforation in acute lymphoblastic

- leukemia due to mucormycosis - a case report. *Indian J Hematol Blood Transfus* 2009;25:36–9.
- [12] Irga N, Kosiak W, Jaworski R, Komarnicka J, Birkholz D. Hyperthyroidism secondary to disseminated mucormycosis in a child with acute lymphoblastic leukemia: case report and a review of published reports. *Mycopathologia* 2013;175:123–7.
- [13] Sankar J, Arun S, Sankar MJ, Seth R, Thavraj V, Kabra SK, et al. Primary cutaneous mucormycosis during induction chemotherapy in a child with acute lymphoblastic leukemia'. *Indian J Pediatr* 2009;76:1161–3.
- [14] Popa G, Blag C, Sasca F. Rhinocerebral mucormycosis in a child with acute lymphoblastic leukemia: a case report. *J Pediatr Hematol Oncol* 2008;30:163–5.
- [15] Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Infect Dis* 2005;41:634–53.
- [16] Herbrecht R, Letscher-Bru V, Bowden RA, Kusne S, Anaissie EJ, Graybill JR, et al. Treatment of 21 cases of invasive mucormycosis with amphotericin B colloidal dispersion. *Eur J Clin Microbiol Infect Dis* 2001;20:460–6.
- [17] Hayes-Lattin B, Maziarz RT. Update in the epidemiology, prophylaxis, and treatment of fungal infections in patients with hematologic disorders. *Leuk Lymphoma* 2004;45:669–80.
- [18] Bjorkholm M, Runarsson G, Celsing F, Kalin M, Petrini B, Engervall P. Liposomal amphotericin B and surgery in the successful treatment of invasive pulmonary mucormycosis in a patient with acute T-lymphoblastic leukemia. *Scand J Infect Dis* 2001;33:316–19.