Medical Mycology Case Reports 11 (2016) 16–20

Contents lists available at ScienceDirect

Medical Mycology Case Reports

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

Current strategies against invasive fungal infections in patients with aplastic anemia, strong power and weak weapon, a case report and review of literature

Omid Reza Zekavat [a,b], Ali Amanati [c,d,*], Fazl Saleh [b], Babak Abdolkarimi [b], Gholamreza Fathpour [b], Parisa Badiee [c], Bita Geramizadeh [e]

[a] Hematology Research Center, Namazi Hospital, Karimkhan Zand St., Shiraz 7193711351, Iran
[b] Department of Pediatric Oncology, Amir Oncology Hospital, Farhang Shahr, Shiraz 7187915998, Iran
[c] Professor Alborzi Clinical Microbiology Research Center, Namazi Hospital, Karimkhan Zand St., Shiraz 7193711351, Iran
[d] Department of Pediatric Infectious Diseases, Namazi Hospital, Karimkhan Zand St., Shiraz 7193711351, Iran
[e] Department of Pathology Transplant Research Center, Namazi Hospital, Karimkhan Zand St., Shiraz 7193711351, Iran

ARTICLE INFO

Article history:
Received 26 February 2016
Accepted 7 March 2016
Available online 8 March 2016

Keywords:
Anemia, Aplastic
Mucormycosis
Aspergillosis
Antifungal agents

ABSTRACT

We report an 18 year old boy with Aplastic anemia complicated by serious fungal rhinosinusitis. Despite prompt treatment and early repeated surgical debridements, he died after about more than 6 weeks of hard challenges with fungal infections. Current strategies against invasive fungal infections (IFIs) in patients with Aplastic anemia may be inadequate for the management of serious complications. Antifungal prophylaxis is highly recommended in pre-transplant period for severe form of Aplastic anemia.

1. Introduction

Aplastic anemia is characterized by bone marrow failure and marked decrease in all marrow elements. In severe form of *Aplastic anemia*, rapid bone marrow transplantation after primary workup is life saving; however, protected environment and prevention of opportunistic infections may be difficult in these cases [1].

Most patients with *Aplastic anemia* experience repeated episodes of infection during their life. Gram positive (predominantly gram-positive cocci) and gram negative organisms (especially Multi-Drug Resistance (MDR) negative bacilli) are the most common causes of infections, but IFIs remain the main cause of death and increase the mortality among respective patients [2,3]. *Aspergillosis* and *Mucormycosis* are the most common mold infections in patients with *Aplastic anemia* [2].

In reported case series by Valera (2011), in 32 patients with acute invasive fungal rhinosinusitis, all deaths were reported among patients with *Aplastic anemia* despite surgical debridement and systemic antifungal therapy [4].

Severe neutropenia predisposes these patients to more severe forms of IFIs with a wide range of clinical manifestations. Gastrointestinal [5], upper air way [6], musculoskeletal [7] cardiac [8], renal [9], disseminated infection [10] and Rhinocerebral/sino-orbital/rhinosinusitis [11] among the most common reported manifestations of IFIs in patients with *Aplastic anemia*. Of these conditions, the last one is the most serious and fatal [4]. We report on a serious fungal infection in a case of *Aplastic anemia* and offer an appropriate strategy for the treatment and prevention in such patients.

2. Case

An 18 year old boy, known case of *Aplastic anemia* since 7 years ago, admitted with severe headache and fever in emergency ward. He was a candidate for bone marrow transplantation because of standard treatment failure that included corticosteroid, anti-thymocyte globulin (ATG) and cyclosporine, and put on in transplant waiting list. He had frequently received blood and platelet transfusion due to low hemoglobin (Hb) level and often nose bleeding.

On admission, he had severe leukopenia [white blood cell count (WBC): 100 (without cell differentiation)], anemia (Hb: 6.5) and severe thrombocytopenia (platelet count: 6000). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were 130 and 48, respectively.

After initial assessment, broad spectrum antibiotics (Piperacillin-Tazobactam) were started for him. Two days later, he developed pain, swelling and redness of the right side of face.

* Corresponding author at: Department of Pediatric Infectious Diseases, Namazi Hospital , Karimkhan Zand St., Shiraz 7193711351, Iran.

http://dx.doi.org/10.1016/j.mmcr.2016.03.003

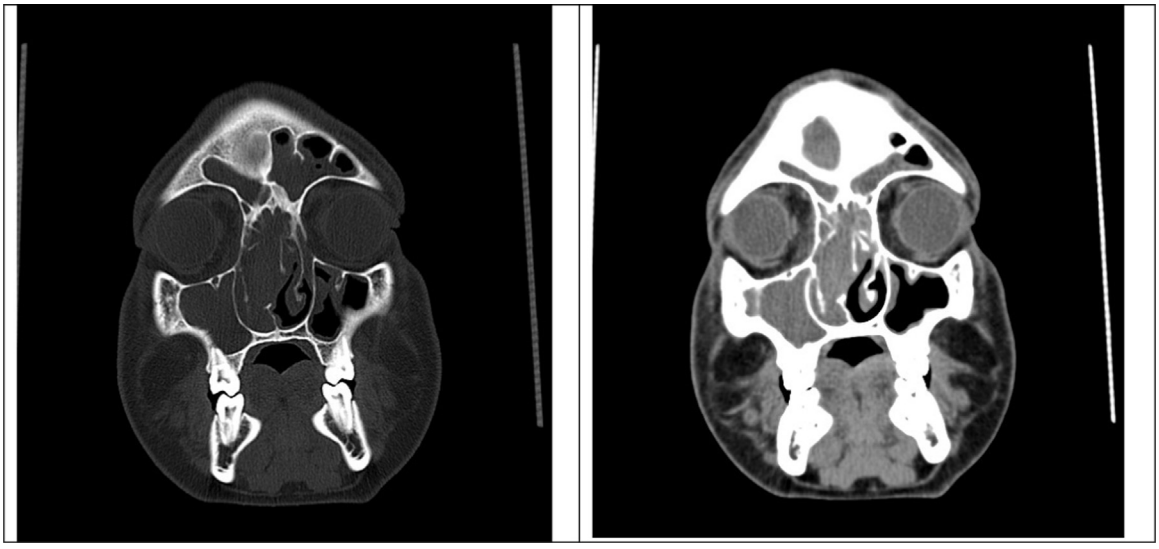

Fig. 1. Para-nasal CT scan (PNS CT) of patient before second surgical debridement which revealed complete right maxillary sinus opacity and involvement of bilateral ethmoid sinuses without any obvious bone destruction.

Gradually, the patient exhibited high grade fever, chills, intolerable headache and periodic disorientation, so due to poor clinical response, an antifungal agent (Amphotericin-B deoxycholate) was added to his antibiotic regimen on fifth day of admission.

In serial physical examination (after primary unilateral face swelling and cellulitis), he developed necrotic lesions in soft and hard palate followed by nasal septum, right alar groove and right nasolabial fold necrosis.

Tomography scan (CT scan) was requested, which revealed right maxillary and ethmoidal sinus involvement (Fig. 1).

Surgical consult has been also requested for diagnostic aspiration and evaluation for surgical debridement. Despite low platelet count, after receiving single donor platelet transfusion, right maxillary sinus debridement was performed and samples were sent for pathology. Fungal elements similar to mucoral hyphae were reported by pathologist.

After primary aspiration, right maxillary sinus debridement was performed during single donor platelet transfusion and samples were sent for pathology. Upon early surgical debridement and short time clinical improvement, all signs and symptoms exacerbated again after few days. Caspofungin was added and second surgical debridement planned 10 days after the first one, and has been organized for short interval surgical sinus debridements during platelet transfusion, till it becomes completely clear.

In the next surgical debridement tissue samples were cultured on Sabouraud dextrose agar (Merck, Darmstadt, Germany) and also examined for Aspergillus and Candida DNA by real time polymerase chain reaction (PCR) and Mucoral by nested PCR [12,13]. Bacterial culture and specimen were sent for microbiology and pathology, respectively.

Other successful debridements were done twice in short intervals. Finally, all involved sinuses, nasal cavity and overlying soft tissue were completely removed by anterior and posterior ethmoidectomy and sphenoidectomy. Also, posterior part of septum was removed. Detailed information about time and results of clinical samples were included in Table 1.

Adjuvant therapy with gamma interferon 100 μgr/day in combination with Granulocyte-colony stimulating factor (G-CSF) [300 μgr/day primarily and then with full dose of 600 μgr/day in two divided doses] was added to the broad antibacterial and antifungal treatments.

Other assessments including blood culture and urine culture were negative and chest x-ray, abdominal ultrasonography and echocardiography were normal in primary evaluations.

However in serial chest x-rays, early possible signs of pulmonary involvement detected in about 3 weeks after his admission (Fig. 2).

Bilateral well-circumscribed ground-glass gray opacities were detected in these chest x-rays confirmed by spiral chest CT scan (Fig. 3).

Our further investigation into fungal infection revealed positive *Mucormycosis*, *Aspergellosis* and *Candidiasis* by PCR and positive fungal culture for *Aspergillus flavus* and *Candida albicans* in repeated debridement (Fig. 4C).

No positive culture was obtained from *Mucormycosis*. During admission, the patient had several positive blood cultures (Table 2). His antibiotic was changed based on antibacterial susceptibility test. Sinus debridement during antifungal treatment was done in four times, but the patient's condition gradually worse and eventually expired.

Table 1
Summary information of repeated debridement and direct mycology test results.

	Date*			pathology	Tissue PCR *Aspergillosis*	Tissue PCR *Mucormycosis*	Tissue PCR *Candida*	Culture
First surgical debridement	20	July	2015	*Mucormycosis*	Not sent	Not sent	Not sent	
Second surgical debridement	30	July	2015	*Mucormycosis*	+	Neg.	Neg.	
3th surgical debridement	7	August	2015	*Mucormycosis*	+	Neg.	+	+**
4th surgical debridement	21	August	2015	*Mucormycosis*	+	+	+	

* Admission date: 13 July 2015.
** Aspergillosis Flavus.