

Spontaneous pneumothorax followed by reversed halo sign in immunocompromised patient with pulmonary mucormycosis

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ABSTRACT

Mucormycosis, an invasive fungus with a variety of clinical presentation, is a devastating infection in immunocompromised host. Here an unusual case of pulmonary mucormycosis is introduced in an immunodeficient patient in which pneumothorax was followed by reversed halo sign (RHS). The clinicians, who visit immunocompromised persons with pneumothorax, should be considerate to take immediate imaging and pathologic measures to confirm or reject mucormycosis.

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1. Introduction

Mucormycosis is a ubiquitous fungus that lives in spoiled vegetation and soil. Human can be infected through inhalation, ingestion and skin inoculation [1,2]. Immunocompromised patients might bear a variety of presentations such as rhino-orbito-cerebral, pulmonary, gastrointestinal, cutaneous, central nervous system and disseminated form [1]. Rhino-orbito-cerebral and pulmonary mucormycosis are the most common forms; the latter progresses rapidly to devastating diseases [1].

Presentation of pulmonary mucormycosis may be confused with several infectious and non infectious diseases; therefore its diagnosis is difficult [3]. Chest CT scan of a patient with pulmonary mucormycosis might demonstrate such presentations as air crescent sign, CT halo sign, solitary or multiple pulmonary nodules or masses, bronchopulmonary fistula and pulmonary artery pseudo aneurysm [1,4].

The occurrence of pneumothorax and its subsequent RHS along with sinusitis, supported by radiology and pathology in a 33 years old patient, is considered as a rare case of pulmonary mucormycosis.

2. Case

Following is the treatment history of a man, 33 years old in July 2014 (day +14), when he died in our hospital as a result of multi-organ failure. He was a farmer, married, with no history of alcohol consumption, illicit drugs use and extramarital relationships.

On day –330: Because of edema he visited a medical center in another city, where he was admitted and membranous glomerulonephritis was diagnosed. Consequently the followings administered; prednisolone and cyclosporine for 2 months, cellcept for 1 month, prednisolone and cyclophosphamide for 7 months.

On day –75: Because of progressive generalized edema he was admitted again. He was discharged under treatment with prednisolone (50 mg/daily) and tacrolimus (1 cap/BD). During the next 2 months he was feeling fine. On day –28, he travelled to village for a few days and he had close contact with sheep. On day –14 the patient reported fever, cough and dyspnea with mild erythema and pain in right eye. Anorexia, weakness, dyspnea and conjunctivitis developed and persisted despite of outpatient anti-biotic treatment.

In the emergency department (day 0): The patient suffered from dyspnea, weakness and right eye pain. On examination, he was agitated but completely conscious with diaphoretic skin. The vital signs have been as follows; temperature, 36.7 C; blood pressure, 100/60 mmhg; pulse rate, 99 beats per minute; respiratory rate, 22 beats per minute and oxygen saturation in air

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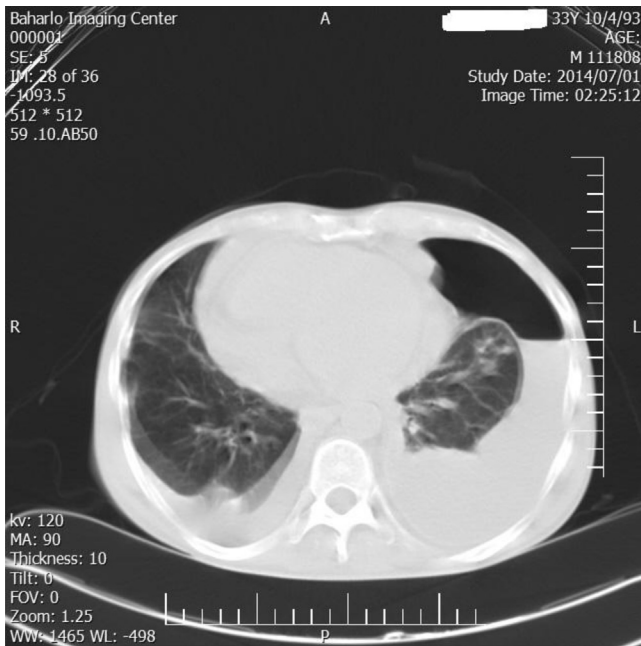


Fig. 1. Axial noncontrast chest computed tomography (CT) image on day 0: showing large pneumothorax with pleural effusion.

room, 99%. He had suprasternal retraction with nasal flaring. In right eye, there was moderate conjunctivitis with eyelid erythema; its movement was normal. The tongue and buccal mucosa were covered with multiple white vegetative lesions. The left lung vesicular sounds decreased with fine rales in both bases. The abdomen was distended without tenderness. There was +3 pitting edema in extremities.

The first day chest CT scan revealed large pleural effusion with pneumothorax in the left side and a shift of mediastinum to the right side. There were also multiple pulmonary nodules with right side pleural effusion (Fig. 1). Consequently drainage with chest tube was administered by the surgeon immediately. Because of the immunocompromised state of the patient, parenteral trimethoprim-sulfamethoxazole (160 mg/IV/TDS) and meropenem (1 g/IV/BD) were administered for pneumocystis jiroveci and multi drug resistant organisms. We also started fluconazole for oral lesions.

On day +3, right eye erythema was extended with small size necrosis in right nasal ala without bleeding (Fig. 2). The tongue's white vegetative plaques turned to brown. With doubt of rhino-orbital mucormycosis, biopsies of tongue and nasal septa were carried out and amphotericin B deoxycholate (1 mg/kg/daily) was administered. On day +4, paranasal sinuses (PNS) CT scan revealed soft tissue density lesion in left ethmoid sinus and nasal passage with extension to left orbit (Fig. 3).

On day +4, he was transferred to Intensive Care Unit (ICU)



Fig. 2. Right eye conjunctivitis with medial side necrosis and black scar in right nasal ala.

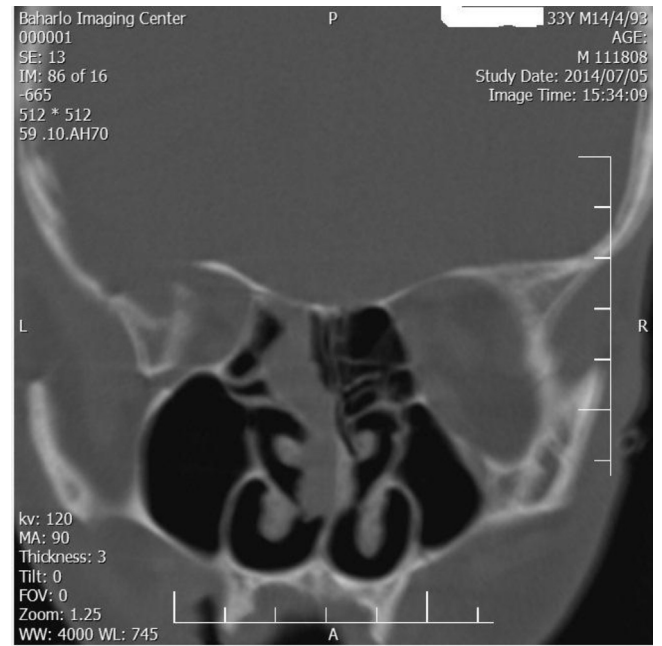


Fig. 3. Coronal PNS CT scan shows soft tissue density lesion in ethmoid sinus with extension to orbit without bone destruction.

because of respiratory distress and was intubated after 48 h; his conscious level was 14+T/15. Smear of sputum for acid fast bacilli, stain and culture of sputum for pneumocystis jiroveci were negative. HIV antibody test, D-dimer Enzyme-Linked Immunosorbent Assay (ELISA) and collagen vascular diseases screening tests were negative (Table 1). Pleural fluid cytologic examination and Polymerase Chain Reaction (PCR) for fungi were negative.

On day +6, laboratory results revealed pancytopenia (Table 1), however in peripheral blood smear there was no schistocyte or immature cells. Bone marrow biopsy which could help in finding the cause of pancytopenia was nevertheless postponed due to the patient's poor condition and low platelet count. Meanwhile his blood pressure was decreased and we started inotropic drugs. Hemodynamic instability of the patient prohibited further attempts such as bronchoscopy and CT guided lung biopsy to identify the causative agent.

On day +9, chest CT-scan showed RHS with multiple nodules (Fig. 4). This was considered as indicating invasive pulmonary mucormycosis. The patient's condition was downgraded on day +11. His level of consciousness suddenly decreased to 4+T/15. Also, in right eye lid, nose and trachea, bleeding appeared. Unfortunately, he died on day +14.

Histopathology of tongue biopsy, revealed mucormycosis (Figs. 5 and 6). Section of tongue biopsy showed ulcerated squamous epithelial mucosa with subepithelial fibro fatty tissue and skeletal muscle fibers of tongue that is on site of ulceration. The nonseptate short and wide hyphae of mucormycetes were present. The inflammatory granulation tissue and inflammatory multinucleated giant cells were also seen in Gimsa staining, but no cyst and trophozoite of pneumocystis jiroveci were identified.

3. Discussion

Pulmonary mucormycosis is a devastating infection when it affects immunocompromised patients such as diabetes mellitus, hematologic malignancies, chronic renal failure, post transplantation and immunosuppressed persons [5]. Herein, we present a

Table 1

Blood tests results obtained In the day 0, day +6, day +11, day +13.

Variable	Reference range	Day 0	Day +6	Day +11	Day +13
White blood cell (per mm ³)	4000–10000	5300	8800	3600	2700
Hemoglobin (g/dl)	13–17	9.4	12	8.2	7.3
Platelets (per mm ³)	140000–400000	102000	143000	22000	25000
Sodium (mmol/Liter)	134–147	130	143	142	139
Potassium (mmol/Liter)	3.5–5.5	4.2	3.9	3.9	4.2
Urea nitrogen (mg/dl)	19–44	164	43	153	182
Creatinine (mg/dl)	0.5–1.4	2.4	0.9	1.4	2
Aspartate aminotransferase (IU/L)	Up to 37	143	36		
Alanine aminotransferase (IU/L)	Up to 41	41	46	17	
Serum Albumin (gm/dl)	3.5–5.5	3.9	3.9	2.8	
Erythrocyte sedimentation rate (mm)	Up to 20		24		90
C-Reactive protein (mg/L)	Up to 10			38.2	80
Anti ds-DNA Ab (CLIA)				2.5	
ANA (CLIA)	Positive > 10			1.2	
C3 (Immunoturbidimetric) (mg/dl)	90–180			45	
C4 (Immunoturbidimetric) (mg/dl)	10–40			16	
CH50 (ELISA) (%)	≥ 90			90	
ANCA c	Up to 1/8			Negative	
ANCA p	Up to 1/8			Negative	



Fig. 4. Chest CT scan on day +9 hospital day after tube thoracostomy: showing the reversed halo sign (RHS): a ring of consolidation (black arrow) with central grand glass opacity and bilateral pleural effusion.

rhino-orbital mucormycosis with pulmonary involvement. The first chest CTscan imaging showed pneumothorax that was followed by RHS. Reticulation inside the RHS, presence of pleural effusion, multiple nodules and concomitant rhino-orbital mucormycosis as well as documented pathology [6,7], collectively were considered as indicating that pulmonary involvement has been due to mucormycosis. The pathological finding is achieved by tongue tissue; lung biopsy has not been possible due to poor condition of the patient.

Our case was an immunocompromised patient with documented rhino-orbital mucormycosis (Figs. 3, 5 and 6). Chest CT scan showed bilateral pleural effusion, multiple nodules and RHS with thin reticulation (Figs. 1 and 4). All these findings guided us to pulmonary mucormycosis. Although histopathology findings are usually needed to establish the diagnosis of pulmonary mucormycosis, using CT imaging and clinical presentation we can avoid the invasive procedures such as lung biopsy [8].

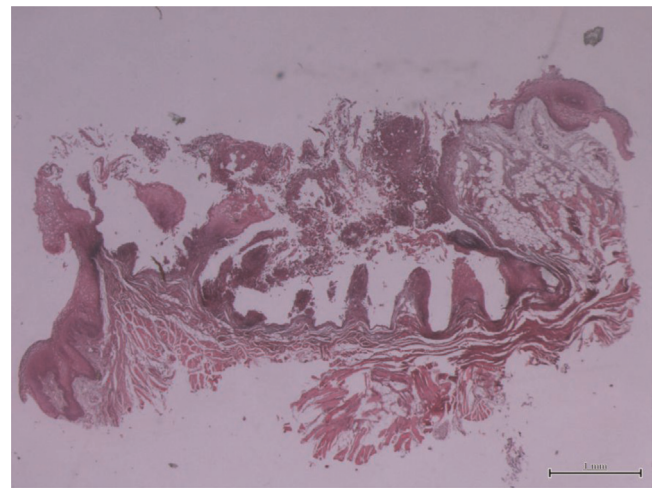


Fig.5. Section of tongue biopsy: showing ulcerated squamous epithelial mucosa with subepithelial fibro fatty tissue and skeletal muscle fibers.

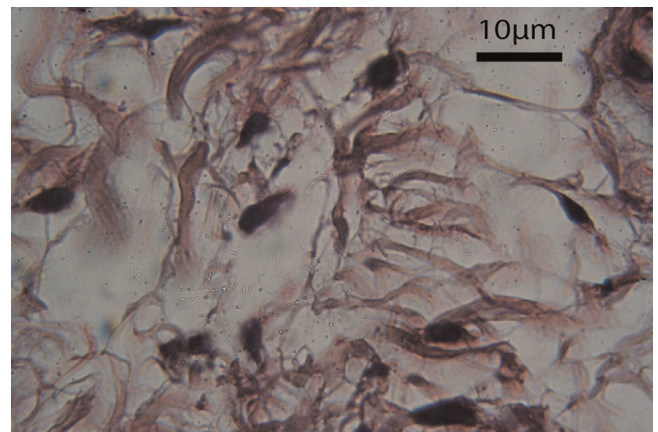


Fig. 6. The nonseptate short and wide hyphae of mucormycetes.

There are few case reports of pneumothorax in pulmonary mucormycosis, some of which are iatrogenic during mechanical ventilation and bronchoscopic procedure [9–11]. Combined mucormycosis and methicillin-resistant staphylococcus aureus (MRSA) were found to be responsible for life threatening

pneumothorax in an immunocompromised patient [12]. Mucormycosis and aspergillus have been recognized as leading to pneumonia and pneumothorax in a dialysis patient [13]. However, spontaneous pneumothorax in pulmonary mucormycosis that is followed by RHS seems to be a unique case.

Based on patient's background and clinical signs, amphotericin B deoxycholate (1 mg/kg/daily) was started immediately. The lower dose of antifungal drug has been due to the patient's renal insufficiency. Ambisome would have certainly been a better choice than amphotericin B; however, the former has not been available in Iran. However the lack of bone erosion in sinus CT scan, delay in pathologic result and patient's poor clinical condition, lead into the reluctance of surgeon for extensive debridement that had negative impact on patient's prognosis.

Pneumothorax which is due to mucormycosis can be fatal particularly in immunocompromised persons, so clinicians should take immediate measures (follow up imaging and pathology) to confirm or reject the presence of invasive fungal infection. If confirmed, antifungal therapy is necessary as soon as possible.

Conflict of interest

The authors declare that there is no conflict of interest.

Ethical form

The form has been filled and submitted alongside this manuscript.

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References

- [1] M. Martinello, A. Nelson, A. Bignold, D. Shaw, We are what we eat. Invasive intestinal mucormycosis: a case report and review of the literature, *Med. Mycol. Case Rep.* 1 (2012) 52–55.
- [2] A.M. Sarrami, M. Setareh, M. Izadinejad, N. Afshar-Moghaddam, M. M. Baradaran-Mahdavi, et al., Fatal disseminated mucormycosis in an immunocompetent patient: a case report and literature review, *Int. J. Prev. Med.* 4 (12) (2013) 1468–1471.
- [3] A. Busca, G. Limerutti, F. Locatelli, A. Barbui, F.G. De Rosa, M. Falda, The reversed halo sign as the initial radiographic sign of pulmonary zygomycosis, *Infection* 40 (2012) 77–80.
- [4] H.P. Mc Adams, M.R. De christensone, D.C. Strollo, E.F. Patz JR, Pulmonary mucormycosis: radiologic findings in 32 cases, *Am. J. Radiol.* 168 (1997) 1541–1548.
- [5] S. Sarkar, D. Jash, A. Maji, M.K. Maikap, Solitary pulmonary nodule: a rare presentation of pulmonary mucormycosis in an immunocompetent adult, *Lung India* 31 (1) (2014) 70–72.
- [6] E. Marchiori, E.M. Marom, G. Zanetti, B. Hochegger, K.L. Irion, M.C.B. Godoy, Reversed halo sign in invasive fungal infections; criteria for differentiation from organizing pneumonia, *Chest* 142 (6) (2012) 1469–1473.
- [7] S.P. Georgiadou, N.V. Sipsas, E.M. Marom, D.P. Kontoyiannis, The diagnostic value of halo and reversed halo sign for invasive mold infections in compromised host, *Clin. Infect. Dis.* 52 (2011) 1144–1155.
- [8] M.C.B. Goddoy, C. Viswanathan, E. Marchiori, M.T. Truong, M.F. Benveniste, S. Rossi, et al., The reversed halo sign: update and differential diagnosis, *Br. J. Radiol.* 85 (2012) 1226–1235.
- [9] Y. Morimatsu, A. Sano, N. Yukutake, K. Nishimura, H. Aizawa, A case of recipient of kidney transplantation presenting life threatening pneumothorax due to the rupture of intrapulmonary multiple infections cavities caused by *Absidia corymbifera* and methicillin-resistant *Staphylococcus aureus*, *Kansenshogaku Zasshi* 78 (11) (2004) 984–988.
- [10] H. Nagakava, H. Igar, K. Konishi, F. Kashizaki, M. Aoyama, A. Watanabe, et al., An autopsy case of tension pneumothorax due to the rupture of intrapulmonary cavity by mucormycosis during treatment with ventilator, *Med. Mycol. J.* 54 (3) (2013) 285.
- [11] J.G. Sales-Badia, V.Z. Hervas, J.M. Galbis-Caravajal, Importance of the reversed halo sign for the diagnosis of angioinvasive pulmonary aspergillosis, *Arch. Bronconeumol.* 45 (5) (2009) 256–261.
- [12] Y. Morimatsu, A. Sano, N. Yukutake, H. Imaoka, K. Nishimura, H. Aizawa, A case of recipient of kidney transplantation presenting life threatening pneumothorax due to the rupture of intrapulmonary multiple infections cavities caused by *Absidia corymbifera* and methicillin resistant *Staphylococcus aureus*, *Kansenshogaku Zasshi* 78 (11) (2004) 984–988.
- [13] Y. Imai, Y. Adachi, T. Kimura, C. Nakano, T. Shimizu, M. Shi, et al., An autopsy case of pulmonary fissure induced by zygomycosis, *Int. J. Gen. Med.* 6 (2013) 575–579.