Case Report

Pulmonary Mucormycosis Disseminating Locally to Cause Spinal Mucormycosis: An Autopsy Study

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Abstract

A thirty-six-year-old male, known case of disseminated pulmonary tuberculosis post anti-tubercular therapy, diabetes mellitus type 3C, chronic pancreatitis, and alcohol dependence syndrome, presented with cough and shortness of breath. Chest X-ray and non-contrast computed tomography showed features of pneumonia involving the right upper lobe of the lung. Laboratory investigations revealed features of diabetic ketoacidosis. Later, a high-resolution computed tomography of the thorax revealed consolidation with cavitation in the right upper lobe and multiple nodules with a rim of ground-glass haze (halo sign).

During management, he developed a rapidly progressive motor deficit in the lower limb, followed by a sensory deficit and loss of deep tendon reflexes. Magnetic resonance imaging of the thorax and cervico-dorsal spine showed consolidation and cavitation in the right lung apex, with contiguous ipsilateral soft tissue edema of the chest wall, paravertebral soft tissues, and marrow edema along the right side of the vertebrae. The spinal cord from the C5 to D2 vertebrae was also swollen and edematous.

He followed a downhill course and succumbed to the illnesses. Postmortem examination revealed a cavitatory lesion with invasive pulmonary mucormycosis involving the apex of the right lung and locally spreading to the ipsilateral thoracic wall, paravertebral soft tissue, intervertebral disc, vertebral bone marrow, and spinal cord corresponding to the D1–D2 thoracic vertebrae, leading to spinal mucormycosis.

Spinal mucormycosis is uncommon, with the present case being the twelfth case. To the best of our knowledge, only one case of contiguously spreading pulmonary mucormycosis leading to spinal mucormycosis has been reported to date.

Keywords:

Pulmonary mucormycosis, spinal mucormycosis

Introduction

Invasive mucormycosis is an uncommon but fatal opportunistic fungal infection common in clinical settings like malignancy, neutropenia, use of immunosuppressive agents, metabolic acidosis, uncontrolled diabetes, starvation, severe trauma, or other debilitating conditions that result in an immunocompromised state [1].

Potential sources of infection include soil, decaying vegetation, hay, stored seeds, horse manure, house dust, or dirty carpets. It

enters the airway through inhalation of sporangiospores, and germination of spores occurs due to impaired phagocytic activity of alveolar macrophages and neutrophils in diabetics. On top of that, the hyperglycemia and acidic environment act as a culture medium for fungal growth [2]. The acidic environment increases the release of iron from transferrin, which in turn leads to hyphal growth [3]. Mycotic invasion of the blood vessels leads to occlusion, followed by tissue infarction and necrosis [4], mediated by fungal proteases, lipases, and mycotoxins, finally resulting in cavitary lesions. Vascular invasion commonly results in disseminated mucormycosis.

However, this case highlights an unusual finding of locally invasive pulmonary mucormycosis from the apex of the right lung to the ipsilateral thoracic wall and vertebra to cause spinal mucormycosis. To the best of our knowledge, only one such case has been reported to date [5].

Case Report

A thirty-six-year-old male, a known case of disseminated tuberculosis post-anti-tubercular therapy, diabetes mellitus type 3c, alcohol dependence syndrome, and chronic pancreatitis, presented with cough and breathlessness for ten days. Initial examination revealed oxygen saturation of 94% at room air with a pulse of 124 beats per minute. Random blood sugar was 405 mg/dL, with ketone bodies in urine and high anion gap metabolic acidosis on ABG analysis. The total leukocyte count was 11,500/mm³ with toxic changes in neutrophils. Chest NCCT and X-ray showed features of pneumonia in the right upper zone. Hence, he was admitted and treatment was started for DKA with right upper lobar pneumonia in the form of empiric broad-spectrum intravenous antibiotics, insulin infusion, intravenous fluids, and other supportive care.

On day 1, HRCT of the thorax was performed and showed consolidation with cavitation in the right upper lobe. Multiple nodules of soft tissue attenuation associated with a rim of ground-glass haze (halo sign) were also noted in the right lung (Fig. 1). Based on these imaging findings, a possibility of fungal infection was suggested, and consequently, an antifungal drug was added to the treatment.

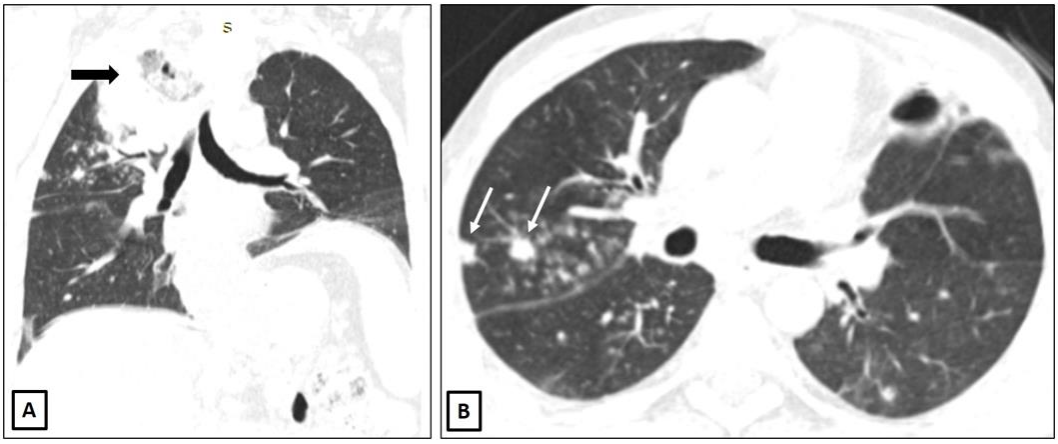

Figure 1: Panel of CT images: (A) Coronal and (B) axial images in the lung window show an area of consolidation with cavitation in the right upper lobe (thick black arrow) and multiple nodules with a rim of ground-glass haze 'halo sign' (thin white arrows), respectively.

On the same day, he developed numbness and weakness in his right upper and lower limbs, with decreased power to four/five grade in his right lower limb, which further decreased to one/five within 24 hours. Gradually over three days, he developed sensory

and motor deficits in both lower limbs with loss of deep tendon reflexes. Given the neurological signs, an MRI of the spine was performed. Short Tau Inversion Recovery (STIR) coronal images showed consolidation and cavitation in the right lung apex with contiguous ipsilateral soft tissue edema of the chest wall, intercostal muscles, and paravertebral soft tissues. Marrow edema was noted in the right half of the vertebral bodies in continuity with the chest wall soft tissue abnormality. T2-weighted and T1-weighted sagittal images of the cervical spine revealed swollen and edematous cord from the level of C5 to D2 vertebrae (Fig. 2).

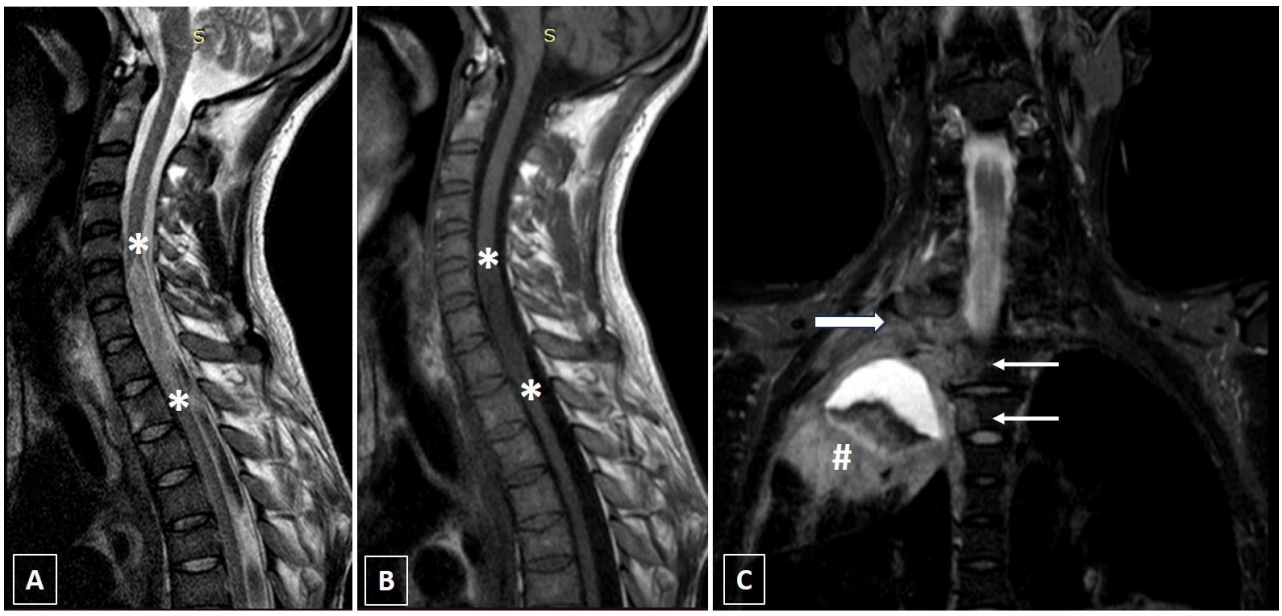

Figure 2: Panel of MRI images: (A) T2-weighted, (B) T1-weighted sagittal images of the cervical spine reveal swollen and edematous cord (white asterisks) from C5 to D2 vertebrae. (C) STIR coronal image shows consolidation with cavitation in the right lung apex (#), contiguous soft tissue oedema of the ipsilateral chest wall extending to paravertebral soft tissues (thick white arrow), and marrow oedema along the right side of the vertebrae (thin white arrows).

On day 5, the CSF examination revealed total protein: 188 mg/dL; glucose: 109 mg/dL; increased globulin; adenosine deaminase: 6.6 U/L; total cell count: 430/µL; with WBC: 206/µL and lymphocyte pleocytosis. However, Gram stain, ZN stain, and culture showed no organism, and the polymerase chain reaction for tuberculosis was also negative.

On day 6, he was put on mechanical ventilation owing to persistent desaturation and gradually deteriorating general condition. Bronchoscopy revealed mucous plugs and purulent secretions in the trachea and right bronchus, suggestive of empyema in the right lung upper lobe. Upon culture of bronchoalveolar lavage (BAL) fluid, multi-drug-resistant Klebsiella pneumoniae ssp. pneumoniae was isolated, and microscopic examination did not show acid-fast bacilli or fungal elements. Further, serum galactomannan was within the normal range, ruling out invasive aspergillosis. Hence, treatment with appropriate broad-spectrum antibiotics was continued, and antifungal treatment was discontinued.

Subsequently, MRI of the thorax was performed and revealed right-sided pleural effusion. Upon culture of pleural fluid, Klebsiella pneumoniae ssp. pneumoniae was isolated. Peripheral blood culture on day 8 also showed multi-drug-resistant Klebsiella pneumoniae ssp. pneumoniae.

On day 10, he developed cardiac arrest leading to his demise despite resuscitative measures.

Postmortem Findings:

Gross Examination: The most significant findings were confined to the lungs, thoracic cavity, and spine. Right-sided pleural effusion with approximately 200 mL of straw-colored pleural fluid was noted. Both the lungs were heavy and boggy, with the right and left lungs weighing 1060 g and 634 g, respectively.

The apex of the right upper lobe showed consolidation with blackish discoloration over the pleural surface, which on cut section showed a large cavity measuring 5 cm in diameter with blackish-gray necrotic material in the lumen (Fig. 3). Multiple smaller cavities were also noted nearby with tan-brown necrotic material. These features corroborate with imaging findings of consolidation with cavitation, and multiple cavities with luminal necrotic material correspond to the 'halo sign.'

On removing the right lung, the thoracic wall at the apex showed a large blackish area extending medially towards paravertebral soft tissue and thoracic spine corresponding to the D1–D2 segment (Fig. 4). The affected spinal segment was dissected out and showed thick purulent fluid exuding from the spinal cord region.

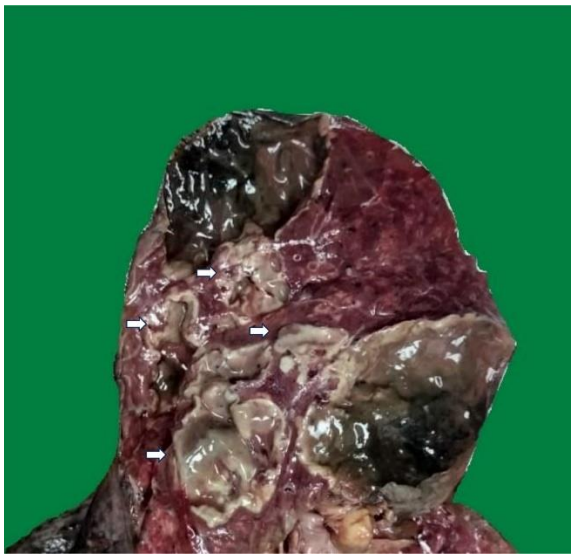

Figure 3: Showing a large, 5 cm diameter, cavitatory lesion filled with blackish pigment and necrotic debri in apex of right upper lobe of lung also involving the pleural surface. Multiple smaller cavities are seen with tan brown necrotic material in the lumen (white arrows) which correspond to the 'halo sign' on CT scan.

Microscopic Examination: The cavitatory lesion showed degenerated cells with dense mixed inflammation and numerous broad, aseptate, ribbon-like hyphal forms of Mucor scattered in the lung parenchyma and also invading into the surrounding blood vessels (Fig. 5A). Grocott stain and KOH mount highlighted the hyphae of Mucor (Fig. 5B, 5C). Sections from the nearby smaller cavities showed necrotic lung parenchyma with mixed inflammation and surrounded by a rim of hemorrhage leading to the 'halo sign' on imaging (Fig. 5D). Sections from the rest of the lung parenchyma show features of diffuse alveolar damage.

Sections from the vertebral column from the D1–D2 segment showed Mucor hyphae infiltrating into the paraspinal soft tissue with angioinvasion (Fig. 6A), annulus fibrosus of the intervertebral disc (Fig. 6B), and vertebral bone marrow (Fig. 6C). The cell block preparation from the exuded spinal cord purulent fluid also showed hyphae of Mucor surrounded by necrotic tissue (Fig. 6D), establishing the diagnosis of spinal mucormycosis.

The gross and microscopic features aptly support the MRI findings of contiguous soft tissue edema of the apical chest wall extending to intercostal muscles, paravertebral soft tissue, and the marrow in the vertebral body.

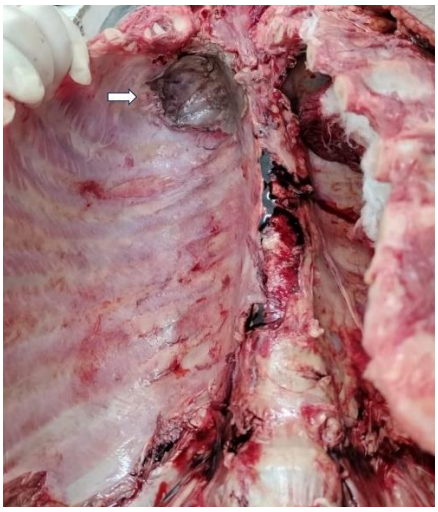

Figure 4: After removing the right lung, a large area of blackish discolouration over the apex of the right thoracic wall (white arrow) extending medially towards the paravertebral soft tissue and thoracic spine corresponding to the D1-D2 segment is seen.

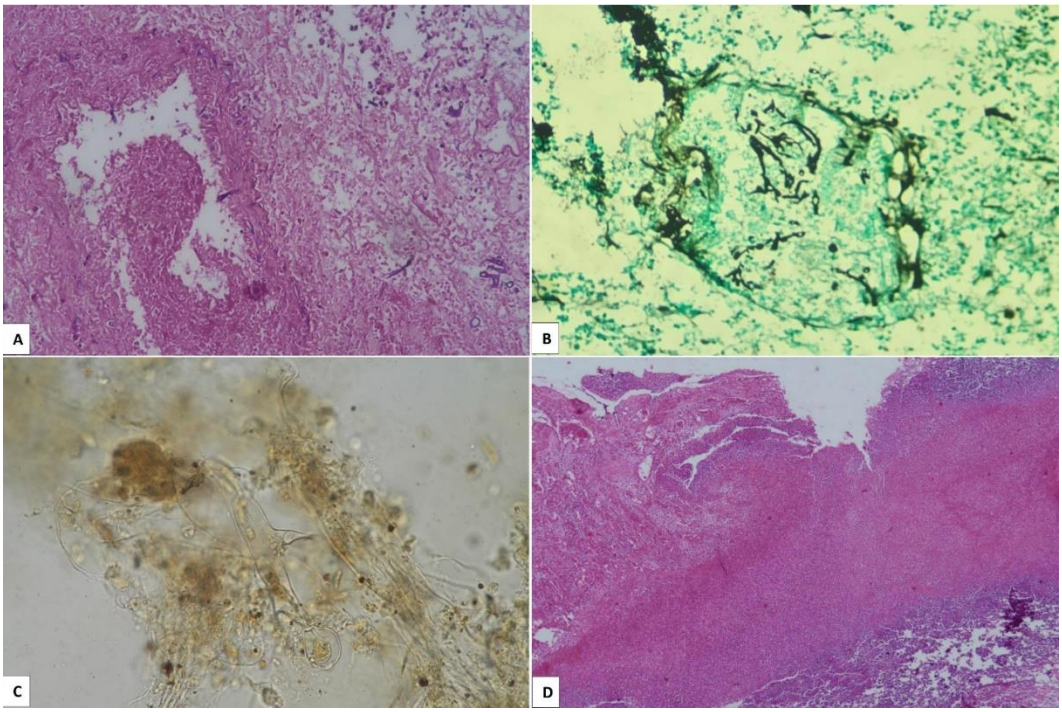

Figure 5: Panel of microscopic images from lung: (A) From blackish cavitatory lesion showing Mucor hyphae in the lung parenchyma with angioinvasion (H&E, 200x). (B) Fungal hyphae highlighted by the Grocott stain also showing angioinvasion (400x). (C) KOH mount showing characteristic fungal hyphae (400x). (D) From the nearby smaller cavities showing necrotic lung parenchyma with mixed inflammation and surrounded by rim of hemorrhage leading to 'halo sign' on imaging (H&E, 40x).

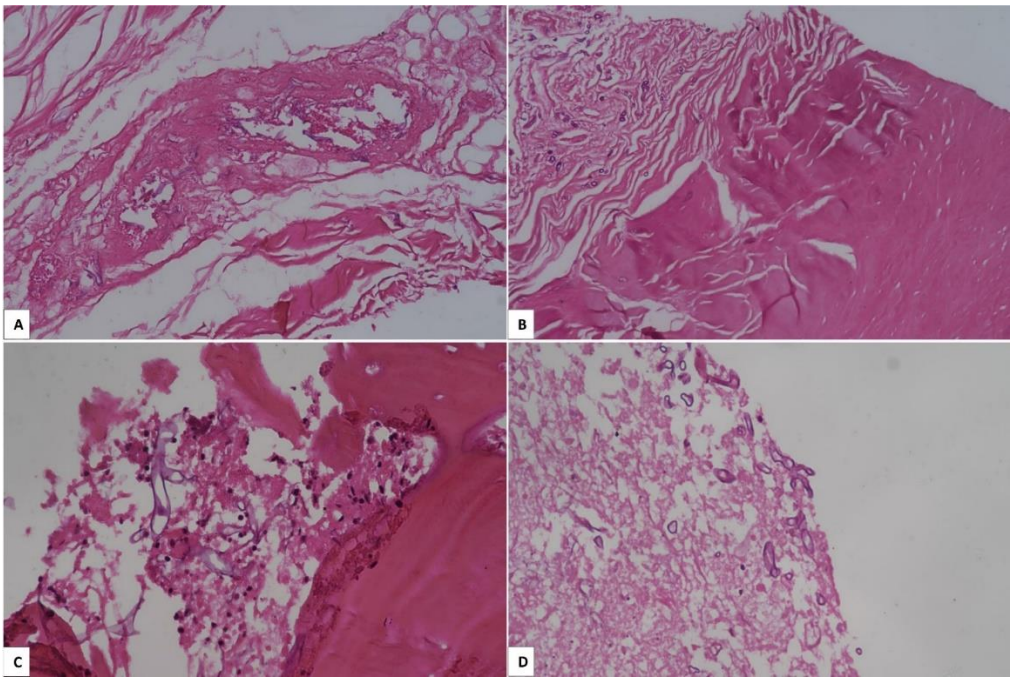

Figure 6: Panel of microscopic images from D1-D2 spinal segment showing Mucor hyphae infiltrating into (A) Paraspinal soft tissue also showing angioinvasion (H&E 200x), (B) annulus fibrosus and surrounding soft tissue (H&E 200x), (C) vertebral body bone marrow (H&E 400x), and (D) spinal cord on cell block preparation from exuded purulent fluid (H&E 400x).

Discussion

Most of the cases with pulmonary mucormycosis have uncontrolled diabetes at the time of infection [6] and present with non-specific symptoms like fever, cough, dyspnea, and breathlessness, as in our case. Hemoptysis can occur when the cavitary lesion communicates with the bronchus.

The imaging findings are also vague, although there are certain clues like the ‘halo sign’ and ‘reverse halo sign’ on CT scan, which are indicative of angioinvasive fungal infection [7]. The ‘halo sign’ is characterized by ground-glass opacity surrounding a pulmonary nodule or mass, and histopathologically it corresponds to necrotic lung parenchyma (as nodule) surrounded by hemorrhage (as halo of ground-glass opacity) [7]. The ‘halo sign’ is commonly associated with invasive pulmonary aspergillosis; however, there is a long list of pulmonary diseases, including other fungal, viral, bacterial, mycobacterial, or parasitic infections and neoplastic diseases, including mucormycosis [8], with similar CT findings. In the ‘reverse halo sign’, a rounded area of ground-glass opacity is surrounded by a crescent or ring of consolidation and is most commonly associated with pulmonary mucormycosis, in addition to a spectrum of other pulmonary diseases.

Therefore, based on the presenting respiratory symptoms with upper lobe involvement in an immunocompromised host with a past history of pulmonary tuberculosis, relapse of pulmonary tuberculosis and community-acquired bacterial pneumonia were considered as common differential diagnoses. This was aptly supported by positive bacterial culture reports on BAL fluid, pleural fluid, and peripheral blood, and appropriate broad-spectrum injectable antibiotics were given. Pulmonary aspergillosis and mucormycosis were also considered due to similar predisposing factors and the ‘halo sign’ on imaging; however, being uncommon

infections with no evidence of fungal infection on various body fluid examinations and serum galactomannan being within the normal range, treatment was discontinued considering the high toxicity and life-threatening adverse effects.

Microscopy and culture are the cornerstones for the diagnosis of mucormycosis. The fungus can be identified in sputum, bronchoalveolar lavage, or pleural fluid in suspected cases; however, the sensitivity of these tests is very low. In our case also, these samples were examined, but no fungal elements were noted. Therefore, percutaneous needle biopsy, bronchoscopic biopsy, or open biopsy should be performed in cases with a high index of suspicion. However, the non-availability of a chest physician at our center precluded invasive tissue biopsy in this case. Molecular-based techniques for the detection of fungal DNA can help in the early diagnosis, but these facilities are not readily available.

Few reports on spinal mucormycosis exist in the literature, and the study done by Patel et al. [9] summarizes all the cases of spinal mucormycosis reported to date, with the present case being the twelfth case. Symptoms of spinal mucormycosis include pain, limb numbness, and weakness to paralysis, depending upon the site and extent of involvement. Our patient initially developed numbness and weakness in the right upper and lower limbs, which rapidly progressed to motor deficit in both lower limbs, followed by sensory deficit and loss of deep tendon reflexes. These features can also be seen in cases with spinal tuberculosis, Guillain-Barré syndrome, or transverse myelitis.

Similarly, radiological findings of spinal mucormycosis are also non-specific. Therefore, if the radiological findings are suggestive of pulmonary fungal involvement with contiguous chest wall, paravertebral, vertebral, and spinal cord involvement, locally disseminating or invasive fungal infection must be suspected, and a biopsy must be obtained to establish the diagnosis.

In addition to the diagnostic challenges, the treatment of fungal infections with spinal involvement is also difficult owing to poor response to standard antifungal therapy. Therefore, early diagnosis, aggressive surgical debridement, and systemic antifungal therapy are the hallmarks of management. Even so, the success rate of combined medical and surgical management is low.

Conclusion

This case highlights an extremely rare finding of invasive pulmonary mucormycosis with contiguous spread to the thoracic wall, paravertebral soft tissue, intervertebral disc, vertebral bone marrow, and spinal cord, resulting in spinal mucormycosis. Owing to the rarity of the condition, few case reports exist in the literature, which precludes the development of optimal management strategies and favorable outcomes.

Abbreviations and Symbols:

ABG: Arterial Blood Gas
NCCT: Non-contrast Computed Tomography
DKA: Diabetic Ketoacidosis
HRCT: High-Resolution Computed Tomography
MRI: Magnetic Resonance Imaging
STIR: Short Tau Inversion Recovery
CSF: Cerebrospinal Fluid
ADA: Adenosine Deaminase
WBC: White Blood Count
PCR: Polymerase Chain Reaction

BAL: Bronchoalveolar Lavage

H&E: Hematoxylin and Eosin

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Competing Interests: None declared

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Ethical Approval: Approved by institutional ethical committee.

Statement of Human and Animal Rights: N/A

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