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Clinical Case Seminar

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A rare cause of pneumonia in an immunocompromised patient

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Abstract

We present the case of a 69-year-old immunocompromised man admitted to our Pulmonology Unit for acute respiratory failure secondary to pulmonary mucormycosis infiltrating and occluding the left main bronchus and pulmonary artery. The patient was treated with liposomal amphotericin B, but developed severe hypokalaemia and anaemia. Despite the treatment, after 63 days, the patient died for cardiorespiratory arrest.

Keywords: acute respiratory failure, mucormycosis, immunocompromised, hypokalaemia, anaemia.

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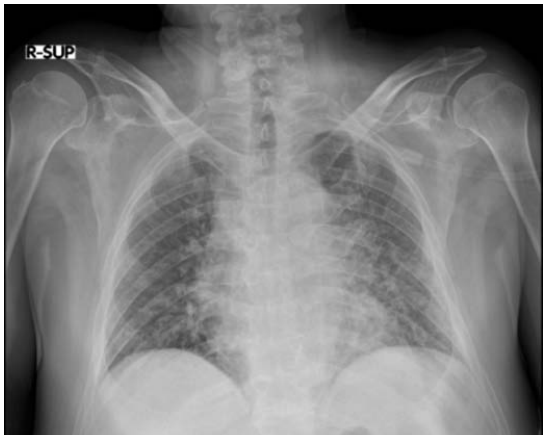
Case presentation

A 69-year-old lifelong non-smoking man, former janitor and prison guard, with a medical history from the 1983 of insulin-dependent diabetes mellitus, complicated by diabetic retinopathy and neuropathy, and from the 2000, of systemic arterial hypertension (treated with olmesartan/hydrochlorothiazide and enalapril) was admitted on the 10th of December 2022 at the emergency room of the University Hospital Gaetano Martino of Messina, Italy (www.polime.it) for confusion and persistent cough with sputum, where he performed: laboratory tests (Tab 1) and a chest X-ray that showed bilaterally multifocal lung opacities with left hilum enlargement (Fig.1).

Fig. 1 Chest X-ray performed at emergency room



Tab.1 Evolution of laboratory data

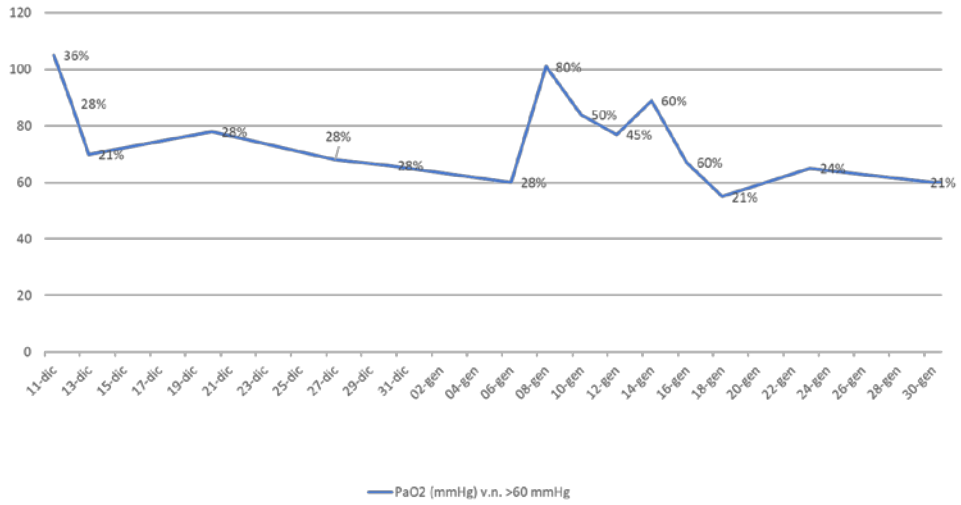
LABORATORY DATA	At emergency room 10th of December 2022	At 40th day after the hospital admission	NORMAL VALUES
Erythrocytes	**4280000**	**31500000**	**4500000-5500000 (cell/mm^3)**
Haemoglobin	**12.5**	**8.7**	**13.5 – 18 (g/dL)**
MCV	**87**	**83**	**80 – 100 (fl)**
MCH	**29**	**27.5**	**25 – 34 (pg)**
Haematocrit	**37**	**26**	**38 – 46 (%)**
Total leukocytes	**23500**	**4300**	**4500 – 9000 (cell/mm^3)**
Neutrophils	**19975**	**1849**	**1500 – 7700 (cell/mm^3)**
Lymphocytes	**2350**	**774**	**1500 – 3500 (cell/mm^3)**
Eosinophils	**235**	**86**	**40 – 500 (cell/mm^3)**
Monocytes	**940**	**215**	**< 1000 (cell/mm^3)**
Basophils	**0**	**0**	**0 – 300 (cell/mm^3)**
Platelets	**450000**	**102000**	**150000 – 350000 (cell/mm^3)**
Serum CRP§	**33.10**	**4.08**	**0 – 0.50 (mg/dL)**
Serum PCT§§	**0.44**	**0.05**	**Bacterial infection of the lower respiratory tract:** **<0.10: absence** **0.10 – 0.25: probable** **0.25 – 0.50: possible** **>0.50: presence of bacterial infection** **Systemic bacterial infection / sepsis:** **<0.50: absence** **0.50 – 10: possible** **>10: high probability of sepsis (ng/mL)**
NT-proBNP	**1006**	**1281**	**0 – 125 (pg/mL)**

C-re C-reactive protein
§§ PCT: procalcitonin

A nasopharyngeal swab for the search of SARS-CoV-2 genome was positive and he was admitted to the COVID-19 Emergency Medicine unit. On admission, his vital signs were: systemic arterial blood pressure 100/60 mmHg, pulse frequency 120/min rhythmic, SpO_2 99% during oxygen therapy with nasal cannulae at a flow rate of 4 L/min with FiO_2 36%, axillary temperature 36.1°C, capillary blood glucose 520 mg/dL. An arterial blood gas analysis performed with the patient breathing oxygen (FiO_2 36%) showed: pH 7.28, PaO_2 105 mmHg, $PaCO_2$ 17 mmHg, SaO_2 97%, HCO_3^- 7 mmol/L. The metabolic acidosis was treated with intravenous infusion of saline, insulin and potassium replacement as the decreased serum potassium levels (Tab. 1). On the 13rd of December 2022 a high-resolution computed tomography (HRCT) of the chest showed the presence of a left peri-hilar opacity with both solid and "ground glass" appearance with associated partial atelectasis of the homolateral lung parenchyma. On the 19th of December 2022 a fibreoptic bronchoscopy (FBS) showed the partial occlusion of the left main bronchus with the presence in its lumen of necrotic material. The procedure was terminated prematurely due to a severe oxygen desaturation of the patient. A bronchoalveolar

lavage (BAL) performed on the 23rd of December 2022 showed the presence of many aseptate hyphae suggestive of Mucorales, bronchial biopsies from the left main bronchus were also collected. Therefore, was started therapy with liposomal amphotericin B at a dosage of 5 mg/kg intravenously. During the hospitalization in the COVID-19 Emergency Medicine unit, the patient has developed acute respiratory failure treated with oxygen therapy administered with nasal cannula or Venturi mask with a variable FiO_2 as summarized in fig. 2.

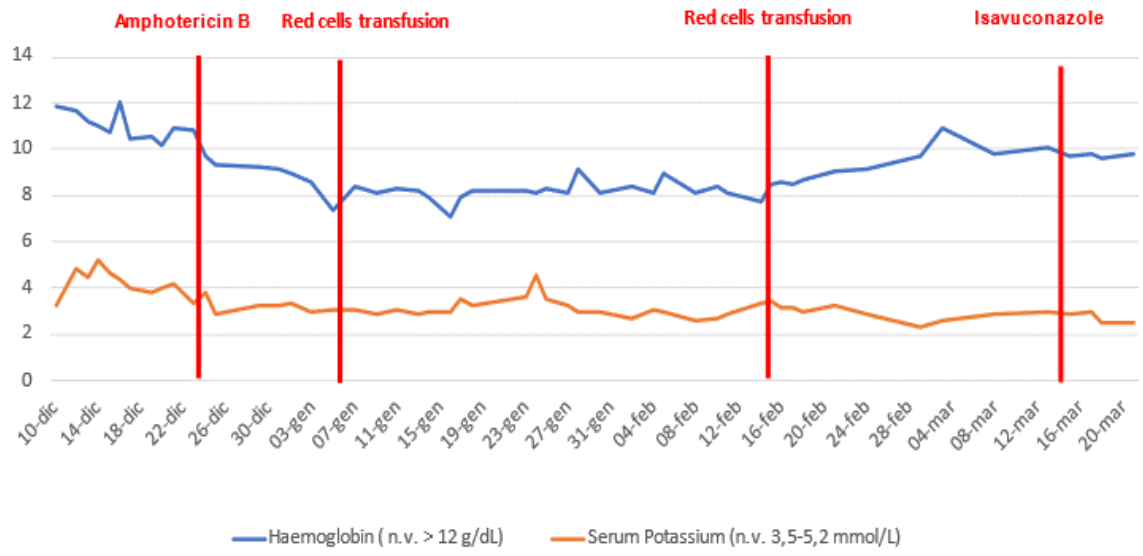
Fig.2 Evolution of acute respiratory failure evaluating PaO_2 and FiO_2



On the 10th of January 2023, the nasopharyngeal swab for SARS-CoV-2 genome was negative and the patient was transferred to our Unit of Pulmonology.

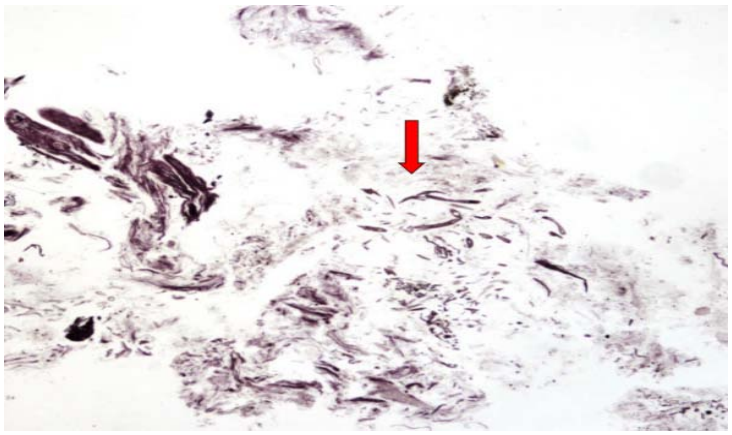
Auscultation of the chest showed all over the left hemithorax decreased vesicular sounds with expiratory wheezing and bilaterally inspiratory basal crackles. Laboratory tests performed in our ward showed persistent severe hypokalaemia despite the intravenous potassium replacement and anaemia needing several hemotransfusions (Tab 1 and fig. 3).

Fig. 3 Temporal changes of haemoglobin and serum potassium



The pathological examination of the bronchial biopsies showed necrotic foci and presence of fungal hyphae even inside the vessels lumen without neoplastic cells (the 11th of January 2023) (fig.4).

Fig.4 Pathological examination on bronchial biopsies showing hyphae of mucorales, 200x, silver impregnation

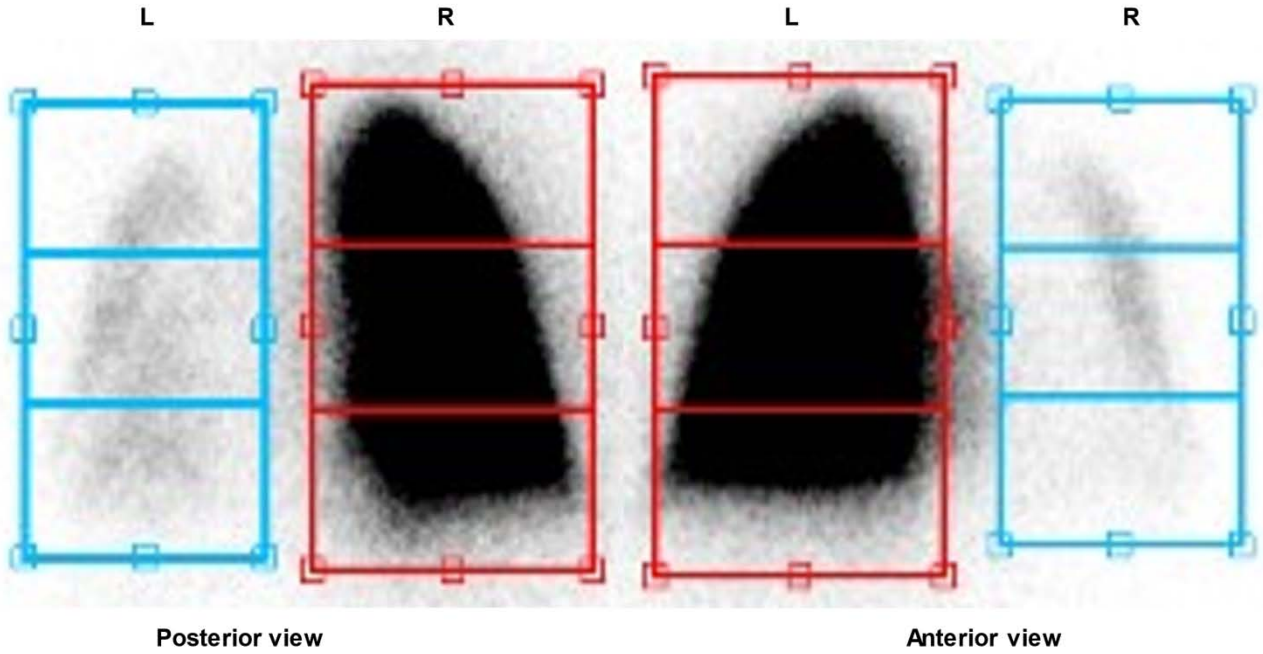


On the 24th of January 2023, an arterial blood gas analysis was performed that showed the resolution of the acute respiratory failure. The patient no longer required oxygen therapy, maintaining SpO2> 90%.

On the 27th of January 2023 another FBS (video) showed an almost complete occlusion of the left main bronchus and both BAL and bronchial biopsies were collected showing the absence of fungal hyphae with the presence in the bronchial mucosa of ulcerative and granulomatous-like inflammation without acid-fast bacilli.

On the 16th of February 2023 a pulmonary scintigraphy showed severe hypoperfusion (5%) of the left lung, whereas the right lung had almost normal (95%) perfusion (fig. 5).

Fig. 5 Lung perfusion scintigraphy



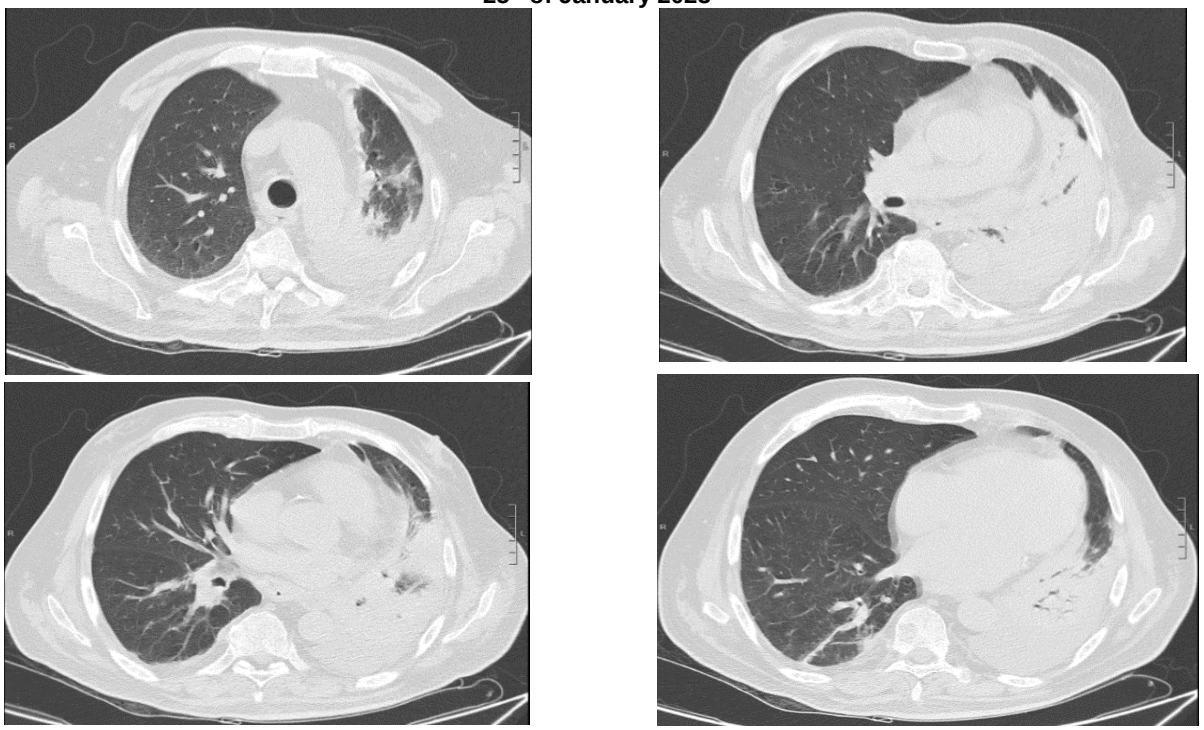
On the 4th of March 2023 the patient developed again acute respiratory failure (SpO_2 88%) starting

oxygen therapy with nasal cannulae at a flow rate of 1 L/min.

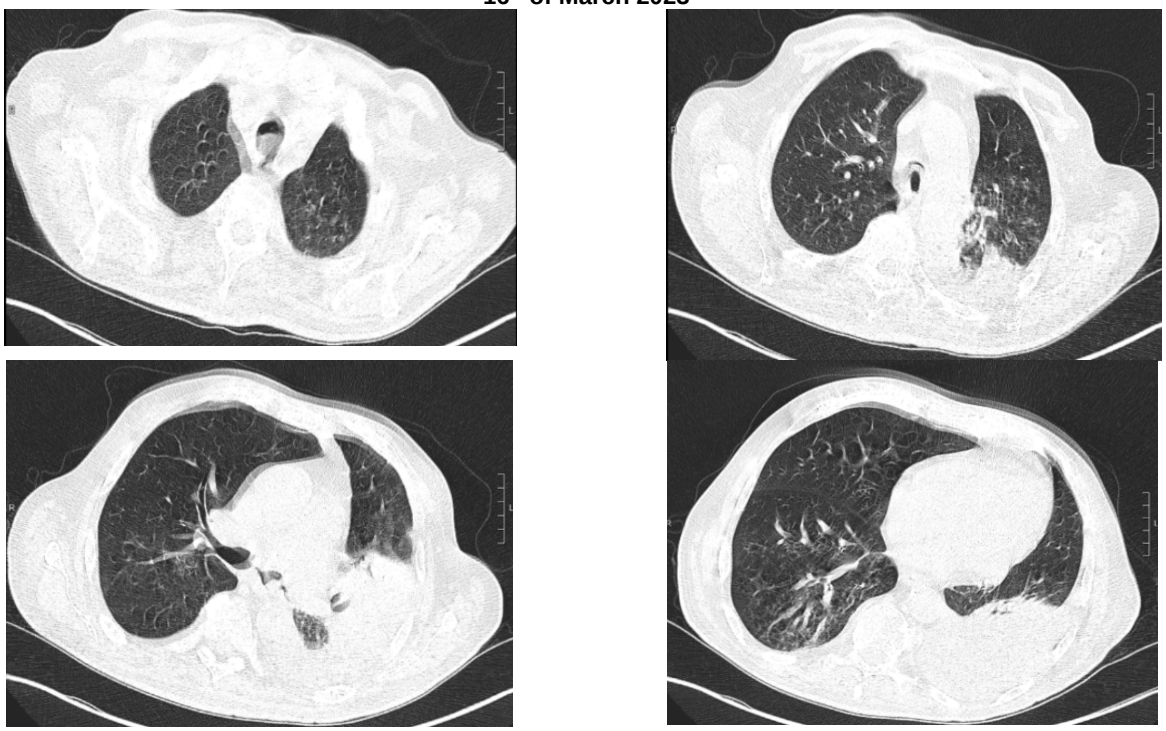
Another HRCT of the chest performed on the 25th of January 2023 showed the complete atelectasis of the left lung and presence of left pleural effusion, the HRCT scan of the chest on the 16th of March 2023 showed a partial re-expansion of the left lung parenchyma and decreased left unilateral pleural effusion (fig 6).

Fig. 6 Evolution of the HRCT scans of the chest

25th of January 2023



16th of March 2023



Pulmonary mucormycosis has a high lethality >60% (1), when feasible, multimodality treatment

approach with both surgical debridement and pharmacological treatment with antifungal drugs may improve the outcome (1). When the development of the total obstruction of a main bronchus (as in our Patient) occurs, the lung ventilation/perfusion ratio is normally maintained without the development of acute respiratory failure. However, when the partial unblocking following the medical therapy occurs, the lung ventilation/perfusion ratio can be altered, correlating with the development of an acute respiratory failure. On the 19th of March 2023 the patient developed paroxysmal atrial fibrillation treated with amiodarone restoring sinus cardiac rhythm. In the 23rd of March 2023, the patient died for cardiovascular arrest.

Discussion

The most common risk factors for the development of pulmonary mucormycosis are represented by immune compromission due to insulin dependent diabetes mellitus, and/or hematologic malignancy and/or solid organ or stem cell transplantation and currently, literature data have shown that only immunocompromised patients could develop this disease (1,4). These fungi growth on decaying food, soil, and animal excrements and the infection occurs through the inhalation of the fungus spores (2). Mucormycosis is more frequent in males and this can be due to the increased humoral and cellular-mediated immune response in females compared to males, including enhanced Th1 responses that may have a fundamental role in promoting mucorales phagocytic activity (3).

A key pathogenetic feature of this fungal infection is represented by the angioinvasiveness with obliteration of the vessels lumen mediating tissue ischemia. This pathogenetic feature is mediated by the increased expression on the endothelium of the glucose regulated protein 78 (GRP78), a specific receptor for the spore coat protein homolog 3 (cotH3), localized on the spores of mucorales fungi; GRP78 increased expression is mediated by hyperglycaemia and increased serum iron levels (1,4).

Liposomal amphotericin B represents the antifungal therapy of first choice against mucormycosis but the long treatment is often associated with the development of several side effects such as severe hypokalaemia and anaemia (5).

Chest CT scan of pulmonary mucormycosis can show pulmonary cavitation and lung opacities with consolidation, pleural effusion and “reserved halo” sign; concomitant severe SARS-CoV-2 pneumonia makes more difficult to identify pulmonary mucormycosis at CT chest scan and is characterized by increased mortality compared to pulmonary mucormycosis alone (6).

Conclusion

We presented a case of pulmonary mucormycosis in an immunocompromised patient with its clinical course complicated by severe anaemia and hypokalaemia secondary to long term liposomal amphotericin B therapy.

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Conflict of interest
The Authors declare no competing interest

Informed consent The Authors declare to have obtained informed consent

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