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ORIGINAL ARTICLE

A Case of Metastatic Malignancy Presenting as Diffuse Alveolar Hemorrhage, a Diagnostic and Management Challenge!

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ABSTRACT

Background: Life-threatening hemoptysis (LTH) is one of the most dreaded respiratory emergencies. If not managed timely, results in inevitable mortality.

Methodology: Documented the case and all the relevant details from the ICU of Liaquat National Hospital, Karachi.

Case: We present a case that was unusual because a young male with no previous comorbidities, and a non-significant exposure history, presented with diffuse alveolar hemorrhage (DAH) and life-threatening hemoptysis. He had come with an extremely short presentation and was diagnosed as metastatic carcinoma, of unknown origin after his demise unfortunately even after expanding all possible avenues and approaching via multidisciplinary teams. If more of such cases are reported and documented, an etiology of DAH and LTH as secondary to malignancy can be more established.

Conclusion: While dealing with cases of LTH, a malignancy focus must also be sought. The significance of detailed clinical examination is high.

Keywords: Diffuse alveolar hemorrhage, life-threatening hemoptysis, massive hemoptysis, metastatic malignancy

INTRODUCTION

Hemoptysis is a common presenting complaint in Respiratory Medicine, and is secondary to a wide array of pathologies, ranging from benign diseases to more severe life threatening ones. There is no consensus on defining LTH (formerly massive hemoptysis) on the basis of amount of blood being expectorated in 24 hours or rate of bleeding per hour accurately. The risk of death from hemoptysis has been correlated with the rate of bleeding[1]. About 15% of patients presenting with hemoptysis will have life-threatening hemoptysis [2]. It is difficult to quantify the amount of blood which is why life-threatening hemoptysis also includes hemoptysis that results in life threatening complications such as respiratory distress, significant abnormal gas exchange, a substantial drop in hemoglobin or hemodynamic instability. For the treatment, airway must be protected; appropriate oxygenation must be ensured on priority. Once the airway is stabilized, a quick diagnosis and control of bleeding site is targeted as well as volume is replaced.

The most common etiologies of life threatening hemoptysis are Tuberculosis, Bronchiectasis [3] (which could also be a consequence of Tuberculosis), especially in South Asia, and then less frequently bronchogenic carcinoma, fungal infections, pneumonia and other viral illnesses.

CASE PRESENTATION

28 year old male with no known co-morbid condition, never smoker, trained as a commercial airline pilot who recently took up poultry farming as a business, had no previous admission history and presented with hematemesis 1 week before presenting to our hospital, with 3 to 4 episodes of fresh blood, approximately ½ cup each time. He was managed at a periphery hospital and upper gastrointestinal endoscopy came back normal and was cleared for a source of upper gastrointestinal bleed. He then developed low grade fever, and 2-3 episodes of hemoptysis approximately 2-3 teaspoons in quantity which later settled. He was being managed along the lines of complicated COVID pneumonia at a different periphery hospital receiving intravenous fluids and antibiotics. His condition kept deteriorating and he developed worsening shortness of breath with significant drop in oxygen saturation.

He presented to our emergency with initial vitals showing a respiratory rate of 35, normal blood pressure and heart rate of 125 and oxygen saturation of 75% on room air. Chest X-ray showed bilateral nodular pulmonary infiltrates of varying sizes on all zones. Patient was admitted into our intensive care unit and was maintaining saturation on 8 liters of oxygen. His examination findings were unremarkable except for a swelling at the lateral aspect of right chest wall in mid axillary line. The patient mentioned on further history taking that there was foul smelling discharge from that lesion several months ago, with no associated fever or tenderness.

Patient then progressively deteriorated and required NIV. Later he became increasingly irritable finally requiring mechanical ventilation after he started expectorating small amounts of blood while in ICU with worsening tachypnea.

Initial laboratory investigations showed elevated LDH i.e. 739, elevated TLC i.e. 23000 with mildly elevated CRP and mildly elevated D-Dimer. His initial urine DR and Renal and Liver Function tests were within normal limits.

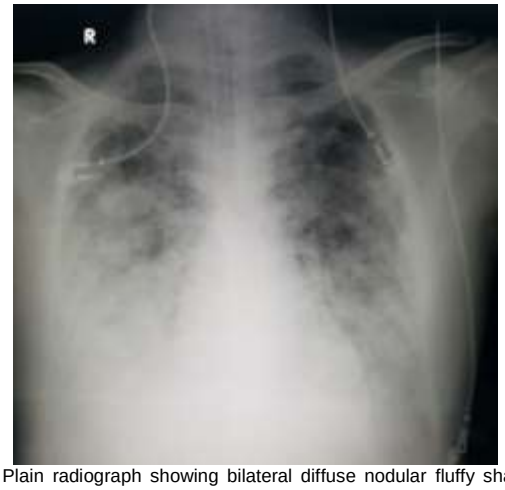

Fig. 1: Plain radiograph showing bilateral diffuse nodular fluffy shadowing mainly involving mid and lower zones

Given the nature of the pulmonary infiltrates evident on his Chest X-ray (Fig. 1), patient was planned for CT Chest and Abdomen with contrast and due to his history Viral PCRs and Dengue, Chikungunya Serologies were sent. CT scan showed multiple soft tissue nodules in both lungs with patchy air space opacification with ground glass opacities diffusely involving the both lungs and multiple enlarged lymph nodes were seen in mediastinum and bilateral hilar regions – suggestive of alveolar hemorrhage and possibility of Tuberculosis (Fig. 2,3). There was lymphadenopathy visible in the abdominal cuts too. We had

immediately made a multidisciplinary team for his management that comprised of an internist, an infectious diseases' expert, a radiologist, a critical care consultant along with us, the pulmonologists.

It was a difficult intubation, as view of the patient's vocal cords was obstructed by large amounts of fresh blood, and after successful passage of endotracheal tube into the trachea, patient was unable to maintain saturation above 80% on 100% FiO2 initially. Intermittent suctioning with ambo-bagging allowed us to bring up oxygenation to 90-92%, while approximately 1.5-2L of fresh blood was removed. Patient was transfused multiple packed cells, but he kept dropping hemoglobin. He was given Factor VII in order to maintain hemostasis, nebulized adrenaline, and tranexamic acid but to no avail. He was started on IV Antibiotics, plasmapheresis, and pulse steroid therapy for 5 days, anti-fungal as well as anti-viral (Oseltamivir).

Patient's inflammatory markers continued to rise, and oxygenation failed to improve. Workup for ANCA, ANA, Cultures (Blood, Urine, and Tracheal), MTB Gene Xpert, and fungal smear, all came back negative.

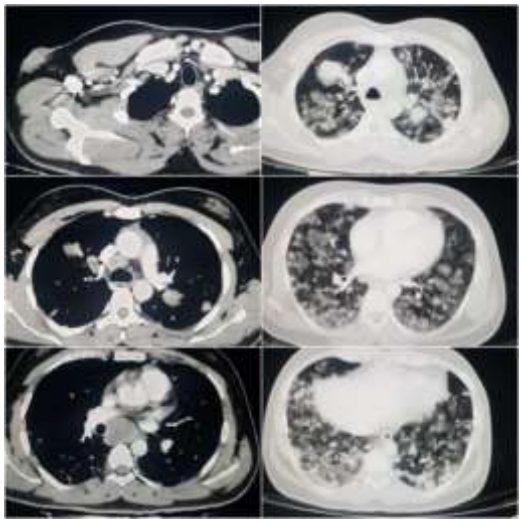

Fig. 2: Computed tomography scan with contrast, axial images of chest, showing multiple soft tissue nodules and patchy ground glass opacities involving both lungs

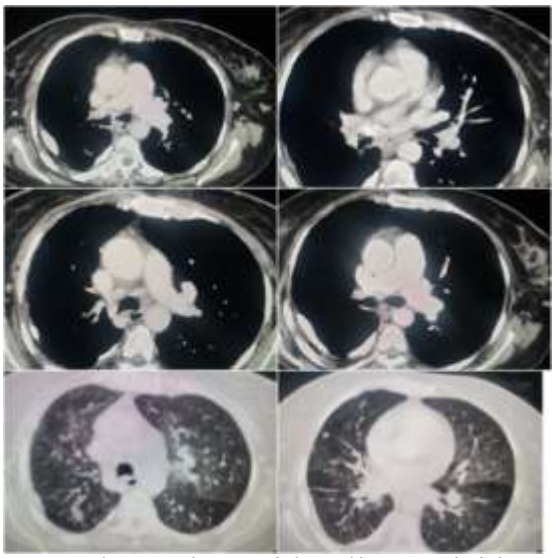

Fig. 3: Computed tomography scan of chest with contrast depicting multiple enlarged lymph nodes in mediastinum and bilateral hilar regions

He then suddenly developed anuria, and went into shock. Patient deteriorated so rapidly that transportation in order to perform hemodialysis was impossible. Moreover he went into atrial fibrillation and then cardiac arrest. Resuscitation attempts were unsuccessful and patient succumbed to his illness. Therefore asphyxia and later hypovolemic shock lead to his death.

The biopsy result of axillary swelling showed results consistent with malignant neoplasm with immunohistochemical profile favoring undifferentiated carcinoma (Fig. 4).

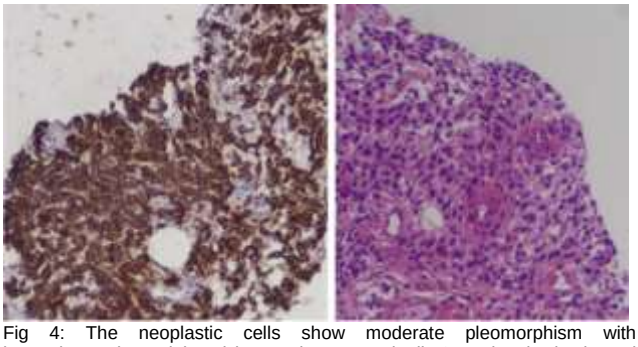

Fig 4: The neoplastic cells show moderate pleomorphism with hyperchromatic nuclei and inconspicuous nucleoli. Occasional mitosis and necrosis is seen. Immunohistochemically positive for CK AE1/AE3 and CK7.

DISCUSSION

The reason this case has been brought up and presented is the unusual course that this patient took and the unlikely diagnosis based on this patient's age and history. DAH's initial presenting symptom is considered to be hemoptysis [4,5,6], but in our patient majorly hemoptysis became apparent during hospital stay, which is similar to the results shown by Rabe et all [7] where hemoptysis was not a prominent feature in majority of patients (97%). Their results also showed that patient with non-immune induced DAH had a significantly worse prognosis, and majority of classical DAH cases are immunologically mediated. These findings were also supported by the case reports by Yang et al [6], where patients with the rare cardiac angiosarcoma presented as DAH, with an extremely poor prognosis. Interestingly, another research revealed contrary findings in this regard that younger patients with immune DAH not only have severe presentation but also worse outcomes[8].

In our patient, there was no investigation that came back positive, which could have potentially guided us in providing directed therapy, but we attempted to treat the patient along the lines of most major etiologies. We initiated intravenous antibiotics to cover Staphylococcus Aureus and Gram Negative bacteria, as well Anti-Tuberculous Treatment; and then proceeded to escalate them when no improvement was being seen as well as adding anti-fungal and anti-viral medications but to no avail. There have been a few documented cases of DAH secondary to Covid 19 infection [9,10], but in our patient 2 sets of Covid PCR were negative, but there was a growth on non-pandemic Coronavirus on our Viral Panel – which seemed to be unlikely as the primary cause of the patient's condition and severity.

Patient gave a non-significant drug history prior to his deterioration – which is why drug induced etiologies were ruled out. Immune mediated DAH, would include pulmonary hemorrhage secondary to APS, SLE, ANCA and other Vasculitic disorders. With negative serologies and lack of a significant response to corticosteroid pulse, recombinant-activated human factor VII therapy and plasmapheresis we did not consider adding another immunosuppressive medication in our patient, as recommended by many clinicians as a form of management with rituximab and cyclophosphamide as considerable options[11].

With the development of renal failure and need for hemodialysis with no response to any of the therapies provided, our patient continued to deteriorate and the only insight we got into the possible etiology of the disease process was from a biopsy of a

chronic lesion in the patient's right axilla – which showed undifferentiated carcinoma as a cause. For our young patient this diagnosis came as a surprise, especially when the CT scan had not given any definitive clue of metastasis in the parenchyma but only lymphadenopathy. In our case, it would seem that knowing the etiology most likely would not have made a difference as seen by the clinical course the patient took during his short ICU stay. Bronchoscopy could not have added any value to our patient care because he needed airway control and the CT imaging could not localize the bleeding site as is concluded by Kathuria et al in their article on practical approach to LTH [12].

CONCLUSION

In such a brief hospital stay, the only thing that could help us in diagnosis of this gentleman was the swelling that we biopsied. So if such a lesion as a clue could be picked earlier in the disease course, a timely diagnosis could be made. This emphasizes the significance of physical examination above all the investigations in order to direct prompt management.

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