

CASE OF THE MONTH

Treatment of Pulmonary Embolism with Chemotherapy in a Case of Newly Diagnosed Osteosarcoma

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Abstract

A 21-year old female, recently diagnosed with osteosarcoma of right humerus, presented to the emergency with history of fever, productive cough, chest pain and progressive respiratory distress for six days. Initial investigations suggested pneumonia but she did not respond to parenteral antibiotics. CT pulmonary angiogram revealed bilateral pulmonary artery embolism. Thrombolysis was performed using alteplase, which failed to improve the clinical condition. In view of underlying malignancy, a possibility of tumour-embolism was considered and she was started on chemotherapy for osteosarcoma. There was dramatic improvement in her respiratory symptoms after the first chemotherapy cycle, along with radiological resolution of the embolism. This case highlights the importance of suspecting tumour embolism in a known case of malignancy with respiratory distress.

Introduction

Patients with an underlying malignancy are prone to develop hypercoagulable state and subsequent pulmonary thromboembolism. Rarely,



Fig. 1: Chest radiograph at presentation: Multiple bilateral ill-defined air space opacities with a right-sided wedge shaped opacity in the lower zone along with a lytic sclerotic lesion involving the right humeral head and anterior dislocation of the right humerus

the embolus may consist of tumour cells and hence, will not respond to thrombolysis and anticoagulation. There have been very few cases reported till date, of an osteosarcoma being described as a cause of pulmonary tumour embolism. Most of these patients had a fatal outcome. Accurate ante-mortem diagnosis and successful treatment for the embolism has been rare.

Case Report

A 21-year old female presented to medical emergency with complaints of fever, productive cough, chest pain and progressively increasing respiratory distress for six days. She had been diagnosed with right proximal humerus osteosarcoma 20 days back and was treatment naïve.

At admission, she was normotensive but had tachycardia (heart rate of 120/min), tachypnea (respiratory rate of 40/min) and hypoxemia (resting oxygen saturation at room air of 74%). Investigations revealed neutrophilic leucocytosis and arterial blood gas

analysis suggested respiratory alkalosis with type I respiratory failure. Chest radiograph revealed multiple bilateral ill-defined air space opacities with a right-sided wedge shaped opacity in the lower zone (Figure 1).

Considering the clinical possibility of community acquired pneumonia, she was started on intravenous antibiotics and high flow oxygen by mask. She did not show significant response to the initial treatment. The electrocardiogram on day 2 showed changes suspicious of pulmonary thromboembolism (sinus tachycardia, a right axis deviation, a RV strain pattern and T wave inversion in chest leads V1-V4).

Computed Tomography Pulmonary Angiogram (CTPA) done on Day 2 revealed a large saddle shaped thrombus involving both right ascending and descending pulmonary artery and left descending pulmonary artery along with parenchymal infarcts (Figure 2A).

Echocardiogram revealed dilated right atrium and ventricle, with a 23x9 mm mobile thrombus prolapsing into the right ventricle, causing moderate right ventricular dysfunction, mild tricuspid regurgitation with severe pulmonary artery hypertension. Anticoagulation with low molecular weight heparin (1 mg/kg BD) was started. One hundred milligrams of Recombinant-tissue plasminogen activator (alteplase) was administered for thrombolysis on day two of hospitalization.

Despite thrombolysis, her respiratory distress continued to worsen, mandating non-invasive bi-level positive pressure ventilation (Table 1). Venous Doppler scan of bilateral lower limbs was normal. Upper limb Doppler revealed thrombosis

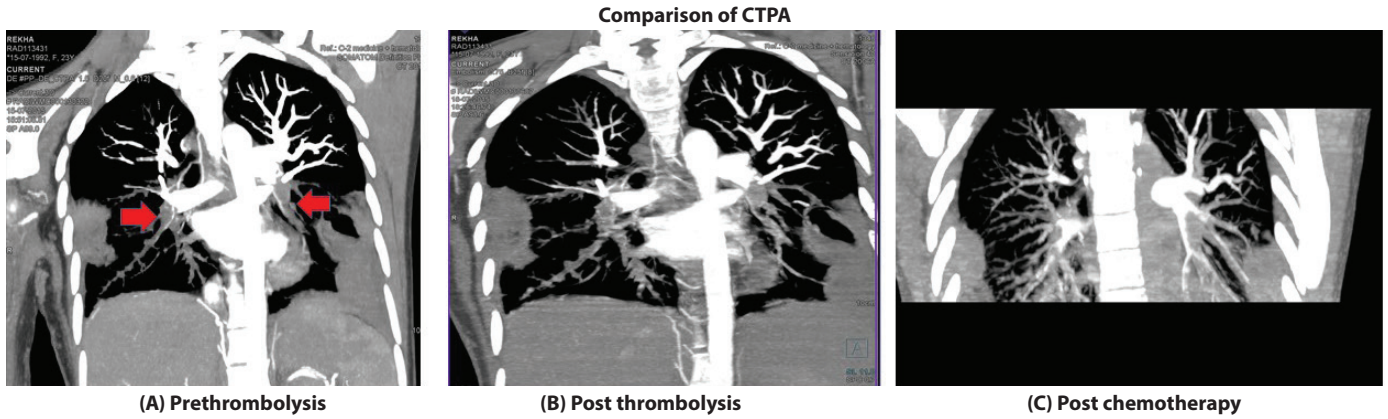


Fig. 2: Computed Tomography Pulmonary Angiogram (CTPA) Images: (A) CTPA done at presentation, shows a large saddle shaped thrombus (red arrows) involving both right and left pulmonary artery along with pulmonary infarcts. (B) CTPA done post-thrombolysis shows no change as compared to previous scan. (C) CTPA done post chemotherapy shows significant recanalization of the right ascending and descending pulmonary artery (nearly 60%)

Table 1: Arterial Blood Gas (ABG)

	Day 1	Day 2	Day 3	Post chemotherapy day 4
Status	Room air	On O2 at 10 litres/ min	On Non Invasive Ventilation (NIV)	Room air
FiO ₂	0.21	0.4	0.30	0.21
pH	7.50	7.48	7.536	7.38
PaO ₂ (mm Hg)	55	82.9	60	92
PaCO ₂ (mm Hg)	23	35.6	18.1	36
SpO ₂ %	76	90	92	97
HCO ₃ (meq/L)	17.2	29.3	24	26
PaO ₂ /FiO ₂	261	207	200	438
Impression	Respiratory alkalosis with compensatory metabolic acidosis	Mixed respiratory and metabolic alkalosis, type 1 failure	Respiratory alkalosis	Normal

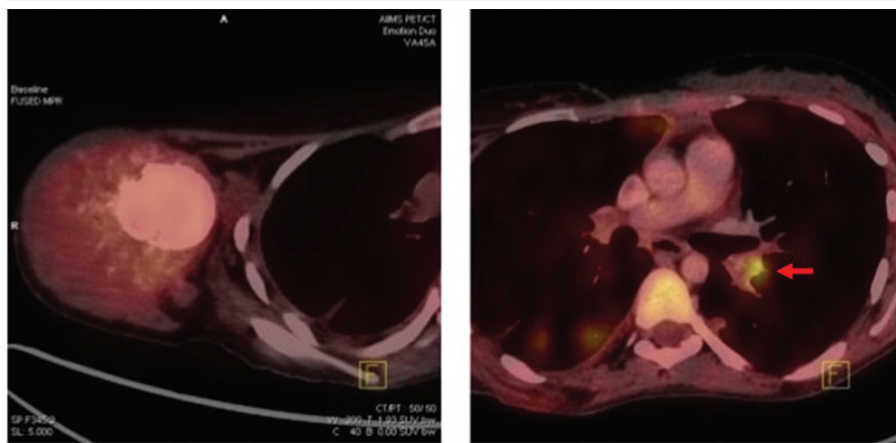


Fig. 3: 18-Fluorodeoxyglucose Positron Emission Tomography Scan (18-FDG PET scan): Metabolically active primary malignant disease involving right humerus. Multiple parenchymal and sub pleural cavitory lesions with mild FDG uptake- likely due to pulmonary infarct. Left descending artery shows one sub segmental thrombus (arrow) with FDG uptake likely malignant thrombus

of right brachial and axillary vein. A repeat CTPA done three days later showed no change in the thrombus burden (Figure 2B).

Lack of response to anticoagulation and thrombolysis raised the suspicion of tumour embolism. Surgical thrombectomy could not be performed

due to poor performance status and high surgical risk. She was started on ifosfamide-etoposide based chemotherapeutic regimen (ifosfamide 3000 mg/m² IV OD and etoposide 75 mg/m² IV OD Day 1-4).

After the 4-day chemotherapy cycle, the respiratory distress

started improving. By day 7 oxygen saturation was stable on room air. Post chemotherapy CTPA showed significant resolution of pulmonary embolism and 60% recanalization of pulmonary artery (Figure 2C). PET scan revealed FDG-uptake in the residual thrombus in the left descending pulmonary artery with multiple sub-parenchymal and sub-pleural cavitory lesions attributable to pulmonary infarction, along with FDG avid primary right humeral mass with standardized uptake value (SUV) comparable to the residual thrombus (Figure 3).

The diagnosis of pulmonary tumour embolism was confirmed and patient was discharged after first cycle of chemotherapy. At the time of preparation of this manuscript, the patient has completed the six-course chemotherapy and a resection surgery for the osteosarcoma has been performed.

Discussion

Venous thromboembolism is a well-recognized occurrence in malignancy, and up to a fourth of cases occur in patients with diagnosed cancer.¹ Tumour embolism is a lesser known entity, most frequently described with epithelial solid tumours (breast, lung, gastro intestinal tract and hepatocellular carcinoma).² Pulmonary tumour embolism secondary to sarcoma is uncommon, and a comprehensive search revealed only 21 cases reported with osteosarcoma.³⁻⁷

The Virchow's triad describes the three primary factors for thrombogenesis as endothelial

dysfunction, stasis or turbulence in blood flow and hypercoagulability. Thrombogenesis in malignancy can occur via all the above mechanisms. While benign venous thrombi are composed of activated platelets, fibrin mesh and macrophages; tumour emboli are composed of viable tumour cells.⁸

Tumour embolism can present as an incidental finding during cancer staging or rarely as acute thromboembolic disease. In the latter scenario, tumour emboli and bland venous thromboembolism are clinically indistinguishable entities, hence delaying accurate diagnosis, similar to our case.

Pulmonary thromboembolism is best identified on Computed Tomographic Pulmonary angiography (CTPA). Subtle radiographic clues along with a high clinical index of suspicion can then aid in confirming diagnosis of tumour embolism. Classically, a CTPA in such a setting, is said to show multifocal dilatation and beading.⁹ Ventilation Perfusion imaging can be done, which shows a segmental contour pattern. This is a non-specific finding seen in many other conditions including diffuse pulmonary vasculitis, primary pulmonary hypertension, fat embolism, septic emboli.¹⁰ The role of 18-Fluorodeoxyglucose Positron Emission Tomography Scan (18-FDG PET scan) is increasingly being defined in these patients. It can help in visualization of FDG avid

thrombus arising from solid tumours. Although FDG avidity can be seen in inflammatory cells comprising bland thrombi as well, a recent study by Sharma et al identified cut-off SUV_{max} of 3.63 to differentiate benign from tumour thrombi with a sensitivity of 72% and specificity of 90%.⁸

Histological diagnosis is gold standard, though utility is limited to surgical embolectomy and autopsy. On histology, the tumour emboli are usually concentric and cellular, compared to the non-concentric and serpentine thromboemboli.

Treatment of pulmonary tumour embolism includes chemotherapy for the primary malignancy, and/or surgical embolectomy (attempted in three of the reported cases). The diagnosis of tumour embolism in our case was considered after the patient failed to respond to anti-coagulation and thrombolysis. However, high clinical index of suspicion along with use of modalities such as 18-FDG PET and Fusion PET-CT can help in early differentiation from bland venous thromboembolism. This is important as unnecessary thrombolysis and life-long anti-coagulation can be avoided. Physicians should remember pulmonary tumour embolism when encountered with a case of malignancy presenting with unexplained hypoxia, more so in absence of clinical response to routine management of thromboembolic disease.

Acknowledgements

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