CASE REPORT

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Deep Venous Thrombosis and Miliary Shadows in Lungs: A Rare Entity with an Ominous Outcome

Vivek Pal Singh, Anil Vardani**, Harsh Mittal***, Pawan Kirtani*****

Abstract

Miliary shadows on chest X-ray though uncommon, usually do not pose a diagnostic dillema in day-to-day clinical practice. Tuberculosis being a common aetiology in South-East Asian subcontinant is often a radiological diagnosis of miliary mottling.

Fever, haemoptysis and miliary mottling in young age group aften reaffirms the diagnosis of tuberculosis. We present a case of florid multifocal deep venous thrombosis in a 25-year-old Asian male with haemoptysis as a chief complaint whose chest X-ray showed miliary shadows. The initial clinical and radiological impression was of tuberculosis with DVT, but when he was investigated thoroughly, it came out to be metastatic adenocarcinoma lung. Patient died within a month of the final diagnosis.

Key words: Deep venous thrombosis, miliary mottling, pulmonary embolism, adenocarcinoma lung, metastasis, haematogenous spread.

Introduction

Deep venous thrombosis (DVT), despite having conventional risk factors such as obesity, pregnancy, oral contraceptive pills, prolonged immobilisation, is a recognised complication of systemic malignancy[1]. In fact, patients with malignancy have a higher incidence of DVT and pulmonary embolism. Malignancies of lung have highest incidence rates of venous thromboembolism (VTE)[2]. Age and history of exposure to tobacco smoke are directly linked to development of lung cancer. Adenocarcinoma lung is strongly associated with the development of VTE[3]. However, adenocarcinoma lung with haematogenous spread showing as miliary shadows on chest X-ray and haemoptysis as first clinical presentation in a young non-smoker patient is rarely reported.

Case report

A 25-year-old male, resident of Kabul, Afghanistan, presented to us on April 1st 2018 with history of fever, right upper limb painful swelling and haemoptysis of one week duration. There was history of insidous onset of right lower limb swelling followed by left lower limb swelling approximately one month back. Venous doppler ultrasound of both lower limbs done in Kabul revealed bilateral lower limb DVT. He was given daily subcutaneous enoxaparin which was overlapped with acitrom.

When he reported to us, his vitals were normal except tachycardia (PR: 124 beats/min). Right upper limb along with right upper part of chest and right side of neck was swollen, warm and tender to touch (Fig. 1). Routine haematology, biochemistry was normal. Chest X-ray showed bilateral miliary shadows along with bilateral (right > left) hilar opacities and right paratracheal opacities (Fig. 2). Ulrasound colour doppler of neck and right upper limb showed an echogenic thrombus in right internal jugular, right subclavian, right axillary, right brachial and other veins extending downards. Ultrasound colour doppler of both lower limbs confirmed deep venous thrombosis with partial recanalisation.

A provisional diagnosis of multifocal deep venous thrombosis with miliary tuberculosis was kept and urgent CT pulmonary angiogram was done which revealed bilateral

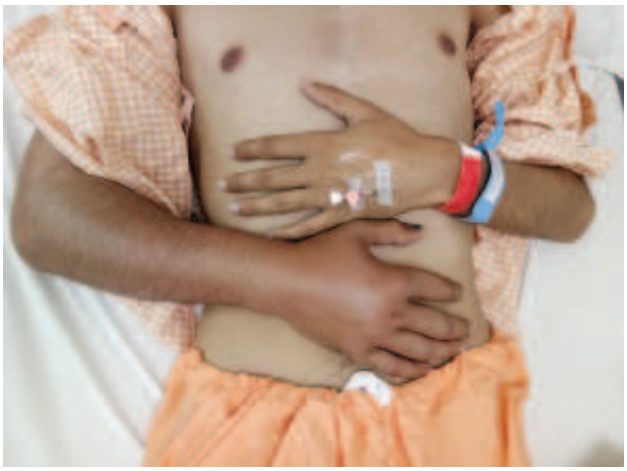

Fig. 1: *Deep venous thrombosis of right upper limb.*

****Consultant, **Senior Consultant, ***Resident, Department of Medicine, ****Consultant Pathology, BLK Super Speciality Hospital, Pusa Raod, New Delhi - 110 005.***

Corresponding Author: Dr Vivek Pal Singh, Consultant, Department of Medicine, BLK Super Speciality Hospital, Pusa Raod, New Delhi - 110 005. Phone: 9818478427, E-mail: drvps78@yahoo.co.in.

pulmonary artery thrombo-embolism with thrombus in right subclavian vein, right internal jugular vein, brachiocephalic vein and in the superior and mid course of superior vena-cava with bilateral multifocal ill-defined patchy air space consolidations, with numerous enlarged necrotic mediastinal and bilateral hilar lymph nodes with multiple enlarged right axillary, right lower deep cervical, supraclavicular, retrocrural, paraaortic, periesophageal and upper abdominal lymph nodes (Fig. 3).

Serolgy for HIV was non-reactive. Mantoux test showed anergy. Sputum for AFB and atypical cells was negative. Endobronchial ultrasound (EBUS) assisted FNAC done from pretracheal lymph node and subcarinal lymph node revealed adenocarcinoma with TTF-1, CK7 positivity and p40 negativity in atypical cells, confirmatory of adenocarcinoma lung (Fig. 4).

PET-CT with contrast revealed multiple metabolically active lesions involving mediastinal, bilateral hilar, bilateral internal mammary, right axillary and abdominal lymph nodes and multiple bones with mild left pleural effusion with features of lymphangitis carcinomatosis in both lungs (Fig. 5).

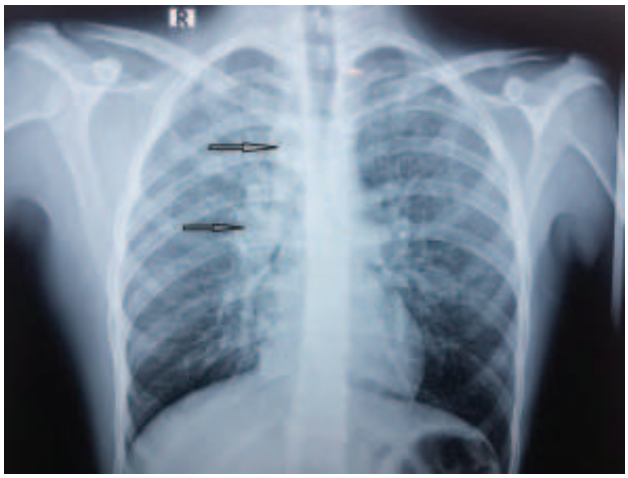

Fig. 2: *Bilateral miliary shadows along with bilateral (right > left) hilar opacities and right paratracheal opacities.*

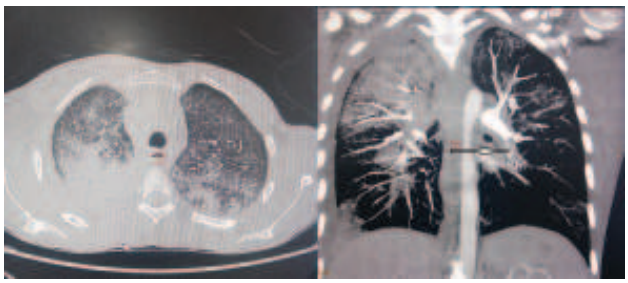

Fig. 3: *Bilateral pulmonary artery thrombo-embolism with bilateral multifocal ill-defined patchy air space consolidation, with numerous enlarged necrotic mediastinal and bilateral hilar lymph nodes.*

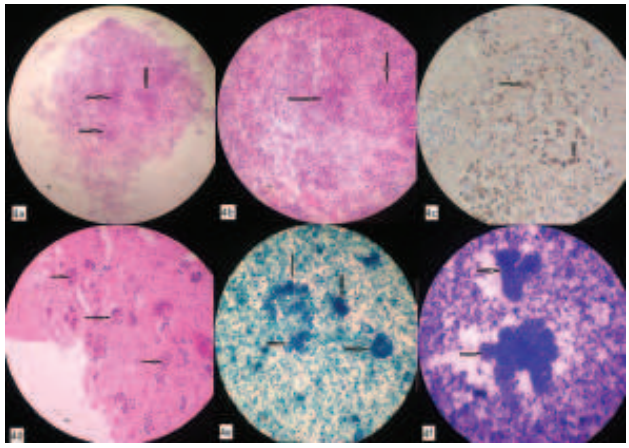

Fig. 4a: *Transbronchial lung biopsy (10 X) showing tumour nest.* ***Fig. 4b:*** *Transbronchial lung biopsy (20 X) showing tumour nest.* ***Fig. 4c:*** *IHC on cell block (40 X) with TTF-1 positivity.* ***Fig. 4d:*** *Cell block (20 X) showing tumour nest.* ***Fig. 4e:*** *FNA smear, Giemsa stain (20 X) showing tumour nest.* ***Fig. 4f:*** *FNA smear, PAP stain (20 X) showing tumour nest.*

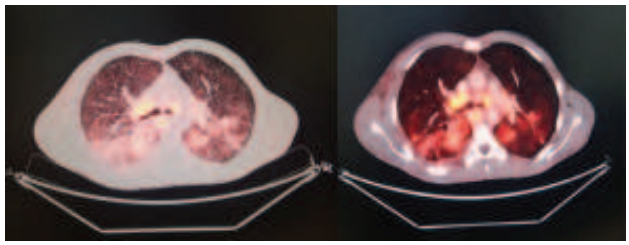

Fig. 5: *PET-CT showing multiple metabolically active lesions suggestive of lymphangitis carcinomatosis in both lungs.*

Advanced nature of the disease and limited therapeutic options were discussed with patient's family members. Palliative Chemotherapy with albumin bound paclitaxel, carboplatin, zolendronic acid and G.CSF support was planned, but in view of poor prognosis patient went back to Kabul and died within a month of final diagnosis.

Discussion

Tumours that arise from the respiratory epithelium (bronchi, bronchioles, and alveoli) are classicaly termed as carcinoma lung or epithelial lung cancers. The incidence of lung cancer is highest between ages of 55 and 65 years. Long-term passive exposure to cigarette smoke increases the risk of development of lung cancer by 1.5-fold. Active smoking increases the relative risk of developing lung cancer by about thirteen-fold[1,2,3].

The standard classification of lung cancer is small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLCs are further divided into three major subtypes: squamous cell carcinoma, adenocarcinoma and large cell carcinoma. Small cell and squamous cell carcinomas commonly present as a central mass with endobronchial

growth, whereas adenocarcinomas and large cell carcinomas present as peripheral nodules or masses often with pleural involvement[4].

Lung adenocarcinomas typically originate in the bronchial epithelium or bronchial glandular epithelium. Their radiological presentations include ground glass nodules, part-solid nodules and solid nodules on chest CT scans. A subtype of adenocarcinomas called bronchioloalveolar carcinomas grow along the alveoli without invasion and can present radiologically as a single mass or a diffuse, multi-nodular lesion or even as fluffy infiltrate[3,4].

Miliary mottling on chest radiographs is rare, and it is a common presentation of miliary tuberculosis. It is also observed in certain fungal infections, sarcoidosis, silicosis, hemosiderosis, fibrosing alveolitis, pulmonary eosinophilic syndrome, and pulmonary alveolar proteinosis, and it is rarely observed in hematogenous metastases of primary cancers of the thyroid, kidney, trophoblasts, and sarcomas. Further, presentation of primary lung cancer as miliary nodules is very rare. There are very few case reports where infiltrating bilateral miliary type of gross morphology of adenocarcinoma has been described[5,6].

Umeki *et al* in 1993 reported five cases of non-smoking bronchogenic adenocarcinoma with bone and miliary pulmonary metastases[1].

Lung adenocarcinoma with miliary pulmonary metastases is usually unresponsive to the platinum drugs paclitaxel, pemetrexed, recombinant human endostatin, etc., which makes it difficult to stop the progression of this cancer. In 2011, Eckart *et al* reported five such cases in whom gene sequencing of epidermal growth factor receptor (EGFR) mutations identified a deletion in exon 19 of the EGFR gene; all five patients had a significant response to EGFR tyrosine kinase inhibitors. Therefore, EGFR tyrosine kinase inhibitors combined with multidisciplinary synthetic therapy are probably useful for the treatment of this carcinoma[1].

Conclusion

Our patient was a young, non-smoking male (25-year-old). He presented with fever, right upper limb painful swelling and haemoptysis. His chest radiograph demonstrated miliary mottling and venous doppler studies showed multifocal DVT. Consequently, miliary tuberculosis with multifocal deep venous thrombosis was considered as an initial diagnosis. Patient was subjected to EBUS-FNAC, which completely changed the diagnosis.

This case re-emphasizes the fact that though DVT has numerous risk factors including malignancy, it is not rare to encounter a patient having florid deep venous thrombosis who is young with no conventional risk factor for DVT or malignancy.

It was interesting to note that our patient developed thrombosis at multifocal sites despite being on anticoagulation. This observation itself is a red flag sign in a patient of DVT. Most of the published literature is about incidence of symptomatic or asymptomatic venous thromboembolism in patients with lung cancers, either at diagnosis or during course of disease and treatment (chemotherapy/ surgery). There are very few cases where a young patient with no conventional risk factors for DVT or malignancy presented with florid multifocal DVT which was progressive despite being on anticoagulation therapy and the chest X-ray gave a confounding picture of miliary mottling. Tuberculosis itself can cause haematological manifestations including thrombosis. However, it is always prudent to get a histopathalogical confirmation of tuberculosis before making a final diagnosis.

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