Case Report

A Male with SLE and Familial Hyperhomocysteinemia: A Rare Presentation

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Abstract

We report a case of a 45-year-old male patient with sudden onset dyspnoea, cough and streaky haemoptysis. The patient was already being treated with anti-tuberculosis drugs by a general practitioner for suspected tubercular pleural effusion for the last 8 months. Computed tomography-pulmonary angiography revealed pulmonary thrombo-embolism. As patient have high plasma homocysteine values, further work-up of the patient including a detailed history taking, physical and laboratory examination established a diagnosis of systemic lupus erythematosus (SLE). Patient was treated with heparin, vitamin B12 and folic acid supplementation in addition to corticosteroids, along with supportive and symptomatic treatment. However, the progressive course the illness resulted in the development of chronic interstitial pneumonia and he succumbed to the illness. **[Indian J Chest Dis Allied Sci 2017;59:35-37]**

Key words: Hyperhomocysteinemia, Pulmonary embolism, Systemic lupus erythematosus, Chronic interstitial pneumonia.

Introduction

Hyperhomocysteinemia is a well known risk factor for venous thrombosis and pulmonary embolism.[1] Previous studies have also reported the association of higher concentrations of plasma homocysteine levels with systemic lupus erythematosus (SLE), especially in male patients.[2] Prevalence of SLE is more common in females, though there is higher propensity of hyperhomocysteinemia in males with SLE.[3] SLE can be responsible for a wide spectrum of pleurapulmonary manifestations, like pleuritis, chronic interstitial pneumonia, acute lupus pneumonitis, acute alveolar haemorrhage, vasculitis, thromboembolism and airway diseases.[4-6] We describe a case of SLE in a male with hyperhomocysteinemia and deep vein thrombosis (DVT) of lower limb with pulmonary embolism and chronic interstitial pneumonia.

Case Report

A 45-year-old non-smoker, non-alcoholic male presented to our hospital with complaints of sudden onset of breathlessness, dry cough and 2-3 episodes of streaky haemoptysis since 3 days. He was on anti-tuberculosis treatment for the last 8 months for pleural effusion under observation of a general practitioner. On examination, he was critically ill with a oxygen saturation of 68% at room air, respiratory rate 40 per minute, blood pressure of 118/84 mmHg and pulse rate 138 per minute. Respiratory examination revealed crackles over bilateral infra-scapular area. General physical examination revealed bilateral swollen and tender thighs and calves. Chest radiograph (postero-anterior view) showed left-sided pleural effusion and pleural haze (Figure 1).

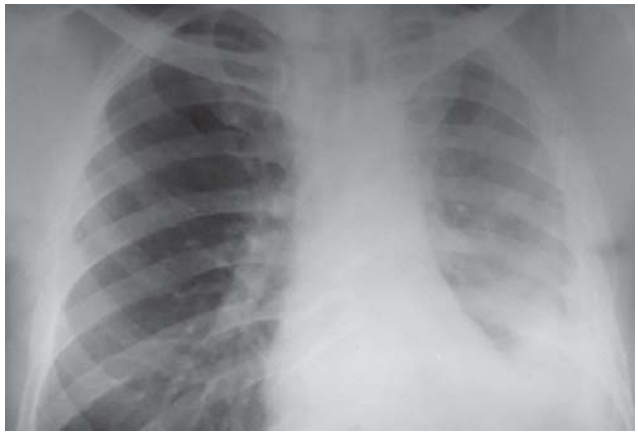

Figure 1. Chest radiograph (postero-anterior view) showing left lower zone haziness.

Electrocardiogram showed sinus tachycardia and 2D-echocardiography revealed dilated right atrium and right ventricle pulmonary hypertension with pulmonary artery systolic pressure of 45 mmHg and a normal left ventricle function. Plasma D-dimer value was 1300 ng/mL. The blood counts, kidney and liver function tests were within normal limits. Due to high index of suspicion of pulmonary embolism, contrast

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enchanced computed tomography (CECT) of the thorax with CT-pulmonary angiography was done which revealed pulmonary thromboembolism in the right upper, middle and lower lobe segmental arteries with partial thrombosis and moderate to severe sub-segmental arterial thrombosis in the right lower lobe. Left lower lung collapse was also observed with pleural thickening (Figure 2).

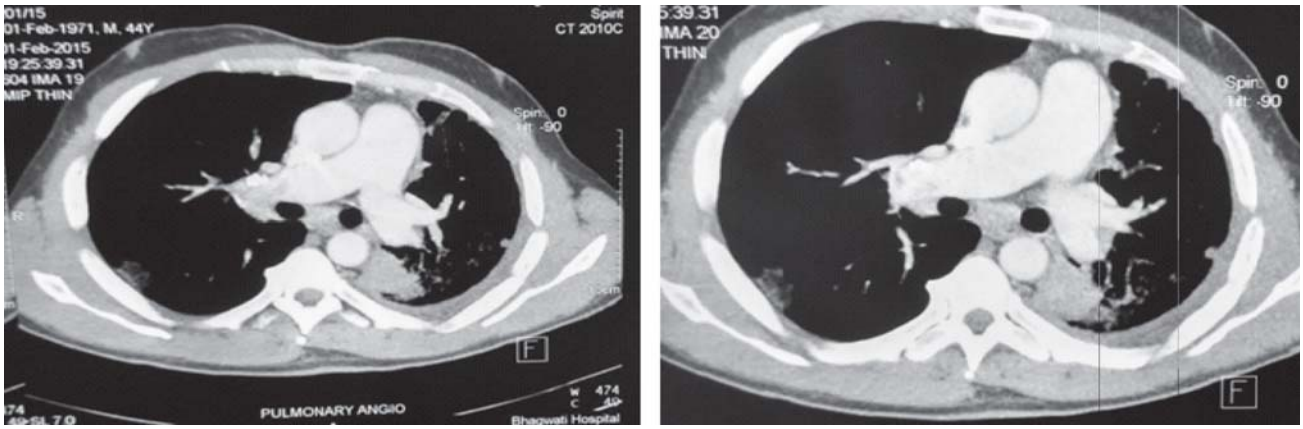

Figure 2. Contrast-enhanced computed tomography of thorax showing filling defects in the right main pulmonary artery.

Bilateral lower limb colour-Doppler revealed DVT involving the distal right superficial femoral vein and posterior tibial vein. Filling defect was also seen in the left posterior tibial vein at the level of ankle. Total plasma homocysteine level was remarkably high at 2096 micromol/L. Both anti-nuclear antibody and anti-ds-DNA (deoxyribonucleic acid) antibodies were found positive.

On subsequent review of history, patient gave history of malar rash and photosensitivity which were demonstrable during his period of admission. Vitamin B12 level was 208 pg/mL (normal 200-500 pg/mL) and folate level was 2.9 ng/mL (normal 3-17 ng/mL). Protein C and protein S activity, fibrinogen level and antithrombin III level were within normal limits. Tests for p-ANCA, c-ANCA, lupus anticoagulant, anti-phospholipid antibody, rheumatoid factor, anti-CCP antibodies, anti SS-A, anti-SS-B, anti-Sm and anti-GBM antibodies were negative.

Patient was treated with oxygen inhalation, low molecular weight heparin (dalteparin at a dose of 200IU/Kg) once daily, vitamin B12 and folic acid supplementation, prednisolone (1mg/Kg) and other supportive and symptomatic therapy. After one month of admission, patient was subjected to inferior vena cava filter placement. However, his general condition continued to deteriorate and repeat CECT of chest with CT-pulmonary angiography revealed chronic interstitial pneumonia, left lower lobe collapse and pulmonary hypertension (Figure 3).

Bronchoalveolar lavage (BAL) fluid cytology was negative for any haemorrhage and pyogenic or fungal growth. BAL for acid-fast bacilli was also negative. Patient did not give consent for transbronchial lung biopsy. A final diagnosis of SLE with hyperhomocysteinemia and DVT with pulmonary thromboembolism and chronic interstitial pneumonia was made. However, due to the intractable illness, patient died.

Patient's first-degree relatives (asymptomatic brother, son and daughter) were also evaluated. His

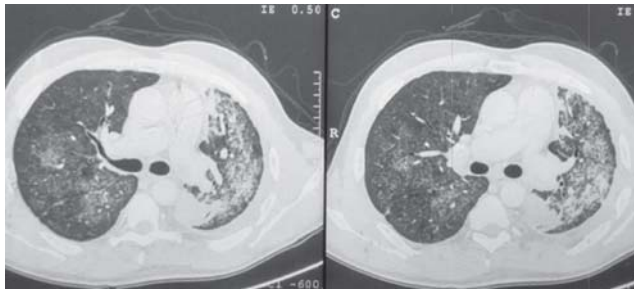

Figure 3. Computed tomography of chest showing patchy areas of ground-glass haze with septal thickening in the left lung, suggestive of interstitial fibrosis.

son and daughter were found to have high levels of plasma homocysteine (44.5 and 30.1 micromol/L, respectively). Vitamin B12 and folic acid supplementation was started for both son and daughter of the patient. Homocysteine levels decreased to less than 10 micromol/L in less than one month. Both of them were advised to remain in follow up.

Discussion

Homocysteine is produced in the body as an intermediary amino-acid in the process of conversion of methionine to cysteine. This homocysteine is normally metabolised by two divergent pathways, namely, remethylation to methionine (requiring folate and vitamin B12) and trans-sulfuration to cystathionine (requiring pyridoxal-5-phosphate). Aberrations in this homocysteine metabolism can be because of genetic factors, nutritional deficiencies (vitamin B12 and folate) and other acquired factors such as exposure to certain drugs like methotrexate,

phenytoin, carbamazepine, theophylline, metformin and niacin.[7] Hyperhomocysteinemia may be associated with co-morbid diseases, like hypothyroidism, renal failure, rheumatoid arthritis, psoriasis, diabetes mellitus and SLE.[7] Homocysteine imparts thrombogenic effect by exerting a toxic effect on clotting cascade, injuring vascular endothelium and antagonising formation and synthesis of nitric oxide.[8]

Risk of vasculo-occlusive disease associated with hyperhomocysteinemia may be classified as moderate, intermediate and severe with homo-cysteine levels 15 to 30 micromol/L, 30 to 100 micromol/L and more than 100 micromol/L, respectively.[9]

In our case, we did not find any other explanation for starting anti-tuberculoris treatment by the general practitioner; except one laboratory report of exudative nature of pleural fluid and history of prolonged febrile illness. As the patient was eventually diagnosed as a case of SLE based on his long history, existing symptoms, signs and corroborative laboratory evidence, we strongly suspect that pleural effusion that prompted the earlier physician to start anti-tuberculosis treatment was a manifestation of SLE. The patient eventually developed chronic interstitial pneumonia which is a known complication of SLE in about 3% to 13% cases.[5,6,10,11]

In conclusion, a high index of suspicion is required to make an early diagnosis of SLE in patients presenting with pleural effusion. There is also a need for screening for hyperhomocysteinemia in patients presenting with hypercoaguable state, like thrombosis. The course of the illness can be altered with an appropriate diagnosis at an early stage of the disease before the development of life-threatening complications. The role of screening of asymptomatic family members in such patients also needs to be emphasised.

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