Superior Vena Cava Thrombosis in a Case of Lung Adenocarcinoma

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Abstract

Superior vena cava syndrome is a common presentation of bronchogenic carcinoma. The mechanism of obstruction is by compression of superior vena cava by the bronchogenic tumor itself or enlarged mediastinal lymph nodes. However obstruction due to intravascular thrombosis is extremely uncommon. Here, we report a rare case of a 65-year-old male smoker who presented with superior vena cava syndrome and bilateral pleural and pericardial effusion with thrombotic occlusion of the superior vena cava in adenocarcinoma of the lung. He was given chemotherapy with carboplatin and gemcitabine with anticoagulant therapy.

Keywords: Adenocarcinoma, Lung, Superior vena cava, Thrombosis

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Introduction

Superior vena cava (SVC) thrombosis is a common phenomenon secondary to subclavian catheterization, however in malignancy it is quite uncommon. Pure intravascular thrombosis is extremely rare and only 0.04% of hospitalized adults have been diagnosed with cancer-related SVC thrombosis.[1,2] Patients that have SVC thrombosis usually present with clinical features of SVC syndrome. We report a rare case of SVC syndrome caused by cancer-related thrombosis.

Case Report

A 65-year-old male presented with progressive swelling of his face and right upper limb for one month. He was a chronic smoker for the past 30 years with a smoking index of 750. He also had dry cough since two months and a dull ache, poorly localized right-sided chest pain since the previous one month. On general survey, there was presence of mild pallor with absence of clubbing. His physical examination revealed facial puffiness, conjunctival redness, non-pulsatile engorged neck veins, and tortuous dilated superficial veins over his chest with venous flow directing above downwards towards the

umbilicus, suggestive of superior vena-caval obstruction. The respiratory system examination was remarkable for decreased chest expansion and bilateral stony dull percussion note over the infra-scapular areas. A chest radiograph showed bilateral minimal pleural effusion with a peripherally located solitary pulmonary nodule at the right lower zone of the lung field (Figure 1). Pleural fluid was pale yellow in color and analysis yielded a total nucleated cell count of 1140/mm^3 (lymphocytes 73%, mesothelial cells 27%) and no malignant cells. Contrast enhanced computed tomography (CT) scan of the thorax showed a nodular lesion in the right lower lobe, bilateral pleural effusion with mild pericardial effusion, and almost complete occlusion of the SVC by thrombosis (Figure 2). The two-dimensional echocardiography showed normal left ventricle (LV) cavity size, mildly impaired LV systolic function (left ventricular ejection fraction of 50%), a mildly dilated left atrium, and mild pericardial effusion. The CT-guided fine needle aspiration cytology (FNAC) of the lung nodule revealed columnar, cuboidal or polygonal cells with a variable quantity of fine vacuolated cytoplasm; the nucleus was of variable size (round to oval), often eccentric with a high nuclear/cytoplasm ratio, and finely granular chromatin, which suggested adenocarcinoma (Figure 3). Immunocytochemistry confirmed the diagnosis of primary adenocarcinoma of the lung, as it was positive for thyroid transcription factor-1 (TTF-1) and negative for p63 and cytokeratin 5/6. Fiberoptic bronchoscopy did not show any intra-bronchial growth or extra-bronchial compression in the bronchial tree. USG doppler of the peripheral venous and arterial system for the both upper and lower limbs showed the presence of a small thrombus only in the right proximal axillary vein with patency of the other venous and arterial systems. However, a coagulation profile did reveal the existence of a hypercoagulable state with prothrombin time of 14.8 s (control: 12.5 s), partial thromboplastin time of 43.6 s (control: 32.2 s), International Normalized Ratio (INR) of 1.13, D-dimer that was elevated at 1018 µg/L

and a fibrin degradation product of 296 µg/ml (normal <10µg/ml). Serum for antinuclear antibody (ANA), IgM and IgG anticardiolipin antibodies, and protein C and protein S were within normal limits. The patient was placed on low molecular weight heparin (LMWH) enoxaparin sodium injections, subcutaneously, at a dose of 40 IU twice daily. After five days of treatment with LMWH, INR was repeated and found to be 2.5. The patient was shifted to daily oral warfarin (5 mg) from LMWH, after 7 days of treatment. His whole body PET scan and bone scan study did not reveal any distant metastasis. He was diagnosed as a case of stage IIIB adenocarcinoma of the lung and treated with a palliative chemotherapy regimen that consisted of carboplatin and gemcitabine. After the first cycle of chemotherapy, the patient was discharged in stable condition with improvement of facial symptoms. Oral warfarin was continued at a dose of 5 mg daily and he was advised to have the INR level checked regularly.
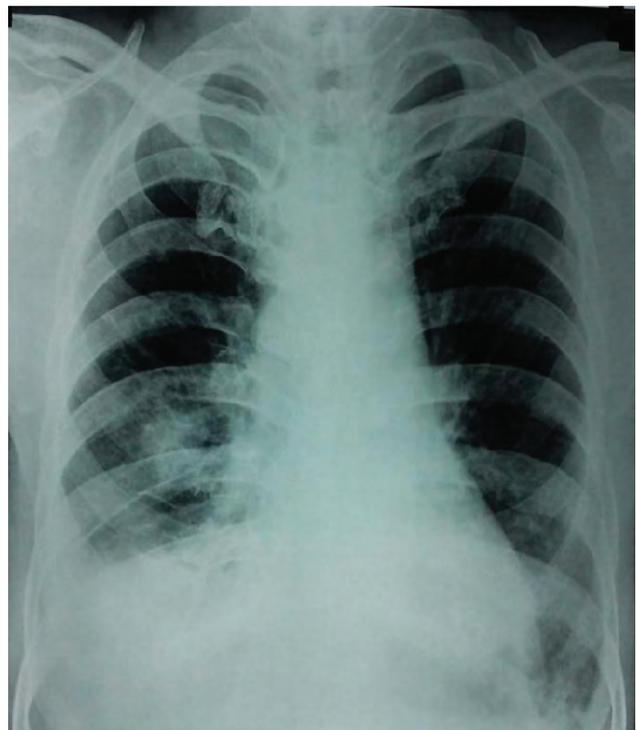

Figure 1. Chest X-ray showing bilateral minimal pleural effusion and a peripherally located solitary pulmonary nodule in the right lower zone of the lung field.

Discussion

Over 85% of SVC syndromes are caused by malignant diseases; among them lung cancer is responsible for 60% of cases, of which most are seen in small cell carcinoma cases followed by squamous cell carcinoma, adenocarcinoma and large cell carcinoma. Other tumors such as lymphoma, mesothelioma and metastatic mediastinal lymphadenopathy are associated with 20% of cases.[3] Other than malignancy, a number of benign conditions are also involved in SVC syndrome, such as benign granulomatous disease, cryptogenic mediastinal fibrosis, intrathoracic goiter or aneurysm.[3] SVC syndromes commonly occur as a result of compression of the vessel from the outside by a mediastinal mass or lymph node and may be due to an inflammatory condition such as tuberculous lymphadenopathy.[4] SVC thrombosis is a rare cause of SVC syndrome, as velocity of the blood flow in the SVC is rapid to allow for the occurrence of thrombosis. It must be suspected when there is absence of superior mediastinal widening on chest X-ray.[1,2,5] Diagnosis is confirmed by volumetric contrast enhanced CT scan of the thorax. SVC thrombosis may be due to hypercoagulable stages, pulmonary arteriovenous malformations, Behcet's disease, chronic lead exposure, thrombosis secondary to thoracic outlet syndrome, and ovarian hyperstimulation syndrome (OHSS) in patients who are undergoing in vitro fertilization following stimulation with a GnRH analog. In patients with neoplastic disease, a syndrome can occur with recurrent thrombosis in unusual areas (including the SVC) which is known as Trousseau's syndrome. Reported varieties of underlying malignancies in patients with Trousseau's syndrome include pancreatic (32.5%), lung (23.6%), gastrointestinal (17.1%) and other cancers (26.8%).[1,6] The main pathophysiologic mechanisms of Trousseau's syndrome are malignancy-related hypercoagulability and tumor cell injury of the vascular endothelium, followed by fibrin formation and platelet aggregation by thrombin production.[7] Takeda et al. have reported the case of a patient with SVC thrombosis in which the major etiologic pathway
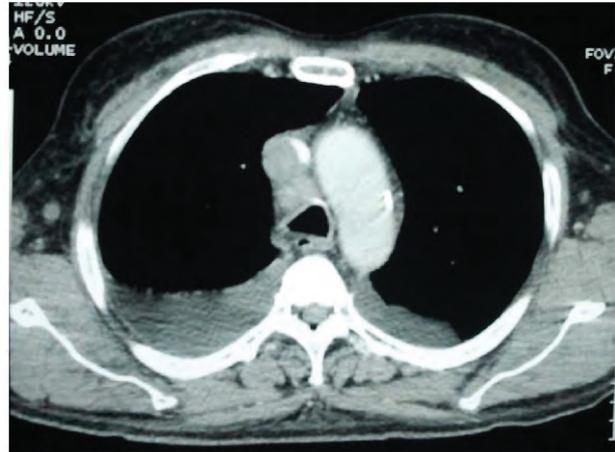
Figure 2. Contrast enhanced CT scan of the thorax showing a nodular lesion in the right lower lobe, bilateral pleural effusion with mild pericardial effusion and almost complete occlusion of the superior vena cava (SVC) by thrombosis.

was suggested to be metastasis of cancer cells to the SVC vessel endothelium from lymphatic drainage through the thoracic duct that lead to the left innominate vein via the left jugulo subclavicular angle.[5] The attachment of metastatic cells to the vessel endothelium was considered as the trigger to thrombus formation, considering the existence of malignant cells in the intra-SVC thrombus.[5]

Cancer (lung) related SVC thrombosis is also reported to be associated with Peutz-Jeghers Syndrome. Peutz-Jeghers Syndrome is characterised by hamartomatous polyposis of the
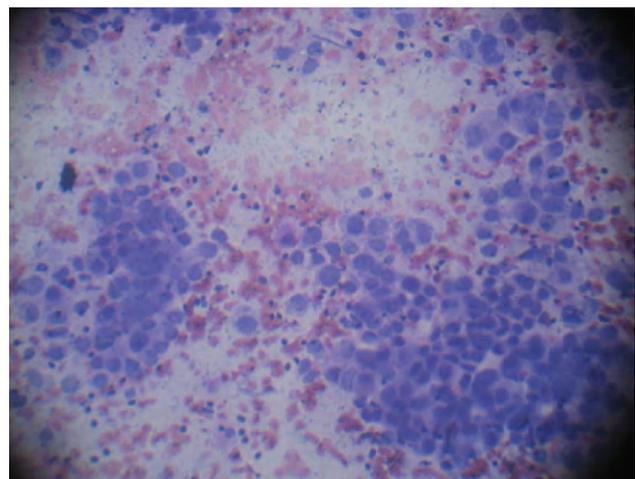

Figure 3. CT-guided fine needle aspiration cytology (FNAC) of the lung nodule showing columnar, cuboidal or polygonal cells with varying quantities of fine vacuolated cytoplasm, variably sized nucleus (round to oval), often eccentric with high nuclear/cytoplasm ratio, and finely granular chromatin suggestive of adenocarcinoma.

gastrointestinal tract and mucocutaneous melanin deposition.[8] In our case there was no lip or intraoral pigmentation and the upper GI endoscopy was normal. Other non-malignant associations of SVC thrombosis are Behcet syndrome, jugular venous catheterization (central venous catheter-ization, pacemaker wires) and systemic lupus erythematosus.[9] Superior vena cava thromboses, though uncommon, is now increasing its frequency because of iatrogenic causes.[10] In our case SVC thrombosis was due to either a cancer-related hypercoagulable state or Trousseau's syndrome.

In SVC syndrome related to malignancy the treatment is usually directed at the malignant disease process. Current treatment modalities include radiotherapy, chemotherapy, steroids and diuretics.[11] Radiation therapy to the malignant process may produce decompression. Steroids are helpful, especially in case of lymphomas that cause SVC syndrome. Here, in this case, chemotherapy (carboplatin and gemcitabine) was the mainstay of treatment. Thrombolysis therapy with anticoagulant is the main treatment modality. Other treatments include percutaneous interventions such as mechanical thrombectomy, transluminal venoplasty and stent placement, and open surgical thromboembolectomy. However thrombolytic therapy and sub-sequent anticoag-ulation for SVC syndrome are more useful in treating central venous catheter-induced acute thrombosis.[12,13] In the past, SVC stents were used when conventional treatment modalities failed. Currently SVC stents have been shown to cause dramatic improvement of SVC obstruction in more than 90% of these patients.[14,15] A few authors have shown excellent outcomes of stenting as an initial therapy in those with malignant SVC syndrome.[16] Complications of stenting include stent thrombosis and stent misplacement. Long term anticoagulation after stenting is advocated.[17] The role of anticoagulation for SVC thrombosis is debatable. Effectiveness of anticoagulation therapy for patients with SVC obstruction or after stenting has never been demonstrated and the type (heparin, warfarin, aspirin or ticlopidine) and the duration of treatment remain controversial.[14,18] In our case we could not perform angioplasty with stenting due to patient's economic condition and his SVC syndrome was improved by the sole use of anticoagulant therapy.

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