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Case report

Occult pulmonary lymphangitic carcinomatosis presenting as 'chronic cough' with a normal HRCT chest

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HIGHLIGHTS

- Asthma, GERD and postnasal drip are the 3 most common causes of chronic cough.
- Constitutional symptoms (weight loss etc.) never occur in chronic cough.
- Pulmonary lymphangitic carcinomatosis can rarely present with chronic cough.

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ABSTRACT

A diagnosis of 'chronic cough' (CC) requires the exclusion of sinister pulmonary pathology, including infection and malignancy. We present a patient with a 3 month history of CC who had an extensive workup including a normal high resolution computed tomography of the chest (HRCT) 6 weeks prior to consultation at our center. He subsequently developed constitutional symptoms including weight loss and loss of appetite 5 weeks after initial consultation. A repeat HRCT chest and a subsequent whole body PET scan found that he had developed extensive pulmonary lymphangitic carcinomatosis (PLC) from a colon primary. Treatment of the colon cancer resulted in significant decrease in metastatic disease burden and cough resolution. PLC is a very rare cause of 'chronic cough' and incipient/occult PLC presenting with chronic cough and a normal initial HRCT chest has not been previously reported.

1. Case

A 66 year old non-smoking Caucasian male with a history of post-nasal drip (PND) and long standing gastroesophageal reflux disease (GERD) presented to our pulmonary clinic for evaluation of a persistent dry cough of 3 month duration. Over the past 3 months, he had failed treatment with inhaled fluticasone/salmeterol, fluticasone nasal spray, omeprazole, loratadine as well as a short course of oral prednisone. He denied wheezing, recent upper respiratory tract infection, fevers, night sweats or weight loss. A chest x-ray (Fig.1) and HRCT of his chest (Fig.2) performed 6 weeks before presentation to our clinic were both normal.

His BMI was 29 kg/M [2] and vital signs were within normal limits. Physical examination was unrevealing. A flexible rhinolaryngoscopic examination revealed some mucus stranding and signs of chronic rhinitis without polyps. Pulmonary function testing (PFT) with methacholine challenge, exhaled oral nitric oxide (FeNO), and sinus CT were all normal. A pH impedance study showed poor symptom correlation to cough along with moderately increased esophageal acid exposure with a DeMeester score of 33.9 (normal < 14.7). A chest CT was not repeated as it had been performed within the past 6 weeks.

Based on the above test results, a treatment regimen consisting of twice daily proton pump inhibitor therapy for GERD and concurrent treatment for PND was undertaken. Several weeks of this regimen resulted in no symptom improvement. A bronchoscopy with random bronchial mucosal biopsies showed chronic inflammation without evidence for infection or malignancy. During a subsequent follow-up visit 5 weeks after the initial consultation, the patient reported new onset weight loss, decreased appetite, and a worsening cough. A repeat HRCT chest (Fig.3) was then obtained and showed interval development of diffuse pulmonary nodules

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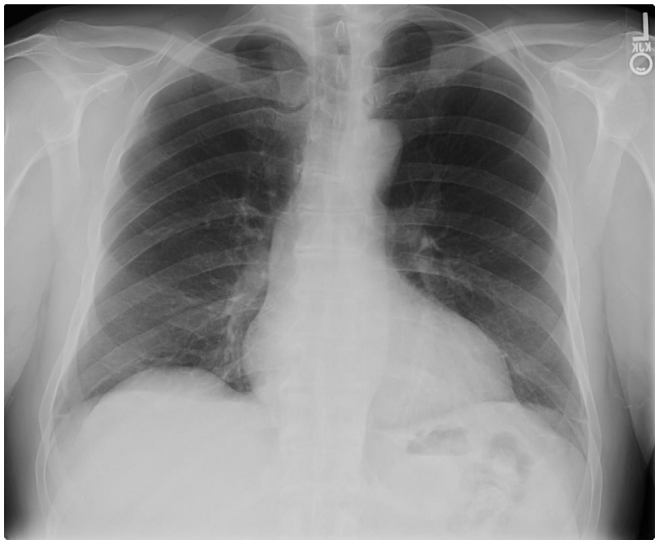

Fig. 1. Baseline chest x-ray.

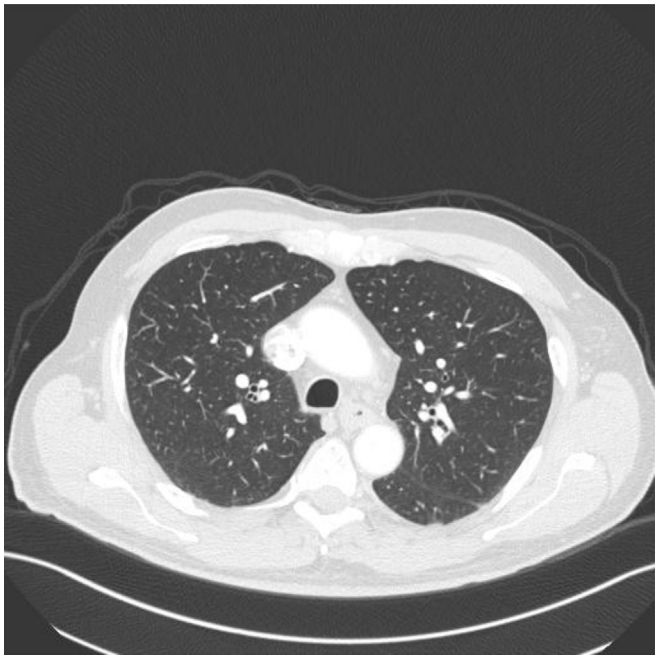

Fig. 2. Baseline HRCT chest.

along with interlobar septal thickening throughout both lungs suggestive of a diffuse hematogenous and lymphangitic metastatic process. New mild bilateral hilar adenopathy was noted without any dominant pulmonary lesion. PET scan revealed intense FDG uptake in the mesenteric wall of the ascending colon with associated wall thickening suggestive of a colon primary. In addition, extensive metastatic disease was noted with FDG avid lesions in multiple lymph nodes in the lower neck, retroperitoneum, skeleton, liver and both lung fields.

A liver biopsy revealed metastatic adenocarcinoma of colorectal origin with immunostains showing tumor cells positive for CK 20 and CDX-2 and negative for CK 7 and TTF-1 (Fig. 4). Palliative chemotherapy was begun with leucovorin, 5-fluorouracil and irinotecan and after several cycles his PLC regressed substantially along with resolution of his cough.

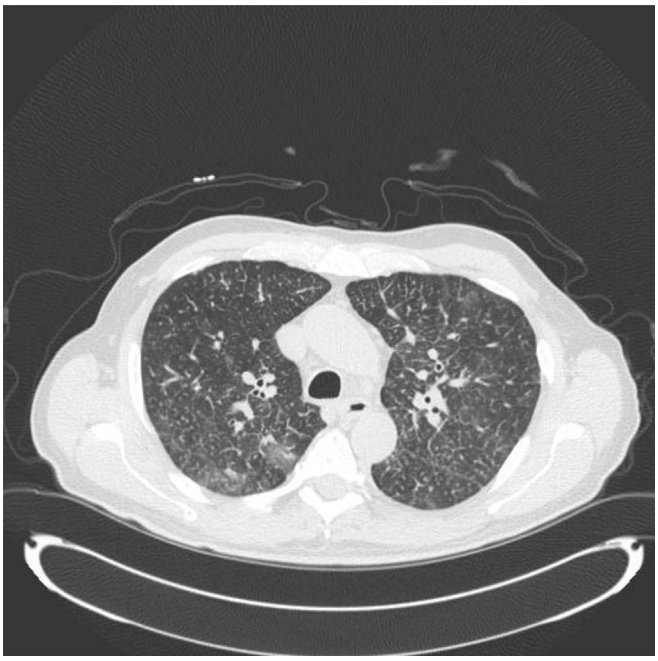

Fig. 3. Follow up CT Chest 4 months after baseline CT.

2. Discussion

The term 'Lymphangitis carcinomatosa' was first used by Troisier in 1873 to describe diffuse infiltration of the lymphatics of both lungs by malignant cells [1]. It is very uncommon pattern of tumour spread occurring in less than 10% of metastatic cancers in the lung [2]. Most PLCs originate from an adenocarcinoma with primaries frequently noted in the breast, stomach, lung, pancreas, and prostate. PLC may develop in a bilateral symmetric fashion following hematogenous emboli initially lodging in smaller pulmonary arteries and subsequently spreading through the vessel walls into the perivascular interstitium and lymphatic vessels [3]. Asymmetric or localized PLC may result from direct extension of tumour from hilar lymph nodes, pleura or from a primary lung malignancy.

Dyspnea typically develops with an insidious onset often followed by a non-productive cough. These symptoms usually progresses rapidly over weeks and often precede the identification of the primary cause. Chest pain, cyanosis and features of pulmonary hypertension have also been described [4]. Cachexia may accompany respiratory features. Auscultation usually reveals either moist or dry crackles.

Plain chest radiography can be equivocal and non-diagnostic in as many as 50% of the cases. Findings often include Kerley A & B lines, nodular shadows, pleural effusions and hilar lymphadenopathy [5]. HRCT chest scan increases the diagnostic accuracy and is excellent in demonstrating both peripheral and central changes. Common findings on HRCT include thickening of inter-lobular septa and bronchovascular interstitium giving a characteristic "dot in box" appearance, sub-pleural nodules, and thickening on the interlobar fissures, pleural effusion(s), pleural carcinomatosis, hilar and mediastinal nodal enlargement (40–50%) with relatively little destruction of overall lung architecture [6].

The pathologic features of PLC include distention of the peribronchial and peri-vascular lymphatics with tumour cells often with intra-vascular tumour emboli and endarteritis of the smaller