INTRODUCTION
Miliary shadowing on chest X-ray has a wide range of differential diagnoses. The cause can be benign like pulmonary sarcoidosis or malignant like metastases from primary or secondary lung cancer and the histological evidence provides the final diagnosis in such cases. Pulmonary metastasis from a primary lung adenocarcinoma is one of the fatal diagnoses which can present in this way. This radiological finding (miliary shadowing) is associated with better clinical prognosis when treated with EGFR (epidermal growth factor receptor) tyrosine kinase inhibitors, in cases of primary pulmonary adenocarcinoma with pulmonary miliary metastases.\(^1\)

CASE REPORT
A 61 years old Caucasian male, non-smoker who was previously fit and well, presented with a 6 months history of weight loss and dry cough. He also complained of gradually worsening shortness of breath over one month and an evening rise in temperature for the last two weeks. There was no significant past medical history except for trauma to left side of chest in a road traffic accident about 28 years ago. There was no history of contact with any known tuberculous patient. He was working as a labourer until a year ago.

On examination, he was tachycardiac, tachypnoeic and was hypoxic at rest with oxygen saturations of 86% on room air. There was a palpable, moderate sized left supra-clavicular lymph node. Chest had bilateral crackles, all over with normal heart sounds and no murmurs. Abdomen was non-tender without visceromegaly or any further lymphadenopathy.

Initial investigations including full blood count and blood chemistry were within normal limits except CRP (which was raised) and arterial blood gas analysis (which showed type-I respiratory failure). Chest X-ray (Figure 1) was performed and later, on the basis of X-ray findings a CT chest study (Figure 2) was carried out. Chest X-ray and CT-scan images were suggestive of bilateral diffuse miliary shadowing. Bronchoscopy was also planned for...
Bilateral miliary shadowing on chest X-ray

this patient, but it was deferred due to his severe hypoxia. Patient underwent supraclavicular node biopsy. Tissue histology and immunohistochemistry studies confirmed metastatic adenocarcinoma of lung origin. Tissue was also positive for EGFR mutation and he was referred to oncologist for further management, where he received treatment with tyrosine kinase inhibitors (TKI).

He initially showed some symptomatic benefit from TKI treatment but unfortunately died after 18 months of diagnosis due to pulmonary complications.

DISCUSSION

The list of differential diagnoses with such a history and radiological finding should include: pulmonary sarcoidosis, miliary tuberculosis, lymphoma, pulmonary alveolar microlithiasis (cannot explain enlarged lymph node), pulmonary histoplasmosis (especially in immunocompromised patients), lung secondaries, lung cancer with pulmonary metastases, talc granulomatosis, early stages of pneumoconiosis and pulmonary hemosiderosis.

Miliary pattern of pulmonary metastases is a rare happening with lung cancer. In cases with pulmonary miliary metastases, the commonest primary lung cancer is adenocarcinoma. In case of lung adenocarcinoma, the presence of diffuse miliary metastases on chest imaging is thought to be a clinical predictor of its response to gefitinib. A dramatic reduction in bilateral pulmonary miliary shadowing is seen in some studies after 250 mg oral gefitinib for couple of months. In such patients, epidermal growth factor receptor (EGFR) gene sequencing identified a deletion in exon 19 of the EGFR gene. Physicians should keep in mind this (rare) sub-group of patients while investigating male never smokers with bilateral micro-nodular shadowing on chest X-ray or CT scan. Although etiology of lung cancer amongst never smokers is unclear, risk factors include environmental tobacco smoke, radon and other environmental exposures.

Adenocarcinoma of the lung is the commonest lung cancer occurring in never smokers. There are certain important differences between lung cancers that occur at molecular level, in smokers and never smokers. Out of these, best understood are the EGFR pathways abnormalities. Lung cancer in never smokers has been found to be more responsive to the agents that inhibit EGFR tyrosine kinase. In lung adenocarcinoma, miliary shadowing is thought to be a clinical predictor of good response to EGFR tyrosine kinase inhibitors. In the past, studies have shown that the predictors of good response to tyrosine kinase inhibitors (TKI) treatment in lung cancer include Asian ethnicity, female gender, never smokers and adenocarcinoma on histology. Keeping in view these six predictors, this patient had three i.e. he was a non-smoker, miliary shadowing on chest X-ray and adenocarcinoma on histology.

REFERENCES