Case Report

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The coexistence of ROS1-rearranged lung adenocarcinoma and pulmonary tuberculosis in a critical ill young patient

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Abstract

The coexistence of lung cancer and pulmonary tuberculosis (PTB) is uncommon in young patients. We report a case of 22-year-old man who presented with a one-month history of chest pain, cough, slight haemoptysis and weight loss. Following two acid fast bacilli positive sputum samples, a diagnosis of TB was concluded. However, his response to anti-TB therapy was inadequate. A CT scan and further laboratory tests assisted the final diagnosis as c-ros oncogene 1 (ROS1) rearranged lung adenocarcinoma and PTB. Despite severe comorbidities, the patient achieved clinical remission following treatment with the anti-cancer drug, crizotinib and anti- TB therapy. Clinicians should be aware that this comorbidity can occur in all age groups and the clinical and radiological symptoms of the two diseases are similar.

Keywords

ROS1, lung adenocarcinoma, pulmonary tuberculosis

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Introduction

Despite the success of molecularly targeted therapies which have improved its prognosis, lung cancer remains the leading cause of cancer-related deaths worldwide[1]. The c-ros oncogene 1 (ROS1) is a receptor tyrosine kinase proto-oncogene that plays an important role in certain tumour types and

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rearrangements of the gene have been reported in 1–2% of patients with non-small-cell lung cancer (NSCLC).[1,2] Pulmonary tuberculosis (PTB) is a common disease which also causes considerable mortality and results in a heavy economic burden for many developing countries[3]. Lung infections, such as TB have been suggested to be contributing factors in the aetiology of lung cancer. [4] However, although studies suggest that there is a two-fold risk of cancer in patients with PTB, [4,5] the coexistence of lung cancer in active PTB cases is reported to be less than 5%.[6]We report here on a rare case of ROS1-rearranged lung adenocarcinoma and PTB in a young adult male.

Case report

A 22-year-old man was admitted to our hospital with a one-month history of chest pain, cough, slight haemoptysis and weight loss. He had received amoxicillin orally from another medical institution but his symptoms had not abated. He had a smoking history of 15 cigarettes/day for four years and his weight and height were 50 kg and 175 cm, respectively. Routine blood tests showed that his haemoglobin level was low (102 g/l) and his white blood cell (WBC) count was elevated (16.25x10^9/l). A chest X-ray showed a mass in the right lung upper zone (Figure 1a). On two occasions, acid fast bacilli were found in his sputum and so a diagnosis of TB was concluded. However, the sputum samples were negative for the culture of TB and common bacteria. His erythrocyte sedimentation rate (ESR, 76mm/h) and C-reactive protein (CRP, 293mg/l) levels were elevated. He was diagnosed initially as having PTB and pneumonia.

He was treated with anti-TB therapy (oral isoniazid 300mg, rifampicin 450mg, ethambutol 1200mg and pyrazinamide 1500mg daily) and an antibiotic (intravenous cefperazone-sulbactam, 3g q12h for one week). However, his response to treatment was inadequate and he began to complain of fatigue, headache, and stomach-ache. Eventually, he became too weak to get out of the bed. Additional laboratory tests were performed and, on this occasion, sputum samples were positive for influenza B. A computed tomography (CT) scan showed a 10.2 x 7.2cm mass in the right upper lung and several small nodules in both lungs (Figure 1b and c). In addition, bilateral hilar and mediastinal lymphadenopathy was observed. An abdominal CT showed multiple nodular enhancing lesions in the liver, kidneys, adrenals, pancreas, mesentery, peritoneum, abdominal wall, lumbar vertebrae, and pelvis. Moreover, brain magnetic resonance imaging (MRI) showed multiple ring-enhancing intracranial lesions (Figure 1d).

A percutaneous lung biopsy guided by CT showed poorly differentiated lung adenocarcinoma. Subsequently, epidermal growth factor receptor (EGFR) mutations were investigated by amplification refractory mutation system (ARMS), and ROS1 and anaplastic lymphoma kinase (ALK) rearrangements were assessed by reverse transcription (RT)-PCR (AmoyDx, Xiamen, China).

Although ROS1 rearrangements were identified, EGFR mutations and ALK rearrangements were not detected. Diagnosis was modified to lung adenocarcinoma T4N3M1C stage IVB[7] (ROS1 rearranged), PTB, pneumonia and influenza B.

Following this diagnosis, the patient received oral crizotinib (250 mg bid, long-term), oseltamivir (75mg bid for one week), anti-TB drugs (as above, long-term) and cefperazone-sulbactam (3g q12h for one week). The patient responded to this treatment and his symptoms eased. After one week, he was able to get out of bed and walk. A subsequent chest CT scan three months later showed that the mass in the

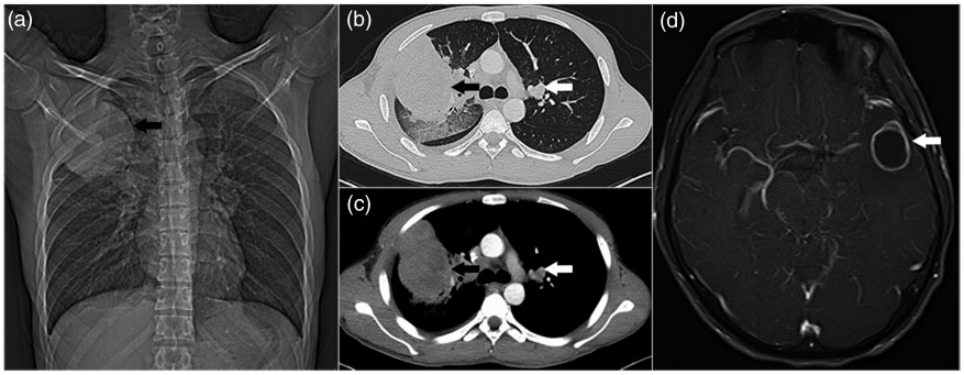

Figure 1. (a) Chest X-ray showed a large mass (black arrow); (b and c) Chest computed tomography (CT) scan showed a mass (10.2 x 7.2 cm, black arrow) in the right upper lung with several nodules (white arrow); (d) Brain magnetic resonance imaging (MRI) showed ring-enhancing intracranial lesions (white arrow).

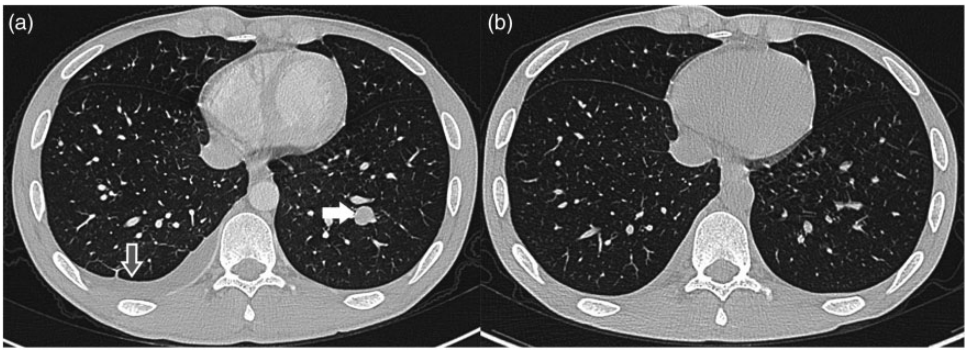

Figure 2. Chest computed tomography (CT) scans showing that the nodule (white arrow) in left lung and pleural effusion (gray arrow) in the right thorax (a) disappeared following treatment (b).

right lung had decreased to 6.8 x 6.0 cm (i.e., 45% decrease in size) , and the nodules in the left lung and pleural effusion in the right thorax had disappeared (Figure 2a and 2b).

Discussion

Lung infections including TB are thought to increase the risk of lung cancer by causing inflammation, which leads to fibrosis, scarring, tissue damage and genetic alterations.[4] One study involving 29,133 Finnish male smokers estimated that the risk of lung cancer was doubled in men with tuberculosis. [4]However, diagnosis of combined lung cancer with PTB may be overlooked because clinical symptoms (e.g., cough, haemoptysis, weight loss, chest pain, dyspnoea) and radiological images (e.g., pulmonary lesions and nodules) are similar in TB and lung cancer. [8]In addition, the prevalence of the comorbidity is low[4,5] and affected patients are likely to be more than 50 years old. [4,9]

In the case reported here, the patient's age, history, clinical symptoms and two

acid-fast bacilli smear-positive sputum samples suggested an initial diagnosis of PTB and so identification of the coincidental lung cancer was delayed. The patient's inadequate response to initial TB therapy resulted in further investigations which ultimately lead to a correct diagnosis. In addition, a chest CT scan provided us with more detailed information compared with the conventional chest X-ray.

To-date, the relationship between lung cancer and PTB has not been thoroughly investigated. However, one study suggested that survival of lung cancer patients with PTB was significantly shorter than those without PTB,[9] and another study concluded that toxicities of lung cancer-related chemotherapy worsened TB.[10] In addition, previous research found that in patients with lung cancer, EGFR exon 19 deletion was reported to occur more frequently in patients with a history of PTB than those without TB lesions.[11]We performed a genetic mutation test for this patient and identified ROS1-rearranged lung adenocarcinoma. Accordingly, we treated the patient with the anti-cancer drug, crizotinib, which is active against ROS1-positive advanced NSCLC.[12] Although the patient had several comorbidities, he achieved clinical remission and at the three months follow-up the lung mass had shrunk by 45%.

In summary, the early recognition of coincidental PTB and lung cancer is important for therapy options and prognosis. Although our data are from only one patient, our report suggests that clinicians should be aware that this comorbidity can occur in all age groups and that a chest CT scan is more useful than a conventional chest X-ray for its diagnosis. In addition, the inclusion of a tuberculin skin test to assist TB detection and the evaluation of TB drug resistance may help determine the most effective anti-TB strategy.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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