

Tuberculosis Masquerading as Recurrent Metastatic Carcinoma of the Cervix

Dear Editor,

The incidences of certain malignancies are increasing and are major causes of mortality. Diagnosis can be difficult and delayed. Most cases are diagnosed at advanced stages making curative therapy impossible. Importantly, infection such as tuberculosis (TB) can manifest with non-specific presentations and mimic malignancies.¹⁻³ In regions where TB infection remains endemic or are found in patients with risk factors, it is very important to consider this infection as it can be easily treated.

A 48-year-old female presented with a 2-month history of chronic cough. She was diagnosed, 9 years before, with carcinoma of the cervix stage 1B. This was treated with a combination of 50.4 Gy over 28 fractions and 33 Gy intra-cervical radiotherapy with complete response. Three years later, she presented with a 3-month history of intermittent fever, night sweats, weight loss, cough and epigastric pain. Chest radiograph (CXR) showed mass lesion in the left lower lobe with a small effusion (Fig. 1a). A computed tomographic (CT) scan of the thorax, abdomen and pelvis (CT-TAP) identified 2 pleural-based masses and an intra-pulmonary mass of the left lower lobe. A trucut biopsy of the pleural based mass showed metastatic squamous cell carcinoma, indicting recurrence of the carcinoma of the cervix. She was treated with 6 cycles of chemotherapy consisting of cisplatin, methotrexate and bleomycin with partial regression. In view of the localised disease, surgical resection was considered. However, the patient declined any surgical intervention and was further treated with another 6 cycles of taxol and carboplatin with good response. Serial imaging and laboratory monitoring showed complete remission of her malignancy. Over the next 5 years, she had 3 episodes of self-limiting haematuria, which was attributed to a combination of urinary tract infection and post-radiation cystitis.

In the current presentation, she had a 2-month history of cough productive of white coloured sputum, which failed to respond to antibiotics. She also had a 1-month history of dysgeusia, loss of appetite and weight loss. Examination revealed fine crackles in the left base of the lung. CXR showed a mass in left hilar region (Fig. 1b). A CT-TAP showed enlarged lymph nodes in paratracheal, hilar and subcarinal regions, while the lungs and pleura appeared clear. Sputum smear and culture for acid fast bacilli (AFB) were negative. Tumour recurrence was suspected. However, she later mentioned that her son-in-law had a chronic cough that had not been investigated, suggestive of possible TB.

She was referred to a respiratory physician for further evaluation. Repeated sputum smear and culture were negative for AFB. Her erythrocyte sedimentation rate (ESR) was elevated and was noted to have a small supraclavicular lymph node. A fine needle aspiration (FNA) of the lymph node was performed and this only showed reactive hyperplasia. After further discussion, it was decided that a mediastinoscopy would be conducted, as the lymph nodes were not amenable by percutaneous route, and endoscopic ultrasound-guided biopsy through either the transbronchial or oesophageal were not available in our centre. Mediastinoscopy showed enlarged friable right para-tracheal lymph nodes (station 4) with mucinous characteristics, suspected to be neoplastic. A frozen section did not show any malignant cells but showed multiple epithelioid cells, Langhan's giant cells and a few caseating granulomas, consistent with TB. Ziehl-Nielsen staining was negative for AFB. Based on the histology and consistent findings, she was treated for mediastinal TB lymphadenitis. She was started on directly observed therapy consisting of rifampicin, isoniazid, pyrazinamide, ethambutol and

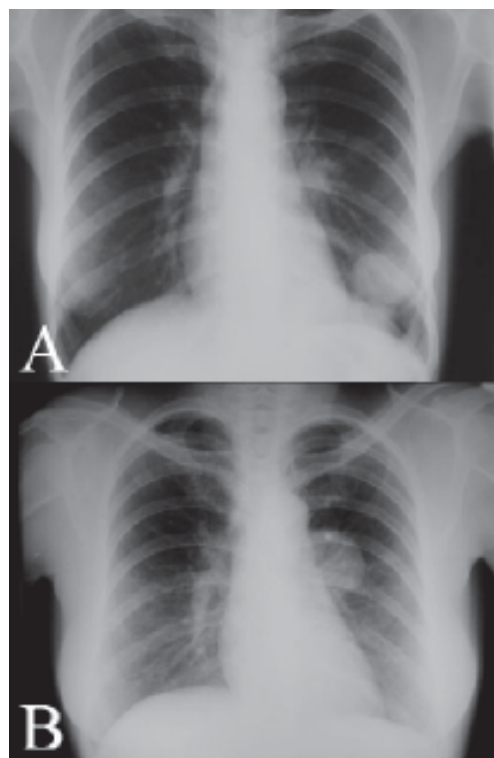


Fig. 1a. Mass in the left lower lobe due to metastatic disease.
Fig. 1b. Mass in the left hilar region secondary to tuberculosis.

pyridoxine. Her symptoms improved with a resolution of her symptoms. She remained well on follow-up 7 months after diagnosis and her latest CXR showed complete regression of the lymphadenopathies.

Our case highlights the importance of considering TB infection in patients with suspected recurrence of malignancy. With the resurgence of TB infection due to the HIV epidemic and an increase in migrations, it will likely contribute to diagnostic dilemma. Co-existence with neoplasms is also more likely to occur.^{4,5} Malignancies or associated treatments increase the risk of reactivation of latent infection or acquisition of TB infection. In our case, the patient probably acquired the infection as previous imaging of her thorax did not show any evidence of previous pulmonary TB and furthermore, her relative had symptoms suggestive of TB.

Misdiagnosis is not uncommon. One study showed that up to 22.9% of patients with known cancers were initially misdiagnosed as having pulmonary metastasis or recurrence.¹ These were later confirmed to be TB infections. Another study showed that TB was the most common infection mimicking cancers on radiological imaging, occurring in 24% of cases.² In our case, the findings from the latest radiograph were similar to those observed when she was diagnosed with recurrence. If our patient had been treated for recurrence without further investigations, the outcome would have been different.

There are many factors that may contribute to diagnostic delay or misdiagnosis. Lack of clinical suspicion, absences of history of previous infections or exposures are contributory factors. Isolation of AFB can be difficult and reliance on AFB isolation to make a firm diagnosis is also contributory. Furthermore, further final culture results are only available until after 6 weeks. Other tests such as Mantoux or heaf tests are widely available but not reliable, and more sensitive tests such as polymerase chain reaction (PCR) is not widely available. It is important to search for other organ involvements and more invasive investigations may need to be considered. In our case, if we had not proceeded to mediastinoscopy, the diagnosis would have been delayed and may affect the outcome.

Our case is also of interest because of the natural history of the disease. Reported 5-year survivals after a relapse of stage 1B diseases have been very poor.⁶ In our own experience, 75% of patients with stage 1B of disease relapse have died and our current patient is the sole survivor. Our patient only had a partial response to first-line chemotherapy, but showed very good response after 6 cycles of second-line chemotherapy (paclitaxel and

carboplatin). Our patient had remained well without any evidence of disease relapse or recurrence 68 months after the last chemotherapy. The exact reasons for our patient's favourable response are unknown. However, tumour characteristics and treatment response are predictive factors. Squamous cell type disease has been shown to be associated with better prognosis, whereas short intervals between disease relapse and poor response to initial treatment are associated with less favourable prognosis.

In conclusion, it is important to consider TB infections in patients with new pulmonary lesions suspected to be metastatic or a recurrence of neoplasm. TB infection remains treatable despite advanced stages at diagnosis. This is especially true in patients residing in areas where TB is still common or with risk factors for TB infections.

REFERENCES

1. Wang JY, Lee LN, Hsueh PR. Factors changing the manifestation of pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2004;9:777-83.
2. Rolston KV, Rodriguez S, Dholakia N, Whimbey E, Raad I. Pulmonary infections mimicking cancer: a retrospective, three-year review. *Support Care Cancer* 1997;5:90-3.
3. Koc S, Beydilli G, Tulunay G, Ocalan R, Boran N, Ozgul N, et al. Peritoneal tuberculosis mimicking advanced ovarian cancer: a retrospective review of 22 cases. *Gynecol Oncol* 2006;103:565-9.
4. Chen CH, Huang CY, Chow SN. Early-stage ovarian carcinoma combined with pulmonary tuberculosis mimicking advanced ovarian cancer: a case report. *Int J Gynecol Cancer* 2004;14:1007-11.
5. Pandey M, Abraham EK, Chandramohan K, Rajan B. Tuberculosis and metastatic carcinoma coexistence in axillary lymph node: a case report. *World J Surg Oncol* 2003;1:3.
6. Tay EH, Yeap ML, Ho TH. A 5-year review of FIGO stage 1B cervical cancer in an Asian population. *Singapore Med J* 1997;38:520-4.

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