An Unusual Cause of Calcific Thoracic Metastases

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Clinical Summary

An 18-year-old male presented with progressive breathlessness and cough of two months duration. He also complained of generalised body pains, low grade intermittent fever, anorexia and weight loss. He was started on empiric daily anti-tuberculosis treatment with rifampicin, isoniazid, pyrazinamide and ethambutol from elsewhere for right-sided pleural effusion one month ago. He presented to us as he did not experience improvement in his condition. There was no other significant medical history. Physical examination showed a 10cm x 8cm, non-tender hard bony mass with ill-defined margins over the upper third of left arm. There was no evidence of digital clubbing or peripheral lymphadenopathy. Respiratory system examination showed features of a right-sided pleural effusion.

Investigations

Routine blood and urine investigations were normal. Serum alkaline phosphate levels were elevated (1176 IU/L). Chest radiograph (Figure 1) showed a right-sided pleural effusion with bilateral pleuro-pulmonary calcific lesions. Antero-posterior and lateral radiograph showed bony mass in the upper third of left humerus (Figure 2). Computed tomography (CT) of chest (Figure 3) revealed bilateral pleuro-pulmonary calcifications with right-sided moderate pleural effusion. On thoracocentesis light yellow-coloured free-flowing pleural fluid was obtained. The pleural fluid was transudative and negative for acid-fast bacilli and malignant cells.
Punch biopsy of bony lesion of left humerus was reported as osteosarcoma (Figure 4). Fine needle aspiration cytology of pleural lesion revealed hyperchromatic nuclei and osteoid formation (Figure 5).

Diagnosis

Left humerus osteosarcoma with pleura-pulmonary calcific metastases and right-sided pleural effusion.

Discussion

Osteosarcoma is the most common primary malignancy of the bone with a peak incidence in the second decade and an additional peak of incidence in elderly individuals. Our patient was in the second decade of life. Osteosarcoma arises from the primitive mesenchymal bone forming cells and the histological hallmark is the presence of malignant osteoid. Distant metastases are evident in 10% of osteosarcoma patients at the time of presentation. Lung is the most common site of metastasis. In our patient, distant metastases to the lung and pleura were evident at the time of presentation. Lung metastases have been observed in more than 90% of patients with osteosarcoma who died. The average interval between the commencement of treatment of primary tumour and the diagnosis of metastatic disease has been observed to be 16 months and an interval of less than one year associated with poor prognosis. In our case, metastases to lung and pleura was observed within two months of occurrence of the primary lesion.

In Japan, annual autopsy database (1981-2002) showed that pleura was involved in 12.1% of patients who died of metastatic osteosarcoma. Though autopsy studies indicating that pleural involvement in metastatic osteosarcoma is not very rare, occurrence of extensive pleural involvement in primary osteosarcoma during life is very rare. Metastatic osteosarcoma presenting with extensive pleural involvement may occur either by direct spread from the underlying lung or by haematogeneous spread. In our case, haematogeneous spread might have resulted in bilateral and extensive pleural involvement.

Pleural calcification may occur due to benign and malignant causes. Benign causes of pleural calcifications include previous trauma or previous pleural infection, haemothorax, calcifying fibrous pseudo-tumour of the pleura and the asbestos exposure. Malignant causes of pleural calcifications include metastatic disease from osteosarcoma, chondrosarcoma, adenocarcinoma, parosteal osteosarcoma and mesothelioma. The mechanism of metastatic calcification in osteosarcoma is not clear. Metastatic calcification deposition can be influenced by the release of excess calcium salts from bone, phosphate concentration, alkaline phosphatase activity, and viscera physico-chemical conditions under alkalosis. The liberated calcium phosphate \([\text{Ca}_3(\text{PO}_4)_2]\) and calcium carbonate \([\text{CaCO}_3]\) salts from the primary site are transported via the blood in soluble form. The increased delivery and precipitation of these salts in distant tissues under alkalosis is thought to result in occurrence of calcification.

Osteosarcoma shows a dramatic response to chemotherapy but 25%-30% may show recurrence. Overall management and prognosis is determined by the number, site and size of the metastasis. Although the histopathological confirmation of lung metastases is essential for proper management and follow-up of the case, it could not be done in our patient in view of his poor general condition and also because the patient was unwilling to undergo the procedure.

The lung metastases are treatable with metastasectomy and adjuvant chemotherapy if the metastatic disease is limited to lung and if complete resection can be obtained with sufficient, i.e., at least
50% post-operative pulmonary reserve. In our case, though the metastatic disease is limited to the thorax, extensive bilateral disease rendered surgical resection impossible. The 5-year survival rate in patients with pulmonary metastasis from osteosarcoma has been observed to be 41% after surgery and systemic chemotherapy. A short time-interval between initial presentation and relapse, recurrence involving more than one organ and bilateral lung and pleural involvement are associated with less favourable outcome. Palliative therapy with neo-adjuvant chemotherapy or radiotherapy was planned in our case. But the patient was severely ill at the time of diagnosis and his parents were not willing for further treatment; he died shortly after confirmation of the diagnosis.

References