

Squamous cell carcinoma of lung with tibial metastasis: A case report



Medical Science

KEYWORDS : Lung carcinoma, Tibial metastasis, Chemotherapy, Bisphosphonates

Dr. Rajib Bhattacharjee MD PGT; Dept. of Radiotherapy; IPGMER, Kolkata.

Dr. Somnath Roy Senior Resident; Dept. of Radiotherapy; IPGMER, Kolkata.

Dr. Ranti Ghosh MD PGT; Dept. of Radiotherapy; IPGMER, Kolkata

Dr. Koushwambi Kar DMRT PGT; Dept. of Radiotherapy; IPGMER, Kolkata.

ABSTRACT

Bone metastasis is common with lung cancer. The most common sites are in the axial skeleton and less common are in the appendicular skeleton but metastasis distal to elbow or knee joints are very rare. As per literature review, there are very few case reports of tibial metastasis from lung cancer, more so with squamous cell histology. Here we report a case of squamous cell carcinoma lung with left tibial metastasis treated with systemic chemotherapy and bisphosphonate and we share our experience regarding treatment outcome and lessons learnt in the process, regarding the need of palliative radiation to the skeletal metastatic site.

INTRODUCTION

Skeletal metastasis are a common occurrence in lung cancer. About 30-40% of lung cancer patients develop skeletal metastases^[1]. The axial skeleton is a more common site of metastasis from lung than the appendicular skeleton^[2]. The most common sites of skeletal metastasis are ribs, spine and pelvis^[3]. Metastasis beyond knee such as in tibia is very rare. Such cases are treated with platinum based chemotherapy. Among bisphosphonates, only zoledronic acid has broad efficacy in the treatment of bone metastases from all solid tumor types, including lung^[1]. Local site palliative radiotherapy is used in some institutes for the bone metastatic site^[4].

CASE REPORT

A 55 years old male chronic smoker attended our out patient's department with complaints of antalgic gait for last 5 months and chronic dry cough for 3 weeks. He was non-diabetic, non hypertensive and without any other co-morbidities. Clinical examination revealed a mild tenderness over the proximal end of left tibia and clubbing on all fingers and toes. No lymph nodes including those in the supra-clavicular area were palpated. X-ray of left knee Antero-Posterior (AP) & Lateral view (figure 1) showed an osteolytic lesion in upper end of left tibia with erosion of medial cortical margin. Chest X-ray Postero-Anterior (PA) view showed a patchy scarry fibrotic opacity in the lower zone of right lung. Contrast Enhanced Computed Tomography (CECT) Scan of thorax (figure 2) revealed an irregular thick walled cavitary lesion in right lower zone with hilar lymphadenopathy. Biopsy from the left tibial lesion (figure 3) showed sheets, clumps, and dense malignant cells having hyper-chromatic pleomorphic nuclei with inconspicuous nucleoli and squamoid differentiation at places on the hemorrhagic background. Few cells showed individual keratinization, suggestive of metastatic squamous cell carcinoma. Fine Needle Aspiration Cytology (FNAC) from the right lung lesion (figure 4) showed clusters of atypical cells, some with squamous cell differentiation in a background of inflammatory cells, a picture suggestive of Squamous cell carcinoma. Other metastatic work ups were within normal limits.

Hence this was a case of squamous cell carcinoma of right lung with left tibial metastasis ($T_2 N_1 M_{1b}$ or American Joint Committee on cancer (AJCC) 7th edition stage IV). As this was a stage IV disease, we started palliative chemotherapy with Carboplatin (Area under Curve 5 i.v D1) and Gemcitabine (1000mg/m² i.v D₁ and D₈) every 21 days for three cycles. We also put the patient on monthly Zoledronic acid i.v 4mg/kg. We also trained him to walk with a walker. As the patient did not have any bone pain, we did not subject him to palliative radiation to the

metastatic site. After 3 cycles of chemotherapy we did a repeat CECT thorax (figure 5) which revealed a decrease in size of the lung lesion but the X-ray of left knee AP & Lateral view (figure 6) showed an increase in size of the lytic bone lesion.

Our plan was to continue systemic chemotherapy and to give palliative radiation to the metastatic site along with supportive care. But the patient did not come back for continuation of treatment.

DISCUSSION

Lung cancer patients present to us with varying complaints. Most present with respiratory symptoms due to the primary lesion, other may present due to general features of malignancy or systemic features of paraneoplastic syndromes. Some present incidentally with a lung lesion in the CXR and many present with symptoms of distant metastasis including bone^[2]. Skeletal metastasis though common, usually involves axial skeleton. Appendicular skeleton when involved spells poorer prognosis^[1].

Bone metastasis is of three types, osteolytic, osteoblastic and mixed. Skeletal metastasis from lung cancer is predominantly osteolytic^[2]. The major complaint is pain which is present in 80% of the cases^[1]. The tumor cells release a variety of factors which stimulates local osteoclasts and osteoblasts. Osteoclast in turn releases growth factor that leads to growth of tumor cells. The osteoclasts resorb bone that causes bone pain^[1]. In our case, the metastatic site did not produce much pain, only pain while walking and mild tenderness. Absence of symptoms due to primary lung lesion delayed diagnosis and lead to presentation in advanced stage.

The current treatment strategy for advanced non small cell lung carcinoma (NSCLC) includes first line chemotherapy with platinum based regimen. Combination of Gemcitabine with carboplatin is effective in advanced NSCLC^[5]. We used this regimen in our patient as he had squamous cell carcinoma, a variety of NSCLC. It is believed that full efficacy benefit for NSCLC is evident after 3-4 treatment cycles and if no response is achieved by then, any further platinum chemotherapy is futile^[5]. We evaluated the patient radio logically after 3 cycles.

Bisphosphonates are pyrophosphate analogues which act directly on bone to inhibit osteolysis and hence prevent skeletal related events (SRE). Berenson et al. opined that Zoledronic acid at doses of 2mg or 4mg and pamidronate at 90mg significantly reduced the need of radiotherapy to bone^[6]. But still it has been seen that SREs occur in a large proportion of patients even with

i.v bisphosphonate therapy [7]. We gave our patient a monthly dose of Zoledronic acid 4mg/kg i.v.

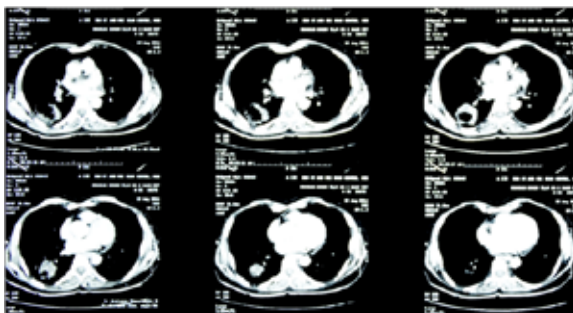
Radiotherapy can provide adequate analgesia in painful bone metastasis. Over 40% of patients can expect at least 50% pain relief, and just fewer than 30% can expect complete pain relief at one month. As analgesics are quite ineffective in bone metastasis, radiotherapy assumes a pivotal role in palliation of skeletal metastasis [8].

In our patient, we used recommended first line palliative chemotherapy and bisphosphonate. The primary lesion in the lung did respond to chemotherapy but skeletal lesion did not. In spite of regression of the lung lesion, the bone lesion continued to grow. As there was not much bone pain, we refrained from applying palliative radiotherapy to the metastatic site. But this situation does raise the question whether or not local radiotherapy should be used for even asymptomatic solitary bone lesion to increase progression free survival.

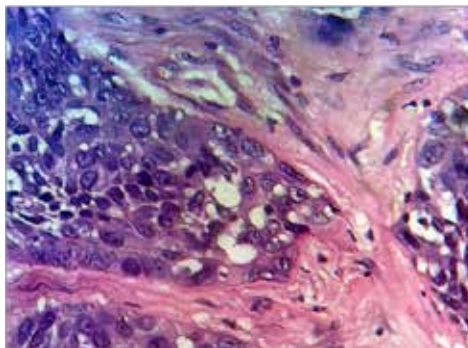
To conclude, NSCLC with distal appendicular solitary bone metastasis is very rare, it will be difficult to accrue enough patients for a prospective trial dedicated to resolve the dilemma regarding treatment in such a scenario.



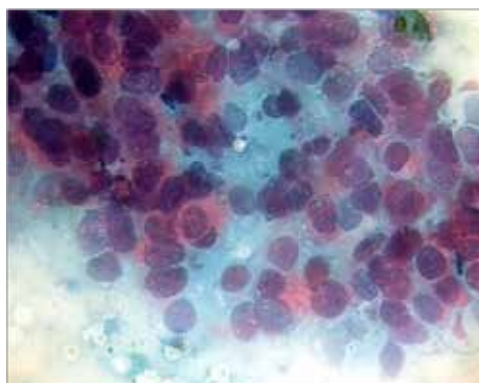
Legends of figure 1: X-Ray Left Knee (AP& Lat view) showing an osteolytic lesion in upper end of left tibia with erosion of medial cortical margin.



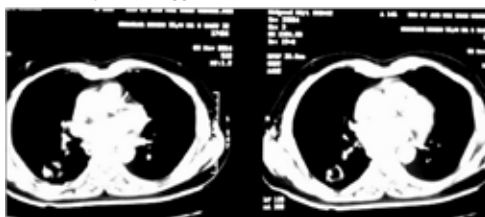
Legends of figure 2: CECT Thorax showing an irregular thick walled cavitary lesion in right lower zone with hilar lymphadenopathy.



Legends of figure 3: Histopathology slide from tibial lesion (high power field) showing sheets, clumps, and dense malignant cells have hyper chromatic, pleomorphic nuclei with inconspicuous nucleoli and squamous differentiation at places on the hemorrhagic background, suggestive of metastatic squamous cell carcinoma.



Legends of figure 4: FNAC from lung lesion showing clusters of atypical cells, some with squamous differentiation in a background of inflammatory cells, suggestive of Squamous cell carcinoma.



Legends of figure 5: CECT Thorax showing decreased size of the lesion in comparison with previous scan.



Legends of figure 6: X-Ray left knee (AP & Lateral) shows increased lesion compared to the previous film.

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