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The Break of Silence: More than Just Giant Cells

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An 88-year-old man presented with a fracture of the left humerus following a trivial trauma. There was no relevant history or comorbidities. He was planned for open reduction and internal fixation. On preoperative evaluation, a suspicious, well-defined radio-opaque lesion was noted in the left mid-zone of the lung on chest X-ray and computed tomography (CT) of the thorax (►**Fig. 1A**). Intraoperatively, a solid lesion was noticed around the fracture site in the adjacent soft tissue (►**Fig. 1B**). A biopsy was performed, and left humerus bone tissue with surrounding soft tissue was sent for histopathological examination following fracture fixation (►**Fig. 1C**). The preoperative X-ray, CT picture, and intraoperative findings were consolidated, and positron emission tomography CT (PET-CT) was advised for further evaluation. PET-CT revealed left lung malignancy with mediastinal lymph node and adrenal and bone metastasis (►**Fig. 1D**). On histopathological examination, the tumor cells were arranged in sheets and nests. Individual cells showed round to polygonal cells with nuclear pleomorphism, increased nuclear to cytoplasmic ratio, moderate eosinophilic cytoplasm, vesicular chromatin with prominent nucleoli admixed with numerous multinucleated giant cells, and areas of necrosis within the nests (►**Fig. 2A, B**). The differentials were metastatic adenocarcinoma and malignant giant cell lesions of the bone. To establish the primary origin of the tumor, a panel of markers was performed by immunohistochemistry (IHC). Surprisingly, IHC showed cytoplasmic and membranous positivity for CK7 only and negative for other markers like TTF1, napsin A for primary lung adenocarcinoma, P63 for giant cell tumor of bone, CK20 for lower gastrointestinal tract neoplasms, inhibin for adrenal cortical tumor, and NKX3.3 for prostate adenocarcinoma (►**Fig. 2C, D**). However, due to patients economic constraints only a limited panel of IHCs were indicated, CD68 to confirm osteoclast-like giant cells (OGC) and molecular profiling could not be performed. Collaborating the radiological findings with histopathological and IHC features, on literature search, it was identified that non-small-cell lung carcinoma with OCG (NSCLC-OCG) is a relatively rare entity that may be negative for primary lung markers and can present upfront with metastasis, masking the primary site of origin and making diagnosis more intriguing. Since the patient was an elderly, curative treatment was deemed inappropriate and palliative care was given. Subsequently, the patient died within 3 months of diagnosis.

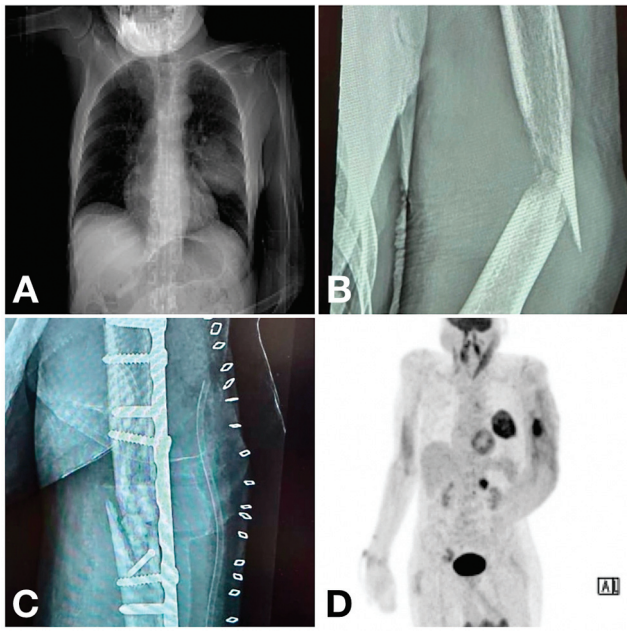

Fig. 1 (**A**) X-ray chest: lesion in the mid-zone of the left lung. (**B**) X-ray: Fracture of the left humerus following a trivial trauma. (**C**) Postoperative X-ray. (**D**) PET-CTwith fluorodeoxyglucose (**FDG**): avid lesion in the left lung, mediastinal lymph nodes, left adrenal gland, and left humerus.

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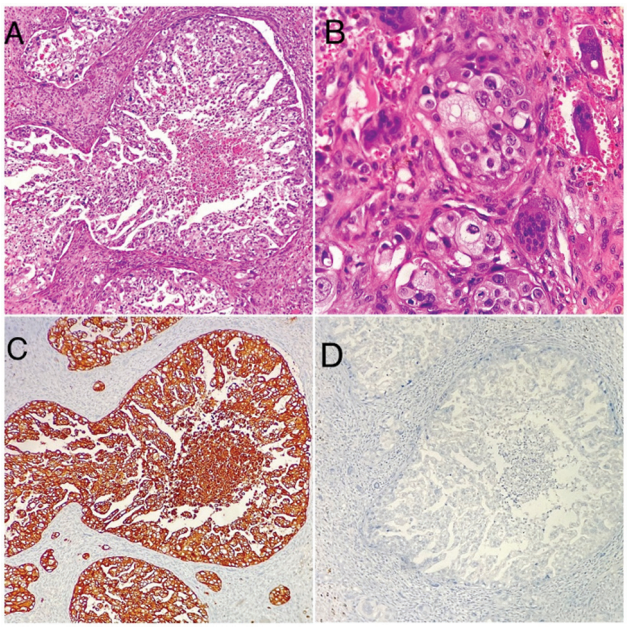

Fig. 2 (**A, B**) Tumor cells arranged in nests admixed with numerous osteoclast-like giant cells (hematoxylin and eosin [H&E] stain; 200X). (**C**) Tumor cells are positive for CK7. (**D**) Tumor cells are negative for P63, TTF1, napsin, inhibin, NKX3.1, and CK20.

NSCLC-OCG are rare, aggressive tumors that can present initially as bone metastases, often complicated by skeletal-related events, which is analogous to our case. Bone resorption by the tumor is initiated with activation of preosteoclasts of the monocyte/macrophage cell line with stimulation of RANK inducing osteoclast formation, activation, and fusion into multinucleated osteoclasts.[1] The bone matrix releases cytokines that activate the tumor growth.[2] Bone metastases from the lung primary are frequently multiple, osteolytic, and can affect any bone, more commonly the spine, followed by long and pelvic bones.[3] These tumors have overlapping features; hence, careful histopathological evaluation aided with IHC is the gold standard to subclassify these lesions appropriately.[4] Prompt and timely diagnosis of NSCLC would aid in early treatment strategies for the prevention of skeletal-related events, thus preserving the quality of life.[5]

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Conflict of Interest
None declared.

References

1 D'Antonio C, Passaro A, Gori B, et al. Bone and brain metastasis in lung cancer: recent advances in therapeutic strategies. Ther Adv Med Oncol 2014;6(03):101–114
2 Nistor C-E, Ciuche A, Cucu AP, et al. Management of lung cancer presenting with solitary bone metastasis. Medicina (Kaunas) 2022;58(10):1463
3 Santini D, Barni S, Intagliata S, et al. Natural history of non-small-cell lung cancer with bone metastases. Sci Rep 2015;5 (01):18670
4 Lindholm KE, Kalhor N, Moran CA. Osteoclast-like giant cell-rich carcinomas of the lung: a clinicopathological, immunohistochemical, and molecular study of 3 cases. Hum Pathol 2019; 85:168–173
5 Ulas A, Bilici A, Durnali A, et al. Risk factors for skeletal-related events (SREs) and factors affecting SRE-free survival for nonsmall cell lung cancer patients with bone metastases. Tumour Biol 2016;37(01):1131–1140

