Letter to the Editor

Isolated regional nodal metastasis in giant cell tumor of the bone: Case report and review of literature

DOI: 10.4103/sajc.sajc_244_19

Dear Editor,

Giant cell tumors (GCTs) of the bone are benign osteolytic tumor commonly occurring in the third to fourth decades with distal femur being the most common site.[1] They form 5% of the primary skeletal tumors.[2] Metastasis though uncommon is usually seen with recurrences. Curettage with intralesional adjuvant therapy with polymethylmethacrylate, liquid nitrogen, and bone graft has been successfully used to reduce recurrences while preserving function.[3] The management of metastasis is still debatable due to the scarcity of literature.

A 47-year-old female who was diagnosed to have GCT of the left radius for which she underwent left distal radius curettage with bone grafting. After 1 year of disease-free interval (DFI), she developed local recurrence and underwent *en bloc* resection of radius with reconstruction using nonvascularized fibula graft with plating. She developed local recurrence in the soft tissue in the next 2 years which was managed by wide local excisions. After a DFI of 1 year, she presented with an enlarged mobile epitrochlear node, fine-needle aspiration cytology of which was suggestive of GCT. Computed tomography of the chest showed no pulmonary metastasis. The patient was discussed in multispecialty board and she underwent epitrochlear nodal dissection. The final histopathology showed five nodes, with one node showing metastatic GCT. There was no perinodal spread. Figures 1 and 2 show the presence of tumor within the lymph nodes. She is on regular follow-up for 1 year and has shown no sign of recurrence.

GCT is characterized by scattered multinucleate giant cells among mononuclear stromal cells, together imparting a syncytium-like appearance causing a typical radiolucent lytic shadow on X-ray.[4] The tumor is known for its propensity for local recurrences which are generally amenable to wide excisions. The potential for metastatic spread was first reported by Jaffe *et al*. in 1940.[5] Distant metastasis is seen in 2%–3% of cases with the lungs being the most common site of distant metastasis and the incidence of pulmonary metastasis varies from 4% to 11% in the literature.[6] Other uncommon sites being the bone, skin, soft tissue, breast, and endobronchial tree have also been reported.[7]

Lymph nodal involvement is very rare in GCT and only 13 cases have been reported in the English literature.[7-19] Table 1 lists the cases of GCT with lymph node involvement. Dyke, in 1931, reported the presence of GCT in lymph nodes in a case with extensive metastatic disease.[8] Since then, majority have reported mediastinal and para-aortic nodal involvement. Only five have reported regional lymph node involvement, of which two were associated with pulmonary metastasis.[7,9-12] Isolated regional node involvement as seen in our case has been reported previously only in three cases.[9-11] Budzilovich *et al*. reported the first regional nodal involvement in 1963.[9] Present *et al*., in 1986, reported a GCT metastasizing to regional lymph node; however, it spread to lungs after a year.[10] In another case reported by Aftab and Umar, there was axillary nodal spread from GCT of the distal humerus without pulmonary involvement.[11]

In one of the largest reviews from a tertiary care center, Viswanathan and Jambhekar retrospectively evaluated 470 patients of GCTs, of which 24 had distant metastasis and only one patient had regional lymph node metastasis to inguinal lymph node. In their patient, the primary site was femur and there were multiple lung metastasis along with lymph node metastasis. The authors concluded that there was no association between clinicopathological variables and the development of metastasis.[12]

The mechanism of pulmonary metastasis has been speculated to be tumor emboli either upfront or during the time of curettage. Lymphatic spread can also be explained similarly by the multiple surgeries performed previously for our patient.

Metastatic GCT has been successfully treated with complete resection of primary and the metastasis. Pulmonary metastatectomy has been routinely performed in resectable patients, with similar principle applied for lymph node metastasis also. All four cases with regional lymph node metastasis have been managed with surgical resection. Connell *et al*. successfully managed a patient with excision of primary patellar GCT along with excision of posterior mediastinal

Table 1: Cases of giant cell tumor of bone with lymph node metastasis

Study	Site of primary	Primary procedure	Setting	Lymph node involved	Other site of metastasis	Treatment
Qureshi *et al*.[7]	Patella	Wide excision (patellectomy)	Recurrent	Regional (inguinal nodes)	Lungs	Surgical resection
Dyke[8]	Patella	Amputation	Recurrent	Distant (mediastinal and peritoneal nodes)	Lungs, spine	None
Budzilovich *et al*.[9]	Femur	Curettage with bone grafting	Recurrent	Regional (popliteal nodes)	None	Surgical resection
Present *et al*.[10]	Femur	Wide excision	Recurrent	Regional	None	Surgical resection
Aftab and Umar[11]	Distal humerus and proximal ulna	Wide excision	Primary	Regional (axillary nodes)	None	Surgical resection
Viswanathan and Jambhekar[12]	Femur	Amputation	Recurrent	Regional (inguinal)	Lung	Surgical resection
Connell *et al*.[13]	Patella	Wide excision (patellectomy)	Recurrent	Distant (mediastinal nodes)	None	Chemotherapy f/b surgical resection
Rock *et al*.[15]	Tibia	Curettage and bone grafting	Recurrent	Distant (mediastinal nodes)	Lungs	Chemotherapy
Kay *et al*.[16]	Tibia	Curettage, phenol application and bone grafting	Recurrent	Distant (mediastinal nodes)	Lungs	None
Lewis *et al*.[14]	Radius	Curettage with bone grafting	Recurrent	Distant (mediastinal nodes)	None	Steroid f/b surgical resection
Goldenberg *et al*.[17]	NA	NA	Recurrent	Distant (mediastinal nodes)	Lungs	NA
Vanel *et al*.[18]	Fibula	Not treated	Primary	Distant (mediastinal node)	None	Radiotherapy
Sung *et al*.[19]	NA	NA	Recurrent	Distant (mediastinal nodes)	None	NA
Present case	Radius	Curettage with bone grafting	Recurrent	Regional (epitrochlear)	None	Surgical resection

NA=Not available, f/b : followed by

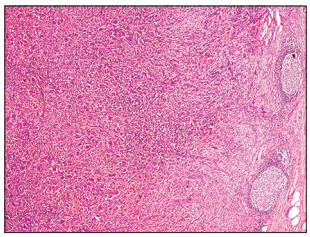

Figure 1: Lymph node replaced by metastatic tumor composed of spatially arranged multinucleate giant cells in a background of mononuclear stromal cells (H and E, ×40)

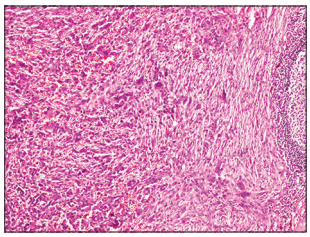

Figure 2: Higher magnification shows uniformly arranged multinucleate giant cells admixed with mononuclear stromal cells with residual lymphoid follicle (right extreme) (H and E, ×100)

nodal mass.[13] Another similar case of GCT of the patella with pulmonary and nodal metastasis treated with metastasectomy.[7] Alternate treatments for unresectable disease have also been attempted with limited success. Lewis *et al*., in 1996, reported a case of distal radius GCT with mediastinal node metastasis. They used high dose steroids to downsize the tumor followed by resection of the mediastinal mass.[14] There are isolated cases where chemotherapy and radiotherapy have been utilized with varied success rates.[18] In the absence of literature, no definitive recommendation can be made.

In the present case, an upfront incomplete surgery followed by multiple recurrences with repeated surgeries would have led to tumor emboli spreading through the lymphatics. The patient was successfully managed by lymph node dissection. The implication of lymph node and distant spread in malignant GCT is not as worse compared to other malignancies and hence should be treated with curative intent if completely resectable.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Kanuj Malik, Anand Raja, Sundersingh Shirley[1]

Departments of Surgical Oncology and [1]Pathology, Cancer Institute (WIA), Chennai, Tamil Nadu, India

Correspondence to: Dr. Anand Raja,
E-mail: dr_anand@yahoo.com

References

1. Turcotte RE. Giant cell tumor of bone. Orthop Clin North Am 2006;37:35-51.
2. Neff JR. Primary tumours of bone. An overview in adults. In: Moosa AR, Schimpff SC, Robson S, editors. Comprehensive Textbook of Oncology. 2nd ed. Baltimore: Williams and Wilkins; 1991. p. 1168-70.
3. Kivioja AH, Blomqvist C, Hietaniemi K, Trovik C, Walloe A, Bauer HC, *et al.* Cement is recommended in intralesional surgery of giant cell tumors: A Scandinavian Sarcoma Group study of 294 patients followed for a median time of 5 years. Acta Orthop 2008;79:86-93.
4. Werner M. Giant cell tumour of bone: Morphological, biological and histogenetical aspects. Int Orthop 2006;30:484-9.
5. Jaffe HL, Lichtenstein L, Partis RB. Giant cell tumour of bone: Its pathological appearance, grading, supposed variants and treatment. Arch Path 1940;30:993-1031.
6. Muheremu A, Niu X. Pulmonary metastasis of giant cell tumor of bones. World J Surg Oncol 2014;12:261.
7. Qureshi SS, Puri A, Agarwal M, Desai S, Jambhekar N. Recurrent giant cell tumor of bone with simultaneous regional lymph node and pulmonary

metastases. Skeletal Radiol 2005;34:225-8.
8. Dyke SC. Metastasis of the "benign" giant cell tumor of bone (osteoclastoma). J Pathol 1931;34:259.
9. Budzilovich GN, Truchly G, Wilens SL. Tumor giant cells in regional lymph nodes of a case of recurrent giant cell tumor of bone. Clin Orthop Relat Res 1963;30:182-7.
10. Present DA, Bertoni F, Springfield D, Braylan R, Enneking WF. Giant cell tumor of bone with pulmonary and lymph node metastases. A case report. Clin Orthop Relat Res 1986;209:286-91.
11. Aftab K, Umar B. Giant cell tumor of bone with lymph node metastases: A rare presentation. Indian J Pathol Microbiol 2011;54:396-7.
12. Viswanathan S, Jambhekar NA. Metastatic giant cell tumor of bone: Are there associated factors and best treatment modalities? Clin Orthop Relat Res 2010;468:827-33.
13. Connell D, Munk PL, Lee MJ, O'Connell JX, Janzen D, Vu M, *et al.* Giant cell tumor of bone with selective metastases to mediastinal lymph nodes. Skeletal Radiol 1998;27:341-5.
14. Lewis JJ, Healey JH, Huvos AG, Burt M. Benign giant-cell tumor of bone with metastasis to mediastinal lymph nodes. A case report of resection facilitated with use of steroids. J Bone Joint Surg Am 1996;78:106-10.
15. Rock MG, Pritchard DJ, Unni KK. Metastases from histologically benign giant-cell tumor of bone. J Bone Joint Surg Am 1984;66:269-74.
16. Kay RM, Eckardt JJ, Seeger LL, Mirra JM, Hak DJ. Pulmonary metastasis of benign giant cell tumor of bone. Six histologically confirmed cases, including one of spontaneous regression. Clin Orthop Relat Res 1994;302:219-30.
17. Goldenberg RR, Campbell CJ, Bonfiglio M. Giant-cell tumor of bone. An analysis of two hundred and eighteen cases. J Bone Joint Surg Am 1970;52:619-64.
18. Vanel D, Contesso G, Rebibo G, Zafrani B, Masselot J. Benign giant-cell tumours of bone with pulmonary metastases and favourable prognosis. Report on two cases and review of the literature. Skeletal Radiol 1983;10:221-6.
19. Sung HW, Kuo DP, Shu WP, Chai YB, Liu CC, Li SM. Giant-cell tumor of bone: Analysis of two hundred and eight cases in Chinese patients. J Bone Joint Surg Am 1982;64:755-61.

How to cite this article: Malik K, Raja A, Shirley S. Isolated regional nodal metastasis in giant cell tumor of the bone: Case report and review of literature. South Asian J Cancer 2020;9:58.