## Letter to the Editor

# Staging investigations in chondrosarcoma: Is evaluation for skeletal metastases justified? Analysis from an epidemiological study at a tertiary cancer care center and review of literature

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Dear Editor,

Chondrosarcoma is the second most common malignant mesenchymal primary bone tumor.[1] Chondrosarcomas which arise *de novo* are primary chondrosarcomas, whereas chondrosarcomas developing on pre-existing benign cartilage neoplasms (enchondromas or osteochondromas) are referred to as secondary chondrosarcomas. They are histologically graded from I to III. Grade I chondrosarcomas are low cellular with an abundant hyaline cartilage matrix, and rarely metastasize. In contrast, Grade III chondrosarcomas are highly cellular with a muco-myxoid matrix and mitoses and high metastases rate up to 70%. These tumors are mainly seen in the adult population, and most commonly involve the pelvis followed by femur and humerus. Surgical excision is the cornerstone of the management of these tumors. They are inherently resistant to chemotherapy and radiotherapy because of the extracellular matrix, low percentage of dividing cells, and poor vascularity. Chemotherapy is reserved only for dedifferentiated and mesenchymal subtypes.[2]

The incidence of metastasis in chondrosarcoma is less as compared to other primary malignant tumors of bone.[3] The axial and proximal lesions are more likely to metastasize than acral and

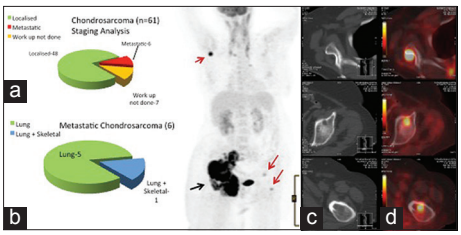


**Figure 1: (a) Staging analysis of all chondrosarcomas seen over a period of 1 year. (b) Site distribution of metastatic chondrosarcomas. (c) Whole body positron emission tomography – computed tomography showing the site of primary lesion in right hemipelvis (black arrow) and distant skeletal metastasis in right gleniod, left acetabulum and greater trochanter of left femur (red arrows). (d) Positron emission tomography images showing intense fluorodeoxyglucose avid lesions at skeletal metastatic sites**

distal lesion with equivalent histology.[4] The lungs are the most common site of metastasis. Skeletal metastasis is very infrequent. They can occur with recurrent, dedifferentiated variants and related to histological grading of the primary tumor.[1]

Conventionally, chondrosarcomas too are by default staged like other bone sarcomas (osteosarcoma and Ewing sarcoma).[5] Staging investigations in high-grade chondrosarcomas include a computed tomography (CT) scan of the chest and a bone scan, or as recently advocated positron emission tomography (PET) CT, or a whole body magnetic resonance imaging.[2]

Prospectively maintained data of all newly diagnosed cases of chondrosarcoma at our institution over a period of 1 year was reviewed. An audit form was devised to capture all the relevant information including patient demographics, symptomatology, site, previous treatment taken, outside diagnosis, stage of disease at presentation, past and family history of cancer, final diagnosis, and final advice on treatment. Whole body positron emission tomography of patient with pulmonary and skeletal metastasis showing uptake at multiple skeletal sites [Figure 1c and d]. All the cases were staged with either a CT scan of the thorax along with a bone scan, or whole body PET-CT. Of 553 cases of primary malignant bone tumors diagnosed during this period, 61 (11%) were a chondrosarcoma. The details of staging workup were not available in 7 cases (11.4%). Of the remaining 54 patients, 48 were nonmetastatic (89%) and 6 cases (11%) had metastasis at presentation [Figure 1a]. Five patients had pulmonary metastasis (9.25%), and 1 patient had combined pulmonary and skeletal metastasis (1.85%) [Figure 1b]. There was no isolated skeletal metastasis. All the patients were evaluated at the multidisplinary clinic, and further treatment plan was formulated.

As in other sarcomas, staging in chondrosarcomas plays a key role in treatment planning and prognosticating ultimate outcomes. A localized resectable chondrosarcoma has a favorable outcome when compared to those which are metastatic at presentation.

Currently, all bone sarcomas are staged with similar staging investigations, which include a bone scan and CT chest or a PET-CT. According to Daw *et al*.'s study on metastatic osteosarcoma, 17% of the patient had skeletal metastasis, 10% had isolated skeletal metastasis, and 7% had skeletal with pulmonary metastasis.[6] Ulaner *et al*.'s study documented, 20% skeletal metastasis in 60 patients with Ewing sarcoma of bone between 2004 and 2012.[7] The frequency of bone metastasis in chondrosarcoma is fewer as compared to osteosarcoma and Ewing sarcoma. The present study showed no cases of isolated bone metastasis in chondrosarcoma. The only case, which had bone metastasis, was with pulmonary metastasis which again emphasis the rare recurrence of isolated bone metastasis in chondrosarcoma of bone. Similar findings have been observed in a few other studies. Douis *et al*. conducted a retrospective audit of 188 cases, of chondrosarcoma operated over 13 years, and observed a 5.3% incidence of pulmonary metastasis with no skeletal metastasis.[8] In another study by Yang *et al*., out of 37 cases of chondrosarcoma seen between December 2005 and March 2008, only 4 patients had pulmonary metastasis and there were no skeletal metastasis.[9] Even though our population was ethnically different from these studies, the results were remarkably similar. In addition, an exhaustive review of the literature revealed only 6 cases of chondrosarcoma with isolated skeletal metastasis. Douis *et al*. also conclude that there is a high chance of false positive results in the bone scan as chondrosarcoma occurs in more aged patient groups than osteosarcoma, and Ewing sarcoma who are at high chance of having concomitant pathologies such as Paget disease and degenerative joint disease.[8]

The extreme rarity of isolated skeletal metastasis questions the applicability in chondrosarcoma of conventional "default" staging investigations as used for other bone sarcomas. This warrants a customized staging approach for chondrosarcoma, one that balances gains in survival versus costs and optimal resource utilization. We believe that there is a justification for restricting staging to only a CT chest in highgrade chondrosarcoma. Only symptomatic patients or those with pulmonary lesions may need further investigations. Such an approach appears to be more evidence-based and cost effective in staging primary chondrosarcoma.

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