CORR Insights

CORR Insights®: Is Needle Biopsy Clinically Useful in Preoperative Grading of Central Chondrosarcoma of the Pelvis and Long Bones?

R. Lor Randall MD

Where Are We Now?

Central cartilage neoplasms of bone are the most common bone tumor encountered in the adult population. From the

distinctly benign, relatively ubiquitous enchondroma to the highly lethal, but fortunately rare, dedifferentiated chondrosarcoma, this family of lesions demonstrates variability in behavior that truly reflects the process of malignant degeneration.

Enchondromas are classically asymptomatic incidental findings. However, if a patient presents with a complaint of atypical bone pain and imaging demonstrates a subtly aggressive central cartilage neoplasm in the bone, one must be concerned about degeneration of an enchondroma into a true low-grade chondrosarcoma. The clinician must carefully scrutinize the images and follow the patient through time to discern the behavior of the lesion. Unless the imaging tests clearly show signs of aggressive behavior (such as substantial or progressive endosteal scalloping,

cortical breakthrough or broad zone of transition), the biopsy often will be useless, as the lesion is likely to have characteristics of a low-grade neoplasm. That is, it is effectively impossible to distinguish an enchondroma from a low-grade chondrosarcoma on biopsy alone. If there is progression over time, it is fair to assume that this lesion is a low-grade chondrosarcoma and aggressive curettage would be appropriate.

When a cartilage tumor undergoes malignant degeneration, the imaging usually makes this clear. Growth of the lesion or cortical compromise are signs of cancer, and when these are observed, the biopsy—though important—generally is only confirmatory; even if the biopsy reveals a lower grade lesion, wide resection is imperative, as the (false-negative) biopsy likely reflects sampling error.

This CORR Insights® is a commentary on the article “Is Needle Biopsy Clinically Useful in Preoperative Grading of Central Chondrosarcoma of the Pelvis and Long Bones?” by Roitman and colleagues available at: DOI:10.1007/s11999-016-4738-y.

The author certifies that he, or a member of his immediate family, has no funding or commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research®* editors and board members are on file with the publication and can be viewed on request.

The opinions expressed are those of the writers, and do not reflect the opinion or policy of *CORR®* or The Association of Bone and Joint Surgeons®.

This *CORR Insights®* comment refers to the article available at DOI: [10.1007/s11999-016-4738-y](https://doi.org/10.1007/s11999-016-4738-y)

R. L. Randall MD (✉)
Huntsman Cancer Institute, 2000 Circle
of Hope Dr., Salt Lake City, UT 84112,
USA

e-mail: lor.randall@hci.utah.edu

Where Do We Need To Go?

We do not yet fully understand how enchondromas arise and develop

CORR Insights

into malignancies. Some suggest that degeneration of an enchondroma may be caused by the loss of normal parathyroid hormone-related protein receptor function leading to increased Indian hedgehog activity [1, 4]. Elevated Indian hedgehog enables cartilage proliferation. This is controversial, however, as some investigators have observed otherwise [2]. Further work is clearly necessary.

If we could arrest progression, or even better, reverse dedifferentiation, we would be able to prevent this insidious process, and save lives. Accordingly, by using improved image guidance, the fidelity of the biopsy is enhanced, definitively sampling the area that was thought to be initially intermediate to high-grade. Such technology would enable the clinician to better assess response to therapy thereby validating any new drug treatment. Present imaging, including fluorodeoxyglucose-positron emission tomography, has improved our ability to measure response to therapy by surrogate indices (loss of radionucleotide uptake), but true histopathologic correlation remains elusive.

How Do We Get There?

Improved imaging that topographically maps a tumor activity and predicts a response to experimental therapy is needed [3]. Accordingly, precision biopsies can then be performed. Further research into the pathogenic degeneration of central cartilage neoplasms of bone into high-grade chondrosarcoma is underway. Investigators have implicated deficiencies in fibroblast growth factor receptor 3 signaling via down-regulation of mitogen-activated protein kinase/extracellular signal related kinase as a possible targetable mechanism [6]. Additionally, deletions in the cartilage tumor suppressor tyrosine-protein phosphatase nonreceptor Type 11 has been shown to result in excessive Indian hedgehog production [5]. However, much more work in this area is needed. With detailed clarification of these pathways, and improved imaging technology, hopefully we will relegate the use of biopsy of chondrosarcoma to that of confirming treatment response.

References

1. Hopyan S, Gokgoz N, Poon R, Gensure RC, Yu C, Cole WG, Bell RS, Jüppner H, Andrulis IL, Wunder JS,

Alman BA. A mutant PTH/PTHrP type I receptor in enchondromatosis. *Nat Genet.* 2002;30:306–310.

2. Rozeman LB, Hameetman L, Cleton-Jansen AM, Taminiau AH, Hogendoorn PC, Bovée JV. Absence of IHH and retention of PTHrP signalling in enchondromas and central chondrosarcomas. *J Pathol.* 2005;205:476–482.
3. Shankar LK, Van den Abbeele A, Yap J, Benjamin R, Scheutze S, Fitzgerald TJ. Considerations for the use of imaging tools for phase II treatment trials in oncology. *Clin Cancer Res.* 2009;15:1891–1897.
4. Tiet TD, Hopyan S, Nadesan P, Gokgoz N, Poon R, Lin AC, Yan T, Andrulis IL, Alman BA, Wunder JS. Constitutive hedgehog signaling in chondrosarcoma up-regulates tumor cell proliferation. *Am J Pathol.* 2006;168:321–330.
5. Yang W, Wang J, Moore DC, Liang H, Dooner M, Wu Q, Terek R, Chen Q, Ehrlich MG, Quesenberry PJ, Neel BG. Ptpn11 deletion in a novel progenitor causes metachondromatosis by inducing hedgehog signalling. *Nature.* 2013;499:491–495.
6. Zhou S, Xie Y, Tang J, Huang J, Huang Q, Xu W, Wang Z, Luo F, Wang Q, Chen H, Du X, Shen Y, Chen D, Chen L. FGFR3 deficiency causes multiple chondroma-like lesions by upregulating hedgehog signaling. *PLoS Genet.* 2015;11:e1005214.