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CORR Tumor Board

CORR® Tumor Board: Do Orthopaedic Oncologists Agree on the Diagnosis and Treatment of Cartilage Tumors of the Appendicular Skeleton?

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What are the surgical and research implications of this study?

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Intramedullary hyaline cartilage tumors include a wide spectrum of disease. On one end are the completely benign enchondromas, which usually are discovered incidentally, and have no imaging findings suggestive of aggressive behavior. These can be left alone without risk to the patient's overall health. On the other end are tumors that present with bone destruction and soft-tissue extension, which represent high-grade chondrosarcomas. These generally call for wide resection for local control, are associated with risk of metastatic disease, and can be a threat to the patient's survival. The tumors in between these two bookends behave variably, and have diverse imaging and pathologic findings. Put in this context, it is challenging to agree on nomenclature, as the current study shows among orthopaedic oncology specialists, and the SLICED group demonstrated among radiologists and pathologists [12].

If we cannot agree on the diagnosis, then agreeing on treatment is next to impossible. We do not have a "gold standard" for these diagnostic decisions, so our treatment recommendations and results end up

A note from the Editor-in-Chief:
We are pleased to present the next installment of The CORR® Tumor Board column. *The* CORR® Tumor Board *column provides multidisciplinary perspective on the themes raised in selected* CORR® *tumor papers. In this column, we will discuss the implications of the highlighted article from the varied disciplines of the Tumor Board members: Orthopaedic surgery, pathology, and radiology. This month's column features the study* "Do Orthopaedic Oncologists Agree on the Diagnosis and Treatment of Cartilage Tumors of the Appendicular Skeleton?" by *Zamora and colleagues available at:* DOI: 10.1007/s11999-017-5276-y.

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heavily biased. We get unscientific input from every aspect of the assessment—from the patient's comfort level and preferences in contending with such uncertainty, to our biases due to our most recent and worst experience with cartilage neoplasms. We also form biases from our training, and from the multidisciplinary teams on which we work. Stated otherwise, we are long on biases, and short on reliable tumor markers that might predict the biologic behavior of a cartilage neoplasm. However, there is some exciting work on that front. Several teams are using molecular genetics to identify such tumor markers for cartilage neoplasms, mainly as a means to develop effective targeted therapy for chondrosarcoma [11]. This type of investigation may lead to the identification of markers that reliably differentiate cartilage neoplasms by local aggressiveness and/or metastatic potential. The goal would be to allow a patient with a cartilage neoplasm to undergo a biopsy for genetic evaluation of the tumor, and on basis of that evaluation, to receive accurate, specific, and effective treatment recommendations.

What issues does this study raise in terms of musculoskeletal imaging?

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Cartilage lesions in bone are fairly easy to identify on imaging as they often contain characteristic stippled "arc and rings" calcifications. However, based on imaging alone, deciding whether the lesion is an enchondroma, low-grade chondrosarcoma, or intermediate/high-grade chondrosarcoma can be challenging. Distinguishing the type of lesion is an important step, as clinical treatment varies for each of the three diagnoses.

Like radiologists and pathologists [12], the study by Zamora and colleagues found that even experienced orthopaedic oncologists have difficulty in making the distinction between the three diagnoses. In fact, the authors had the most difficulty differentiating low-grade chondrosarcomas from enchondromas and high-grade chondrosarcomas, similar to past imaging studies [8, 13]. Endosteal scalloping and soft-tissue formation are likely the most reliable radiographic and CT imaging features for a chondrosarcoma; and the presence of intralesional fat can be more suggestive of an enchondroma on MRI [8, 13]. But many of these imaging features are not conclusive. Recent imaging studies have focused on advanced MRI techniques such as diffusion weighted imaging and dynamic contrast enhancement to help distinguish the various cartilage tumors [5, 6]. Unfortunately, the results are not promising. Positron emission tomography (PET) imaging has excellent discrimination for high-grade chondrosarcomas, as they can have higher metabolic activity than enchondromas or low-grade chondrosarcomas. However, PET cannot distinguish between the two lower-grade cartilage tumors [7].

Until a good imaging, histologic, or clinical biomarker is developed, the best practice for determining the treatment plan for a cartilage tumor, as the authors highlight, is through a multidisciplinary team comprised of orthopaedic oncologists, radiologists, and pathologists. As Aristotle once said, "The whole is more than the sum of each part."

What more does the surgeon need to know about musculoskeletal pathology in order to get the most out of this study?

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The authors of the current study have addressed a subject near and dear to the heart of pathologists: Diagnosis. Specifically, their study provided multiple observers with an identical,

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but limited, set of data points with which to render a diagnosis. In this exercise, pathologic findings (if available) were withheld, and the observers were given clinical and radiologic information with which to formulate their diagnostic impression. Diagnostic discordance was remarkably high.

The authors have done a service to bone tumor diagnostics by demonstrating the difficulty in predicting the behavior of intramedullary cartilaginous neoplasms of the appendicular skeleton. In pathology, measurement of diagnostic accuracy has become a major focus of quality efforts [9, 14]. In fact, improving diagnosis is the subject of a recent comprehensive study by the Institute of Medicine (IOM) [4]. However, diagnostic "error" can be difficult to measure. Absolute certainty in diagnosis is unattainable, and bone neoplasia is a prime example of this principle. In anatomic pathology, review of slides by another pathologist is often used as a surrogate "gold standard" against which to measure diagnostic accuracy [1]. Using peer review and "expert" review to measure diagnostic accuracy can be flawed because variations in diagnostic criteria can potentially result in substantial differences in diagnostic opinion. The authors of the current study raise awareness of this limitation as it pertains to clinical and radiologic findings. Perhaps their study will more-fairly inform malpractice litigation and institutional quality metrics, as well as clinical practice.

Importantly, Zamora and colleagues render an incomplete picture of the ideal diagnostic process. In particular, each observer's diagnostic opinion included only a single physician's perspective at a single point in time and, by requirement, encompassed only one of several discrete diagnostic entities. An ideal diagnostic effort brings together multiple disciplines. As the recent IOM study stressed, "health care organizations should facilitate and support collaboration among pathologists, radiologists, other diagnosticians, and treating health care providers to improve the diagnostic testing process" [4].

In addition, the benefits achieved by longitudinal and iterative consideration of the diagnosis are important. Sometimes a tumor's biologic behavior declares itself over time. Furthermore, the limitations of diagnosis must be acknowledged; there are times when it is more appropriate to simply render a differential diagnosis than to "pull the trigger."

In neoplastic bone pathology, more often than in other types of tumor pathology, integrating the clinical and radiologic findings into the pathologic interpretation is critical. At my institution, it is not uncommon for the pathologist actually to visit the radiology suite for an in-person discussion for difficult diagnoses; likewise, team gatherings around the multiheaded microscope are common. The pathologist will want to consider and reconsider the pathologic impression based on the clinicoradiographic findings, and the orthopedist/radiologist will want to consider and reconsider the clinical and radiologic impressions in light of the pathology findings. It is an integrative exercise. Subsequent findings on longitudinal followup may further inform the diagnostic impression, as the authors note with respect to their group of "benign" intramedullary tumors that lack substantial progression over time.

Tumor boards serve as one way of bringing the disciplines together and encouraging integrative review, and sometimes they even result in reinterpretation of a diagnosis [2, 3, 10]. From this perspective, it is a special pleasure to contribute to this column.

References

1. Association of Directors of Anatomic and Surgical Pathology. Recommendations for quality assurance and improvement in surgical and autopsy pathology. *Am J Surg Pathol*. 2006;30:1469–1471.
2. Chang JH, Vines E, Bertsch H, Fraker DL, Czerniecki BJ, Rosato EF, Lawton T, Conant EF, Orel SG,

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Schuchter L, Fox KR, Zieber N, Glick JH, Solin LJ. The impact of a multidisciplinary breast cancer center on recommendations for patient management: The University of Pennsylvania experience. *Cancer*. 2001;91:1231–1237.

3. Cohen P, Tan AL, Penman A. The multidisciplinary tumor conference in gynecologic oncology–does it alter management? *Int J Gynecol Cancer*. 2009;19:1470–1472.
4. Committee on Diagnostic Error in Health Care; Board on Health Care Services; Institute of Medicine; The National Academies of Sciences, Engineering, and Medicine; Balogh EP, Miller BT, Ball JR, eds. *Improving Diagnosis in Health Care*. Washington, DC: National Academies Press; 2015.
5. De Coninck T, Jans L, Sys G, Huysse W, Verstraeten T, Forsyth R, Poffyn B, Verstraete K. Dynamic contrast-enhanced MR imaging for differentiation between enchondroma and chondrosarcoma. *Eur Radiol*. 2013;23:3140–3152.
6. Douis H, Jeys L, Grimer R, Vaiyapuri S, Davies AM. Is there a role for diffusion-weighted MRI (DWI) in the diagnosis of central cartilage tumors? *Skeletal Radiol*. 2015;44:963–969.
7. Lee FY, Yu J, Chang SS, Fawwaz R, Parisien MV. Diagnostic value and limitations of fluorine-18 fluorodeoxyglucose positron emission tomography for cartilaginous tumors of bone. *J Bone Joint Surg Am*. 2006;86:2677–2685.
8. Murphey MD, Flemming DJ, Boyea SR, Bojescul JA, Sweet DE, Temple HT. Enchondroma versus chondrosarcoma in the appendicular skeleton: Differentiating features. *Radiographics*. 1998;18:1213–1237.
9. Nakhleh RE, Nosé V, Colasacco C, Fatheree LA, Lillemoe TJ, McCrory DC, Meier FA, Otis CN, Owens SR, Raab SS, Turner RR, Ventura CB, Renshaw AA. Interpretive diagnostic error reduction in surgical pathology and cytology: Guideline from the college of American pathologists pathology and laboratory quality center and the association of directors of anatomic and surgical pathology. *Arch Pathol Lab Med*. 2016;140:29–40.
10. Pillay B, Wootten AC, Crowe H, Corcoran N, Tran B, Bowden P, Crowe J, Costello AJ. The impact of multidisciplinary team meetings on patient assessment, management and outcomes in oncology settings: A systematic review of the literature. *Cancer Treat Rev*. 2016;42:56–72.
11. Polychronidou G, Karavasilis V, Pollack SM, Huang PH, Lee A, Jones RL. Novel therapeutic approaches in chondrosarcoma. *Future Oncol*. 2017;13:637–648.
12. Skeletal Lesions Interobserver Correlation among Expert Diagnosticians (SLICED) Study Group. Reliability of histopathologic and radiologic grading of cartilaginous neoplasms in long bones. *J Bone Joint Surg Am*. 2007;89:2113–2123.
13. Yoo HJ, Hong SH, Choi JY, Moon KC, Kim HS, Choi JA, Kang HS. Differentiating high-grade from low-grade chondrosarcoma with MR imaging. *Eur Radiol*. 2009;19:3008–3014.
14. Zhi, Q, Siegal GP, eds. *Quality Management in Anatomic Pathology: Strategies for Assessment, Improvement, and Assurance*. Northfield, IL; CAP Press, 2017.