Clin Orthop Relat Res (2015) 473:3612–3614 / DOI 10.1007/s11999-015-4519-z

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

Published online: 27 August 2015

CORR Insights

CORR Insights®: Should High-grade Extraosseous Osteosarcoma Be Treated With Multimodality Therapy Like Other Soft Tissue Sarcomas?

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Where Are We Now?

Orthopaedic oncology is a specialty defined by uncertainty. Although we are able to diagnose sarcoma subtypes reliably and recommend treatment plans, the reality is that even tumors with the same name can act dramatically differently. Therefore, the clinician must use many details about the individual scenario—grade, histologic subtype, size, depth, location, stage, and patient demographics—to make a logical guess as to the anticipated behavior of the diagnosed condition. As described by Fan and colleagues [3], extraosseous osteosarcoma is a representative example of a common dilemma in orthopaedic oncology: How do we select the most appropriate management strategy when we are unable to accurately predict the natural history or response to treatment in a rare cancer?

The first attempt at understanding a rare tumor is by a simple descriptive case report or case series to reveal general observations about the patients in which the tumor occurs, the common features of presentation, the treatments attempted, and the observations on oncologic outcomes (survival and recurrence). The current study is the most recent in a line of such case series.

In attempt to view this problem from a novel perspective, Fan and colleagues question if extraosseous osteosarcoma behaves more similarly to a soft tissue sarcoma than a skeletal osteosarcoma. This is a reasonable approach, and has worked well for most subtypes of high-grade soft tissue sarcoma as their biologic aggressiveness, response to treatment, and patient outcomes are similar. They found that some features, such as a therapeutic response to radiation, are more characteristic of soft tissue sarcoma than skeletal osteosarcoma. As the authors note, the heterogeneity of treatment increases the difficulty in interpretation, as there was

This CORR Insights® *is a commentary on the article* "Should High-grade Extraosseous Osteosarcoma Be Treated With Multimodality Therapy Like Other Soft Tissue Sarcomas?" *by Fan and colleagues available at:* DOI: 10.1007/s11999-015-4463-y.

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This *CORR* Insights® comment refers to the article available at DOI: 10.1007/s11999-015-4463-y.

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CORR Insights

not one consistent strategy of management throughout the study.

Where Do We Need To Go?

The results of this investigation can be compared to what we know about skeletal osteosarcoma and soft tissue sarcoma. The rate of local recurrence reported in this series with use of adjuvant radiation (43%) appears closer to the limited knowledge of radiation in skeletal osteosarcoma (52%) [5], rather than soft tissue sarcoma (historically 13% to 29%, with modern reports typically less than 10%) [1, 4]. Disease-specific survival, while inferior to classic adolescent skeletal osteosarcoma, is not overly dissimilar from Stage III soft tissue sarcoma and skeletal osteosarcoma in older individuals [2].

What is most striking about this report is the aggressive nature of this disease, particularly in its tendency to recur locally. The data are not conclusive enough to propose a specific treatment algorithm, but are compelling enough to prove that we have not figured out extraosseous osteosarcoma. Despite attempts to improve the oncologic outcomes through various combinations of multiagent chemotherapy and radiation, the rates of local and distant recurrences remain quite poor. These are the primary challenges for improving care, and are approached with different methods.

The high rate of local recurrence, with or without radiation, suggests that the tumors are not being excised completely. Perhaps this tumor is more infiltrative than we assume, and there are unseen microscopic positive margins or satellite lesions unrecognized and unresected at the time of surgery. Knowing the capacity for recurrence, clinicians should approach this entity with a surgical plan for a wide resection at least, with consideration of complete removal of the muscle of origin when the functional deficit is not thought to be substantial. Radiation as an adjuvant is warranted when margins are less than ideal given proximity to an important structure.

The poor overall survival of the cohort, all who presented initially with localized disease, emphasizes the metastatic potential, need for chemotherapy, and inadequacy of our current chemotherapeutic options. Despite our best efforts at expeditious diagnosis and treatment, often the tumor has already entered the circulation by the time it is identified, and if that has happened, no amount of surgery at the primary site will change the outcome. Survival improvements will be gained only with more-effective systemic therapy.

How Do We Get There?

Further improvement in the treatment of extraosseous osteosarcoma cannot be achieved with more retrospective data. Only a prospective, collaborative approach will provide definitive insight into the best treatment strategy. A prospective series across several institutions using a well-defined treatment algorithm may capture enough patients to compare to historical controls. Additionally, research into rare tumors would benefit from a provider-initiated national sarcoma registry or database, which would improve our ability to draw conclusions by optimizing patient numbers and generalizability. A registry would be difficult to organize and maintain, as well as take years before results could be determined. Still, a registry would undoubtedly enhance our knowledge of many rare sarcomas in a similar state of uncertainty as extraosseous osteosarcoma.

Individual surgeons and institutions, within the limitations of their available resources, can also actively pursue and join existing clinical trials investigating novel therapeutics. As "standard" multiagent chemotherapy does not appear to have a substantial impact on the overall survival of extraosseous osteosarcoma, the most-realistic chance to improve survival would be the eventual identification of an efficacious experimental agent. Many clinical trials now in progress, and others in development, allow for inclusion of extraosseous osteosarcoma as a subtype of soft tissue sarcoma. While the effects on rare tumors

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specifically may not be a primary finding of any trial, secondary analysis of the data may yield new and helpful information.

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