Letter to the Editor Regarding "Intraneural Ewing Sarcoma of Fibular Nerve: Case Report, Radiologic Findings and Review of Literature"

Letter:

We read with interest the article "Intraneural Ewing Sarcoma of Fibular Nerve: Case Report, Radiolog Findings, and Review of Literature,"[1] recently published in the journal. In our opinion, some further clarifications are mandatory to provide a correct and complete message. The neoplasm interestingly described in this case report is correctly allocated within the family of extraosseous Ewing's Sarcomas (EES). The rarity is the intraneural site of the tumor. EESs are, by the way, soft-tissue sarcomas (STS) and should be diagnosed and treated accordingly. Recently published European guidelines for the management of STS[2] confirmed that "Surgery is the standard treatment of all patients with an adult type, localised STS. It must be carried out by a surgeon specifically trained in the treatment of this disease. The standard surgical procedure is a wide excision with negative margins (no tumour at the margin, R0). This implies removing the tumour with a rim of normal tissue around it [II, A]."

The diagnosis should be achieved, after an appropriate imaging assessment, with multiple core needle biopsies, possibly by using 14- to 16-G needles. An excision biopsy could be considered for small (<3 cm), superficial, and suprafascial lesions, where wide margins can be obtained without damaging noble structures. An immediate evaluation of the sampled tissue during biopsy may be considered, but a surgical excision with frozen section technique is not suggested. An excision without a diagnosis with frozen section to establish diagnosis and margins cannot allow a definitive diagnosis with a complete immunohistochemical study and does not allow neoadjuvant (preoperative) treatments when feasible.[2]

In EES, the recommended treatment is local with surgery and/or radiotherapy plus chemotherapy.[3] Chemotherapy plays a pivotal role in the treatment of EESs. Neoadjuvant and adjuvant chemotherapies produce comparable results in patients with localized disease.[3] A complete resection predicts a favorable survival, and mutilating surgery may be the choice in some cases.[2,3] Inadequate margins and residual tumor are significant risk factors for local recurrence, and high grade, size greater than 5 cm, and age older than 50 years are significant prognostic factors for overall survival of the patients.

Inadvertent surgical excision of an STS (a so-called "whoops surgery") is not desirable but does not seem to lead to an adverse outcome when a wide re-excision of the area involved has been carried out.[4] Other authors have affirmed that local recurrence of a STS is a devastating complication. Consequently, minimizing the proportion of positive surgical margins, or tumor contamination, during resection is of paramount importance.[5] In another recent study, Qureshi et al.[6] investigated the impact of negative but close resection margins on local recurrence in children with EES. The authors concluded that quantitative extent of negative margins does not influence local control, whereas achieving a 3-dimensional tumor-free margin should be the goal of surgical resection.

Therefore, the golden standard of treatment for localized disease remains surgery, although there is a worse disease-free survival in patients with sarcoma without margin-negative surgery.[3] If a "whoops" surgical procedure is not a universally accepted direct negative factor for overall survival (about 25% at 5 years), it determines a greater rate of local recurrence. However, local recurrence implies a greater risk of dedifferentiation and metastatic disease with a general worse outcome. Other studies indicated, as specific predictors for better survival, a younger age and complete resection.[3]

Biopsy is the key step in the diagnosis of soft-tissue tumors, and it is the first surgical step. An inadequately performed biopsy may fail to achieve a proper diagnosis, have a negative impact on survival, and ultimately necessitate an amputation to accomplish adequate margins of resection. Poorly performed biopsy remains a common finding in patients with musculoskeletal tumors who are referred to orthopedic oncology centers.[7] After an unplanned resection or an incorrect biopsy, patients undergoing re-excision can present evidence of microscopic residual disease on pathologic examination with a significant prognostic effect on multivariable analysis for distant metastases ($P = 0.002$) and, consequently, a negative trend for survival was detected as well.[8]

Unplanned resection is a common problem in the management of STS. Because sarcomas are so rare, they may be misdiagnosed initially as more common benign lesions.[9] These tumors can mimic benign nerve sheath tumors and other STS, their nature is highly aggressive, with local recurrence and a propensity to metastasize; therefore, a high index of suspicion is needed.[10] When the treating surgeon is unaware of or does not adhere to proper surgical principles of orthopedic oncology, an intralesional procedure may be performed without the requisite preoperative imaging, staging, or wide resection margins for optimal management of sarcoma.[9] These sarcomas should be managed before surgery in a multidisciplinary setting, with a team of musculoskeletal radiologists, pathologists, orthopedic and clinical oncologists, and peripheral nerve injury specialists. Obtaining an accurate tissue diagnosis and achieving local control with a combination of neoadjuvant therapy and surgery with wide margins is crucial to the successful management of these sarcomas.[10]

In conclusion, as Mankin affirmed several years ago, during a famous sarcoma course, "You'll never be blamed to do a biopsy!"

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REFERENCES

1. Lavorato A, Titolo P, Vincitorio F, Cofano F, Garbossa D. Intraneural Ewing sarcoma of fibular nerve: case Report, radiologic findings and review of literature. *World Neurosurg*. 2019;123:212-215.

2. Casali PG, Abecassis N, Bauer S, et al, on behalf of the ESMO Guidelines Committee and EURACAN. Soft tissue and visceral sarcomas: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2018;29(suppl 4):iv51-iv67.

3. Galyfos G, Karantzikos GA, Kavouras N, Sianou A, Palogos K, Filis K. Extra-osseous Ewing sarcoma: diagnosis, prognosis and optimal management. *Indian J Surg*. 2016;78:49-53.

4. Kulkarni A, Grimer RJ, Carter SR, Tillman RM, Abudu A. How bad is a whoops procedure? Answers from a case matched series. *Othrop Proc*. 2018;87-B.

5. Biau DJ, Weiss KR, Bhumbra RS, et al. Monitoring the adequacy of surgical margins after resection of bone and soft-tissue sarcoma. *Ann Surg Oncol*. 2013;20: 1858-1864.

6. Qureshi SS, Laskar S, Kembhavi S, et al. Extraskeletal Ewing sarcoma in children and adolescents: impact of narrow but negative surgical margin. *Pediatr Surg Int*. 2013;29:1303-1309.

7. Bickels J, Jelinek JS, Shmookler BM, Neff RS, Malawer MM. Biopsy of musculoskeletal tumors: current concepts. *Clin Orthop Rel Res*. 1999;368:212-219.

8. Fiore M, Casali PG, Miceli R, et al. Prognostic effect of re-excision in adult soft tissue sarcoma of the extremity. *Ann Surg Oncol*. 2006;13:110-117.

9. Tedesco NS, Henshaw RM. Unplanned resection of sarcoma. *J Am Acad Orthop Surg*. 2016;24:150-159.

10. Mohan AT, Park DH, Jalgaonkar A, Alorjani M, Aston W, Briggs T. Intra-neural Ewing's sarcoma of the upper limb mimicking a peripheral nerve tumour. A report of 2 cases. *J Plast Reconstr Aesthet Surg*. 2011;64:e153-e156.