CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 80 (2021) 105676

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Extraskeletal Ewing sarcoma attached to the ulnar nerve: A case report

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ARTICLE INFO

Article history:
Received 17 January 2021
Received in revised form 15 February 2021
Accepted 15 February 2021
Available online 23 February 2021

Keywords:
Extraskeletal Ewing sarcoma
Extremity
Ulnar nerve
Small mass
Malignancy

ABSTRACT

INTRODUCTION: Extraskeletal Ewing sarcoma (EES) of the extremity is uncommon, and only a small number of reported cases have been devoted to the upper-extremity.
PRESENTATION OF CASE: A 65-year-old woman presented with a recurrent EES, a highly malignant tumor, involving the ulnar nerve at the right elbow region which was initially suspected as a benign soft tissue tumor, schwannoma, thus marginal excision had been performed. Due to its malignant behaviour, we treated the recurrent lesion with wide excision and reconstruction combined with chemotherapy. Histological evaluation revealed a monotonous small round cells appearance.
DISCUSSION: EES of the extremity involving the ulnar nerve is fairly uncommon. The tumor was often smaller in the adult than in the child population which was consistent with the present case, thus may mimic a benign tumor. Because of the overlapping histopathological features of EES with other tumors, other investigations such as immunohistochemistry and cytogenetic studies must be performed to allow definitive diagnosis. The result of our study was negative for the *EWSR1-FLI-1* and *CIC-DUX4* fusion gene, however, other less frequent translocations could be found in this case which does not exclude the diagnosis of Ewing sarcoma family.
CONCLUSION: Few cases of EES involving the ulnar nerve have been previously reported. The correct diagnosis of EES involving the ulnar nerve has become particularly important in order to enable the initiation of comprehensive management that have the potential to reduce disease progression and the avoidance of improper and potentially harmful surgical therapy.

1. Introduction

Ewing sarcoma is the second most common type of primary malignant bone tumor in childhood and adolescence. Almost one-fourth of these aggressive tumors originate from soft tissue, regarded as extraskeletal Ewing sarcoma (EES) [1]. EES is usually seen in young adults with a rapidly growing mass in the trunk, paraspinal muscles, or extremities. However, EES of the extremity is uncommon, and only a small number of reported cases have been devoted to the upper-extremity [2–5]. To the best of our knowledge, EES involving the ulnar nerve has never been previously reported. EES tumor may mimic various soft tissue tumors including schwannoma, neurofibroma, embryonal rhabdomyosarcoma, lymphoma, and synovial sarcoma. Differentiation between EES tumor and other soft tissue tumors is essential for appropriate management and estimating future prognosis.

Herein we present a rare case of EES involving the ulnar nerve at the right elbow region which was initially suspected as benign soft tissue tumor underwent wide excision and reconstruction due to its highly malignant nature. The work has been reported in line with SCARE criteria [6].

2. Presentation of case

A 65-year-old right hand dominant woman first noticed a mass on the ulnar side of her right elbow in 2018 approximately 5 months prior to first presentation in our clinic. Per review of initial elbow magnetic resonance imaging (MRI) from elsewhere, there was a small mass of 15 × 10 × 10 mm on the ulnar nerve with low signal intensity on T1W image (Fig. 1A) and high signal intensity on

Abbreviations: EES, Extraskeletal Ewing sarcoma; MRI, magnetic resonance imaging; PCR, polymerase chain reaction.

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https://doi.org/10.1016/j.ijscr.2021.105676

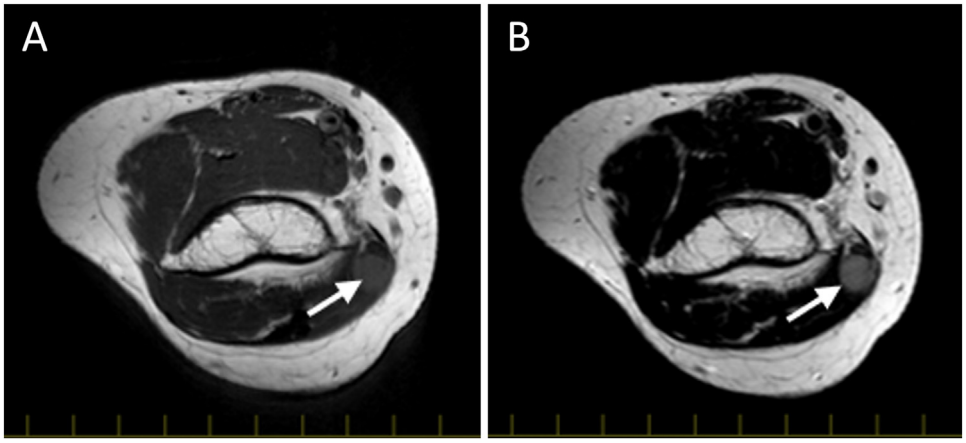

Fig. 1. Initial MRI of the right elbow. T1W image (A) demonstrated hypointense signal intensity. T2W image (B) demonstrated hyperintense signal intensity. The lesion was homogenous and attached to the ulnar nerve.

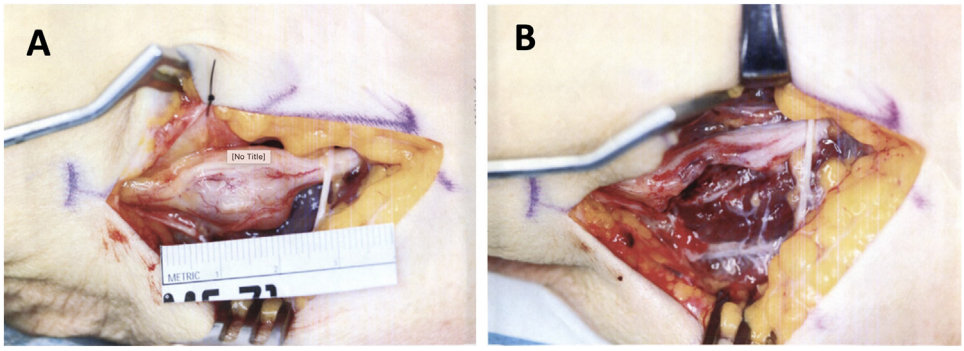

Fig. 2. Intraoperative findings of initial surgery at another hospital before (A) and after (B) tumor marginal excision was performed to preserve the ulnar nerve.

T2W image (Fig. 1B). The lesion was homogenous and not attached to the underlying bone. She was initially treated at another hospital with an excisional biopsy because a benign soft tissue tumor, schwannoma, was suspected. Intraoperative findings showed a subcutaneous mass attached to the ulnar nerve (Fig. 2A) and it did not resemble a schwannoma or neuroma. The mass was excised marginally to preserve the attached ulnar nerve (Fig. 2B). Pathology revealed an EES tumor. The patient was then referred to our clinic 1 week following the index procedure. On physical examination we found an operation scar without any redness, local heat and paresthesia. An elbow MRI evaluation was repeated. The imaging studies demonstrated a lesion of $12 \times 5 \times 5$ mm exhibited contrast enhancement on T1W image after administration of a gadolinium contrast agent (Fig. 3). The lesion suspected as a local recurrence and attached to the ulnar nerve. Subsequently, the patient completed the preoperative chemotherapy course with adriamycin plus ifosfamide (AI protocol).

Since this was regarding as a recurrent case of highly malignant tumor, a recommendation was made for wide resection. A skin margin of 3 cm was obtained. The lesion along with the ulnar nerve and part of the triceps were excised en bloc together (Fig. 4). Afterwards, the nerve transfer was performed at the distal third of the forearm. The radial branch of superficial radial nerve was coapted with sensory branch of the ulnar nerve. The terminal end of anterior interosseous nerve harvested from pronator quadratus muscle was transferred via end-to-end strategy to the ulnar motor fascicle. Moreover, an interpositional nerve graft was sutured by end to side technique between the presumed median and ulnar motor fascicles at the wrist to enhance the motor recovery. Finally, free flap transfer from the anterolateral thigh was performed to reconstruct the soft tissue defect. The specimen was sent for definitive pathology

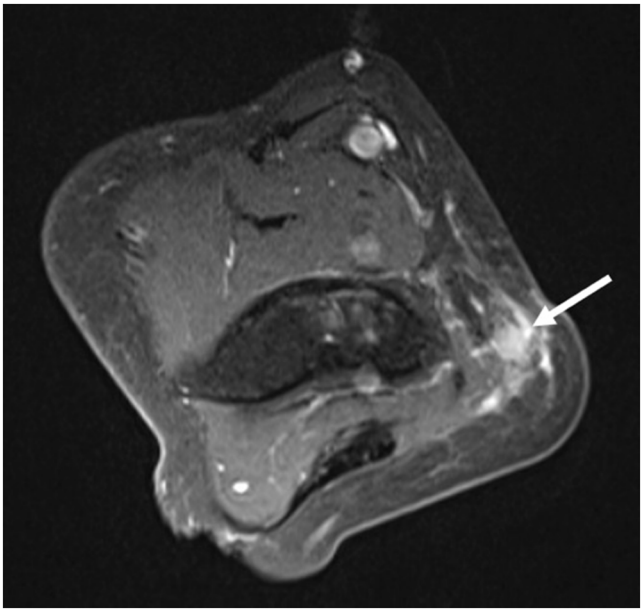

Fig. 3. Contrast-enhanced T1-weighted axial image demonstrated an enhanced lesion(arrow).

evaluation. We also sent tissue samples for frozen section to examine the surgical margins. The result demonstrated that the tumor was completely excised with negative margins all around.

Histological evaluation revealed a monotonous small round cells appearance (Fig. 5). Immunohistochemical staining demonstrated that the tumor was positive for CD99 and INI-1, but negative for

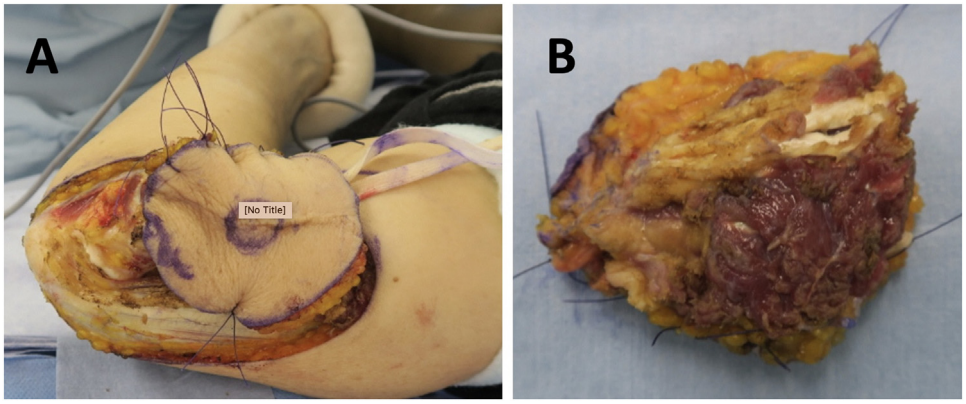

Fig. 4. Intraoperative findings of the second surgery on the inner aspect of the right elbow at our hospital. Wide resection (A) was performed. Resected tumor mass (B) along with ulnar nerve and a part of the triceps muscle.

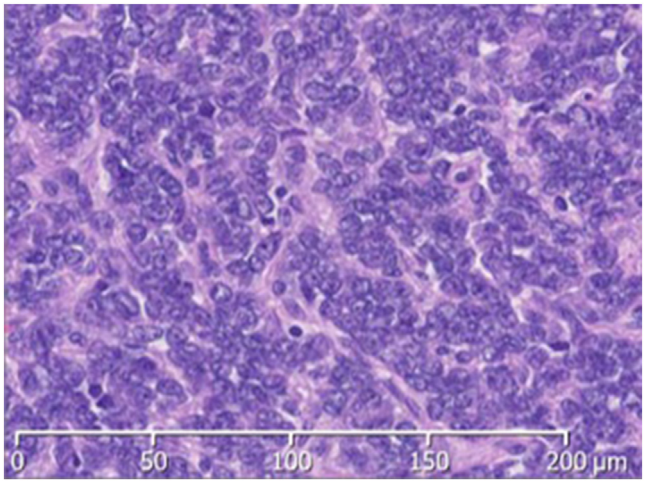

Fig. 5. Histological picture showed monotonous small round cells (hematoxylin and eosin staining, original magnification ×100).

CD34, epithelial membrane antigens, chromogranin A, and WT1. Since it was an unusual and rare case, paraffin blocks were sent for cytogenetic analysis in order to evaluate the translocation of t(11;22)(q24;q12), which is a definite feature of the Ewing sarcoma family tumors. However, cytogenetic test results did not show the t(11;22)(q24;12) translocation and the *CIC-DUX4* fusion gene was not detected by reverse transcription polymerase chain reaction (RT-PCR).

After the last surgery, the patient completed the postoperative chemotherapy courses. At 2 years follow-up, the postoperative limb function including lateral pinch strength was reasonable and did not hinder any activity of daily living. There were no sign of local recurrence and any metastasis until the last follow up.

3. Discussion

Ewing sarcoma is an aggressive tumor with a high incidence of local recurrence and distant metastasis. Some studies have been reported regarding EES to be associated with even poorer prognosis compared with osseous Ewing sarcoma [1]. EES of the extremity is extremely rare, and as far as we know, there are only a few reported cases of EES involving the extremities. Some authors have reported ESS in the shoulder [2], finger [3], sciatic nerve [4], and median nerve [5], however, EES in the ulnar nerve has not been previously reported. In the present case, we describe the first case of EES associated with the ulnar nerve at the elbow region which was initially considered as a benign schwannoma or neurofibroma in the clinical settings. Andrew et al. reported that EES was more common in older women than in younger women, and the tumors were often smaller in the adult than in the child population which was consistent with the present case [7].

The histopathological differential diagnosis of EES includes embryonal rhabdomyosarcoma, lymphoma, and neuroblastoma [1]. The histopathology of EES demonstrates small homogenous, round, or oval cells containing solid material separated by fibrous septation. In addition, EES cells produce vacuoles and are resistant to staining because their cytoplasm contains glycogen [1]. Because of the overlapping histopathological features of EES with other tumors, other investigations such as immunohistochemistry and cytogenetic studies must be performed to allow definitive diagnosis [1].

The role of cytogenetic studies in the differential diagnosis of soft-tissue sarcomas, including EES, is essential. Due to the fact that considerable overlap in clinical and histopathological morphology features of EES with other small round cell tumors, cytogenetics procedures have been proven to be necessary diagnostic tools [8]. Fortunately, many soft-tissue tumors, including EES, are now characterized by chromosomal rearrangements, which aid in precise subclassification, as were performed in the present case [1]. Ewing sarcoma has an *EWSR1-FLI-1* fusion gene resulting from the t(11;22)(q24;12) translocation with positivity rate of approximately 85% [9]. The split signals of *EWSR1-FLI-1* were not detected by fluorescence in situ hybridization (FISH) in the present case and it may be because the EWS gene was fused with other ETS family genes [10]. Despite of the fact that *CIC-DUX4* gene fusion, resulting from either a t(4;9) or t(10;19) translation, is the most common genetic abnormality detected in EWSR1-negative small blue round cell tumors, the gene fusion was not detected by RT-PCR in the present case [11]. The result of our study was negative for the *EWSR1-FLI-1* and *CIC-DUX4* fusion gene, however, other less frequent translocations could be found in this case which does not exclude the diagnosis of Ewing sarcoma family. EES was concluded based on the characteristics of cell morphology in histopathological result and positive expression of CD99 in immunohistochemistry result.

The surgical management of EES may be controversial. Jamshidi et al. reported a case of EES attached to the median nerve treated with marginal excision and no local recurrence occurred after 2 years [5]. Marginal excision of EES attached to the sciatic nerve was reported by Sharma et al., and they found no local recurrence until the last follow-up [4]. Krulik et al. reported two cases of EES located in the sacrum and shoulder areas in which surgery was not performed because of distant metastasis from the first presentation [2]. To our knowledge, EES involving the upper extremity treated by wide excision has never been reported before in the literature. In our study, the patient presented with local recurrence at the

first consultation. Consequently, we considered our case of EES as a highly malignant and aggressive tumor, so we performed wide excision.

Regarding chemotherapy, Raney et al. reported that combination therapy improved the survival of patients with EES [12]. Therefore, we performed chemotherapy with ifosfamide and doxorubicin before and after the surgery [13]. There was no local recurrence and distant metastasis at the last follow-up at 2 years post-surgery.

4. Conclusion

Despite the fact that EES involving the ulnar nerve is extremely rare, it must be considered as an important differential diagnosis due to its highly malignant behaviour and it may mimic benign tumor. A comprehensive preoperative investigations and the multidisciplinary approach are required for accurate diagnosis of unusual presentation of EES. The correct diagnosis of EES involving the ulnar nerve has become particularly important in order to enable the initiation of comprehensive management that have the potential to reduce disease progression and the avoidance of improper and potentially harmful surgical therapy.

Declaration of Competing Interest

The authors report no declarations of interest.

Source of funding

The research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Ethical approval

All investigators ensure that the conduct of this study is in accordance with the ethical standards of their respective institution as laid down in the 1964 Declaration of Helsinki.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

All authors were responsible for the study concepts. Data acquisition, analysis, and interpretation were performed by TS, TF, MPJ, KA and NA. Drafting of the manuscript was the responsibility of TS, TF, MPJ, KA and NA. TS, TF, MPJ, KA and NA approved the final version of the manuscript to be published, and TS, TF, MPJ, KA and NA have agreed to be accountable for all aspects of the work.

Registration of research studies

Not applicable.

Guarantor

Tomohiko Sakuda, MD, PhD.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgment

None.

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