Extraosseous Osteosarcoma: A Case Report and Review of the Literature

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Extraosseous osteosarcoma (EOO) is a rare soft tissue sarcoma that produces osteoid and bone. It is sometimes accompanied by cartilage. It is located in soft tissue without skeletal attachment. A previous study revealed that extraosseous osteosarcoma is a chemoresistant tumor with a poor prognosis and should be distinct from osseous osteosarcoma. Out of more than a hundred of osteosarcoma recorded during 1992 to 2012 in Chiang Mai Hospital, only one was EOO. This is a case report of a 44-year-old Asian man who first noticed a small right thigh soft tissue mass associated with pain. MRI reveals a heterogeneous mass in the quadriceps muscle without continuity with the bone. Wide resection of the tumor was performed. Microscopically, the tumors composed of large size spindle shape and bizarre malignant cell with osteoid production. After the resection, adjuvant radiation by brachytherapy technique, and chemotherapy was performed. At postoperative 24-months follow-up, the patient was free from local recurrence and distant metastasis, compared to seven months of median survival time for patients treated with resection alone in previous case reports.

Keywords: Extraosseous, Osteogenic Sarcoma, Soft tissue sarcoma

Case Report

A 44-year-old Asian man first noticed a small right thigh soft tissue mass associated with pain. The patient had no history of prior radiation, fracture or any local muscular injection at his right thigh. A month later, the mass was excised marginally at a provincial hospital and the first pathological diagnosis was dedifferentiated chondrosarcoma. Four months after the surgery, he developed a progressively enlarged mass at his surgical site and was referred to Chiang Mai University Hospital. Physical examination revealed a large right thigh mass that was warm, tender, smooth, and fixed to the medial fascia of the anterior compartment and measured 15x20 cm. The radiograph
and magnetic resonance imaging (MRI) of the right thigh are described in Fig. 1.

Wide excision of the tumor was performed. Cut sections of the specimen showed a large infiltrative tumor mass, measuring 17x11x10 cm within the soft tissue. The mass revealed white tan firm cut surface with large areas of hemorrhage and necrosis. Microscopically, the tumors composed of large size spindle shape and bizarre malignant cells with osteoid production (Fig. 2). Telangiectatic areas and chondroid differentiation areas were observed. After the resection, adjuvant radiation by brachytherapy technique preformed. He received doxorubicin-base chemotherapy a month after the operation. For 24 months after the treatment, no local recurrence or distant metastasis was observed.

Discussion
Extraosseous osteosarcoma (EOO) is a rare soft tissue tumor and its exact cause is unknown; but the suggested associated factors in development of this tumor include history of prior radiation exposure(5,8,9), previous trauma(10), intramuscular injection(11), myositis ossificans(8,12), heterotrophic ossification of dermatomyositis(13) and previous bone graft(14). Radiation is a documented predisposing factor in many reports. However, trauma is in doubt to be the actual cause due to the clinical history that was long before the development of the tumor. EOO arising in myositis ossificans has been shown by many authors. However, the diagnosis of myositis ossificans was made only on the clinical findings and not supported by tissue pathology. The common presentation is an insidious onset of a painful mass.

Tumor is usually very large before the patient receives treatment. In the series of Chung and Enzinger(12), the median duration of symptoms prior to presentation is six months (weeks to 25 years). Unlike the osseous osteosarcoma (OO), EOO most commonly affected individuals older than 30 years and is rarely encountered during the first two decades of life(13) although some pediatric cases have been documented(6). The series of Chung and Enzinger(12) revealed a slight male: female predominance whereas Sordillo’s series(5) reported equal incidence. The lower extremity

**Fig. 1** (A) The radiograph of the right thigh shows a soft tissue mass (arrow head) containing calcification (arrow). (B) Axial post intravenous gadolinium MRI reveals a heterogenous mass in the quadriceps muscle without continuity with the bone. Note the dark area in the mass (black arrow) corresponding with calcification (F = femur).

**Fig. 2** Section of the tumor showed size malignant cells with anisonucleosis and nuclear pleomorphism. Dense pinkish materials are osteoid, producing by the tumor cells (H&E, x200).
especially thigh represents the most common anatomic site, followed by the upper limb and retroperitoneum, respectively \(^{(7,12)}\). Rare location such as thyroid gland, penis, mediastinum, and kidney were also reported \(^{(1,12,15-17)}\).

Imaging studies play a major role in the tumor evaluation and treatment planning. On radiographs, the classic appearance of the tumor is a soft tissue mass with variable degree of calcification \(^{(18)}\). Calcification, if presented, can be spotty calcification or dense cloud-like opacity. Computed tomography and MRI is essential to identify tumor extent and to exclude continuity of the tumor with the cortex and bone marrow. The continuity with the bone indicates that the tumor is more likely to originate from the bone than the soft tissue. Bane BL et al \(^{(7)}\) found that the common histologic patterns of EOO were osteoblastic, pleomorphic malignant fibrous histiocytoma (MFH)-like and fibroblastic patterns. The other less common patterns were chondroblastic, giant cell type MFH-like, small cell, and telangiectatic patterns. It was shown that the histologic pattern and the other pathologic features did not significantly affect the outcome. In the present cases histologic slide review of the first excised specimen demonstrated that the tumor was actually chondroblastic osteosarcoma. The recurrence tumors were mixed osteoblastic, chondroblastic, and telangiectatic patterns. It was important to separate EOO from the other high-grade pleomorphic soft tissue sarcoma because chemotherapy would benefit the EOO patient. The clues for EOO were osteoid producing malignant cells and the characteristic histologic patterns.

Due to the rarity of EOO cases, therefore, the standard management has not been fully determined. In 1971, Allan and Soule \(^{(2)}\) reported some improvement of survival and rate of local recurrence in 26 EOO cases treated with amputation. However, superior functional outcome and survival of limb-sparing compared with amputation observed in other sarcoma \(^{(19)}\). Ahmed and Patel \(^{(4)}\) reported 82% 5-year local recurrent-free survival rate inpatient with extremity EOO treated with limb salvage procedure using clinical and anatomical criteria as used for patients with other types of sarcoma. Five centimeters margin of wide local excision is recommended to be the treatment of choice \(^{(15)}\). However, if this is not possible due to anatomical location, amputation is suggested.

Radiation is another effective way to combine with surgery in increasing survival rate and delay the recurrence. In Sordillo’s series \(^{(5)}\), median time to first metastasis in patients treated with wide excision followed immediately by radiation was longer (12 months) than treated with wide excision alone (7 months). The median survival time of the former group was also longer than the latter group (60 months vs. 28 months).

Although EOO is a relative chemoresistant tumor with only 15 to 41% of 5-year Survival rate \(^{(2,3,9,20,21)}\), benefit was observed in postoperative adjuvant chemotherapy \(^{(5)}\). In five patients with localized disease, three of them received a combination of doxorubicin, dacarbazine, vincristine, methotrexate, dactinomycin, and leukenan for 18 months. The other two received doxorubicin, vincristine, and cyclophosphamide for nine months. Four patients in this group had no recurrence or metastasis. Hence, in a small number of patients, a combination of doxorubicin based adjuvant chemotherapy may be a treatment of choice. It has been shown that the tumor size (<5 cm vs. ≥5 cm), the age at presentation, and the tumor volume were the major predictors for the patient survival \(^{(5,19)}\).

Conclusion

The EOO has clinically and therapeutically different from OO and there is no conclusion of treatment. The authors recommend that after the definite surgery either wide excision or amputation; additional treatment modalities such as adjuvant chemotherapy and radiation should be administered.

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 journal’s Editor-in-Chief.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

DP carried out to draft manuscript. AP, TL, NP participated in the radiological evaluation and JS participated in pathological studies. All authors read and approved the final manuscript.

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Potential conflicts of interest

None.

References


ออสทีโอซาร์โคมาที่เกิดภายนอกกระดูก: รายงานผู้ป่วยและการศึกษาวรรณกรรม

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ออสทีโอซาร์โคมาที่เกิดภายนอกกระดูกเป็นมะเร็งเนื้อเยื่ออ่อนที่มีการสร้างกระดูกซึ่งพบได้น้อยโดยต้องไม่มีการติดต่อกันกระดูกของผู้ป่วย จากการศึกษาในอดีตพบว่าออสทีโอซาร์โคมาภายนอกกระดูกนั้นไม่เคยตอบสนองต่อการรักษาด้วยเคมีภูมิคุ้มกันและไม่สามารถรักษาได้ ดังนั้นการรักษาผู้ป่วยกลุ่มนี้จึงแตกต่างจากออสทีโอซาร์โคมาของกระดูกจากข้อมูลผู้ป่วยออสทีโอซาร์โคมาของโรงพยาบาลมหาวิทยาลัยเชียงใหม่ ตั้งแต่ พ.ศ. 2535-2555 พบผู้ป่วยออสทีโอซาร์โคมาที่เกิดภายนอกกระดูกเพียงหนึ่งราย รายงานผู้ป่วยฉบับนี้ ผู้เป็นผู้ป่วยชายไทย อายุ 44 ปี มีเหตุการณ์จุดจากคลื่นแม่เหล็กไฟฟ้าที่ช่วงเวลา 2 เดือน โดยไม่มีหลักฐานการติดต่อกันกระดูกปกติ และไม่ได้รับการรักษาด้วยการตัดต่อและการตรวจทางวิทยาการรักษาโรคภูมิแพ้ แต่ตรวจพบเซลล์มะเร็งในเนื้อเยื่อต้นขา ผู้ป่วยได้รับการรักษาด้วยเคมีภูมิคุ้มกัน และการผ่าตัดเพื่อทำการส่งเร่งได้รับการกลับกันไม่ได้รับการรักษาโรคภูมิแพ้และมะเร็งในเนื้อเยื่อต้นขา ผู้ป่วยมีค่าเฉลี่ยของการมีชีวิตอยู่ 24 เดือน เปรียบเทียบกับการศึกษาในอดีตที่มีการผ่าตัดเพื่อการอยู่เดิมพบว่าผู้ป่วยมีค่าเฉลี่ยของการมีชีวิตอยู่ 7 เดือน เท่านั้น