Case Report

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*

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Extraosseous osteosarcoma (EOO) is a rare malignant mesenchymal neoplasm that produces osteoid, bone and sometimes accompanied by cartilage. It is located in soft tissue without skeletal attachment. EOO is accounting for only 1% of soft tissue sarcoma[1,2]. The first case of EOO was reported by Wilson in 1941[3] but fewer than 300 cases have been reported to date[4]. The soft tissue of the lower extremity is the most common affected site. In contrast to osteosarcoma of bone which usually affects young adults and adolescents, EOO usually occurs middle-aged and elderly patients (5^{th}-6^{th} decade of life)[5]. A previous study revealed that EOO is a doxorubicin-resistant tumor with a poor prognosis and should be distinct from osseous osteosarcoma[4]. However, there was onepedriatric chemosensitive case reported by Wodowski in 2003[6]. The diagnostic criteria of EOO are presence of neoplastic osteoid and bone, sometime with neoplastic cartilage[1,3]. The histologic variants of EOO are osteoblastic, chondroblastic, fibroblastic, osteoclastic, small cell, telangiectatic and lately giant cell-MFH like pattern that was added in 1990[7].

The present study demonstrated the case of a 44-year-old Asian male with extraosseous osteosarcoma and its clinical course.

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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.

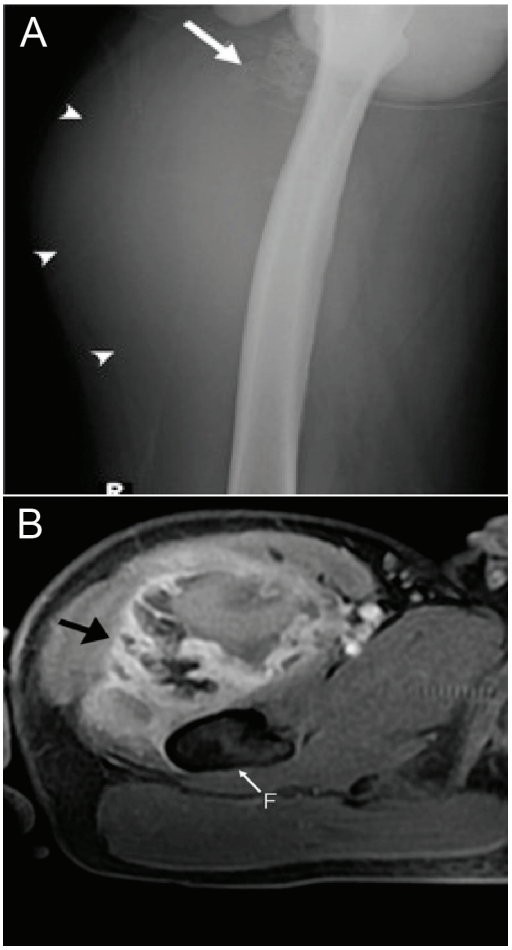

Fig. 1 (A) The radiograph of the right thigh shows a soft tissue mass (arrow head) containing calcification (arrow). (B) Axial post intravernous gadolinium MRI reveals a heterogenous mass in the quadriceps muscle withoutcontinuity with the bone. Note the dark area in the mass (black arrow) corresponding with calcification (F = femur).

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 myosisits 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

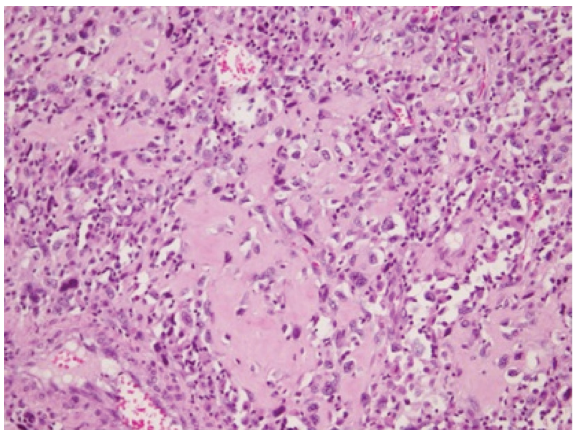

Fig. 2 Section of the tumor showed size malignant cells with anisonucleosis and nuclear pleomorphism. Dense amorphous matrix is osteoid, producing by the tumor cells (H&E, x200).

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 telangietatic 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 is 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 leukeran 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, DP carried out the operation and patient follow-up. 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

1. Weiss SW, Folpe AL. Osseous soft tissue tumours. In: Weiss SW, Folpe AL, editors. Enzinger and Weiss's soft tissue tumours. 4th ed. St. Louis: Mosby; 2001: 1389-417.
2. Allan CJ, Soule EH. Osteogenic sarcoma of the somatic soft tissues. Clinicopathologic study of 26 cases and review of literature. Cancer 1971; 27: 1121-33.
3. Wilson H. Extraskeletal ossifying tumors. Ann Surg 1941; 113: 95-112.
4. Ahmad SA, Patel SR, Ballo MT, Baker TP, Yasko AW, Wang X, et al. Extraosseous osteosarcoma: response to treatment and long-term outcome. J Clin Oncol 2002; 20: 521-7.
5. Sordillo PP, Hajdu SI, Magill GB, Golbey RB. Extraosseous osteogenic sarcoma. A review of 48 patients. Cancer 1983; 51: 727-34.
6. Wodowski K, Hill DA, Pappo AS, Shochat SJ, Kun LE, Spunt SL. A chemosensitive pediatric extraosseous osteosarcoma: case report and review of the literature. J Pediatr Hematol Oncol 2003; 25: 73-7.
7. Bane BL, Evans HL, Ro JY, Carrasco CH, Grignon DJ, Benjamin RS, et al. Extraskeletal osteosarcoma. A clinicopathologic review of 26 cases. Cancer 1990; 65: 2762-70.
8. Laskin WB, Silverman TA, Enzinger FM. Postradiation soft tissue sarcomas. An analysis of 53 cases. Cancer 1988; 62: 2330-40.
9. Lee WR, Laurie J, Townsend AL. Fine structure of a radiation-induced osteogenic sarcoma. Cancer 1975; 36: 1414-25.
10. Berry MP, Jenkin RD, Fornasier VL, Rideout DF. Osteosarcoma at the site of previous fracture. A case report. J Bone Joint Surg Am 1980; 62: 1216-8.
11. Lee JH, Griffiths WJ, Bottomley RH. Extraosseous osteogenic sarcoma following an intramuscular injection. Cancer 1977; 40: 3097-101.
12. Chung EB, Enzinger FM. Extraskeletal osteosarcoma. Cancer 1987; 60: 1132-42.
13. Eckardt JJ, Ivins JC, Perry HO, Unni KK. Osteosarcoma arising in heterotopic ossification of dermatomyositis: case report and review of the literature. Cancer 1981; 48: 1256-61.
14. Park SG, Song JY, Song IG, Kim MS, Shin BS. Cutaneous extraskeletal osteosarcoma on the scar of a previous bone graft. Ann Dermatol 2011; 23 (Suppl 2): S160-4.
15. Dudhat S, Desai S, Borges A, Shinde S. Retroperitoneal extraosseous osteosarcoma. A case report and review of literature. Indian J Cancer 1999; 36: 186-9.
16. Lin SY, Chen WM, Wu HH, Chen WY, Chen TH. Extraosseous osteogenic sarcoma. J Chin Med Assoc 2005; 68: 542-5.
17. Hertel V, Basten O, Bockmuhl U. Extraosseous osteosarcoma of the thyroid gland. Laryngorhino-otologie 2006; 85: 913-6.
18. Kransdorf MJ, Meis JM. From the archives of the AFIP. Extraskeletal osseous and cartilaginous tumors of the extremities. Radiographics 1993; 13: 853-84.
19. Rosenberg SA, Tepper J, Glatstein E, Costa J, Baker A, Brennan M, et al. The treatment of soft-tissue sarcomas of the extremities: prospective randomized evaluations of (1) limb-sparing surgery plus radiation therapy compared with amputation and (2) the role of adjuvant chemotherapy. Ann Surg 1982; 196: 305-15.
20. Fabbri N, Tiwari A, Umer M, Vanel D, Alberghini M, Ruggieri P, et.al. Extraskeletal osteosarcoma: clinicopathologic features and results of multimodal management [abstract 10093]. J Clin Oncol 2010; 28 (Suppl): 15s.
21. Rao U, Cheng A, Didolkar MS. Extraosseous osteogenic sarcoma: clinicopathological study of eight cases and review of literature. Cancer 1978; 41: 1488-96.

ออสทีโอซาร์โคมาที่เกิดภายนอกกระดูก: รายงานผู้ป่วยและการศึกษาวรรณกรรม

อภิรักษ์ แสงสิน, นัทธยา ปัทมภาสพงษ์, จงกลณี เศรษฐกร, ธนินนิตย์ ลีรพันธ์, ดำเนินสันต์ พฤกษากร

ออสทีโอซาร์โคมาที่เกิดภายนอกกระดูกเป็นมะเร็งเนื้อเยื่ออ่อนที่มีการสร้างกระดูกซึ่งพบได้น้อยโดยต้องไม่มีการติดต่อกับกระดูกของผู้ป่วย จากการศึกษาในอดีตพบว่าออสทีโอซาร์โคมาภายนอกกระดูกนั้นไม่ค่อยตอบสนองต่อการรักษาด้วยเคมีบำบัดและมีพยากรณ์โรคไม่ดี ดังนั้นการรักษาผู้ป่วยกลุ่มนี้จึงแตกต่างจากออสทีโอซาร์โคมาของกระดูกจากข้อมูลผู้ป่วยออสทีโอซาร์โคมาของโรงพยาบาลมหาราชนครเชียงใหม่ ตั้งแต่ พ.ศ. 2535-2555 พบผู้ป่วยออสทีโอซาร์โคมาที่เกิดภายนอกกระดูกเพียงหนึ่งราย รายงานผู้ป่วยฉบับนี้ ผู้เป็นผู้ป่วยชายไทย อายุ 44 ปี มาพบแพทย์เนื่องจากคลำพบก้อนบริเวณต้นขาขวาร่วมกับมีอาการปวด การตรวจคลื่นแม่เหล็กไฟฟ้าพบก้อนในกล้ามเนื้อของต้นขา โดยไม่มีส่วนติดต่อกับกระดูกปกติ และได้รับการรักษาด้วยการผ่าตัด ผลการตรวจทางพยาธิวิทยาพบเซลล์รูปกระสวยขนาดใหญ่ และเซลล์มะเร็งร่วมกับมีการสร้างกระดูก ผู้ป่วยได้รับการรักษาเพิ่มเติมด้วยเคมีบำบัด และการฝังแร่โดยไม่พบการกลับเป็นซ้ำ และการกระจายของไปยังอวัยวะอื่นภายหลังการผ่าตัดรักษาเป็นเวลา 24 เดือน เปรียบเทียบกับการศึกษาก่อนหน้าที่รักษาด้วยการผ่าตัดเพียงอย่างเดียวพบว่าผู้ป่วยมีค่าเฉลี่ยของการมีชีวิตอยู่เพียง 7 เดือน เท่านั้น