

Extraskelatal osteosarcoma in right neck subcutaneous tissue: A case report of an extremely rare tumour

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Abstract. Extraskelatal osteosarcoma (ESOS) is a rare soft-tissue sarcoma that is treated with surgical resection, chemotherapy and radiotherapy; however, as it is now considered to be radiation resistance, it is associated with conflicting management principles and poor outcomes. A multimodality approach is currently used to treat ESOS, which entails the incorporation of multidrug chemotherapy and/or radiotherapy coupled with surgery to obtain the best outcome; however, there are many factors that influence the treatment effects and clinical outcomes of ESOS. In the present study, a case of an 81-year-old man who suffered from primary ESOS in the subcutaneous tissue of the right-hand side of the neck was reported. The patient was treated several times with partial resection and once with radiotherapy, and was still living following 3 years of follow-up. Thus, the present case report demonstrated that surgical resection and postoperative radiotherapy regimens may be favourable in the short term with a disease-free survival of ~15 months; however, patients are prone to relapse.

Introduction

Extraskelatal osteosarcoma (ESOS) is a rare subtype of osteosarcoma, with which patients affected have distinct clinical features but similar prognostic factors and poor outcome compared to primary skeletal osteosarcoma (1), and its management principles are not well defined and even conflicting, multimodality treatment remains standard (2-4). ESOS originating in the subcutaneous tissue is a rare occurrence, accounting for <10% of all ESOS cases (5,6). We present a case of ESOS primary in subcutaneous tissue of the right neck with which treated by both local resection and radiotherapy being relapsed several times (a brief summary of therapy on the patient see Table I).

Case report

Patient case. An 81-year-old man admitted to our hospital on May 26, 2014, presented with two weeks history of a mass founded on the right side of the neck, suffering with dull pain and swallowing; the patient provided written informed consent for participation in the present study. There was no history of any surgical procedure, trauma, local radiation exposure in head and neck, any long-term medication or addictions. There was no clinical evidence of metastatic disease. His family history and general physical examination was unremarkable. On physical examination, a hard-mobile subcutaneous mass approximately 4.0x3.0 cm was palpable on the right side of the neck which moved with a slight tenderness. bilateral neck swollen lymph nodes were not touched. Karnofsky performance score (KPS) was 90. Blood count, serum alkaline phosphatase and tumor markers such as CEA and AFP were normal. CT (Fig. 1) scan revealed an uneven density soft tissue masses is of about 4.1x3.0x2.8 cm size in the rear of sternocleidomastoid on the right neck (Fig. 1A and C), contrast-enhanced CT (CECT) shows the mass peripherally enhanced with the necrosis in the center area, adjacent sternocleidomastoid and the right internal jugular vein were showed displaced (Fig. 1B and D).

First operation. A local widely resection was done on this patient in June 4, 2014. The operative procedure was performed under general anaesthesia, a subcutaneous mass with the size

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Abbreviations: ESOS, extraskelatal osteosarcoma; CT, computed tomography; CECT, contrast-enhanced CT; SMART, simultaneous modulated accelerated radiotherapy; RT, radiotherapy; RECIST 1.1, Response Evaluation Criteria In Solid Tumours version 1.1; SD, Stable disease; RTOG, Radiation Therapy Oncology Group; CEA, carcinoembryonic antigen; AFP, α -fetoprotein; CTV, clinical target volume

Key words: osteosarcoma, subcutaneous tissue, extraskelatal, neck, radiation therapy, resection

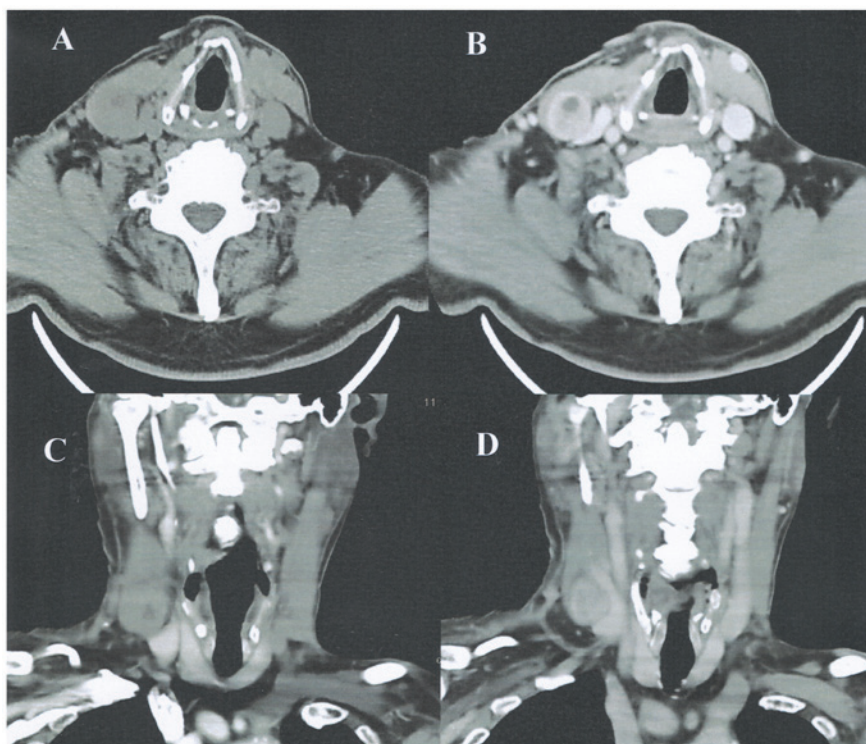


Figure 1. (A and C) CT scan showing an uneven density soft tissue masses in the rear of the sternocleidomastoid on the right neck. (B and D) Contrast-enhanced CT presenting the mass peripherally enhanced, the adjacent sternocleidomastoid and the right internal jugular vein, which were displaced. CT, computed tomography.

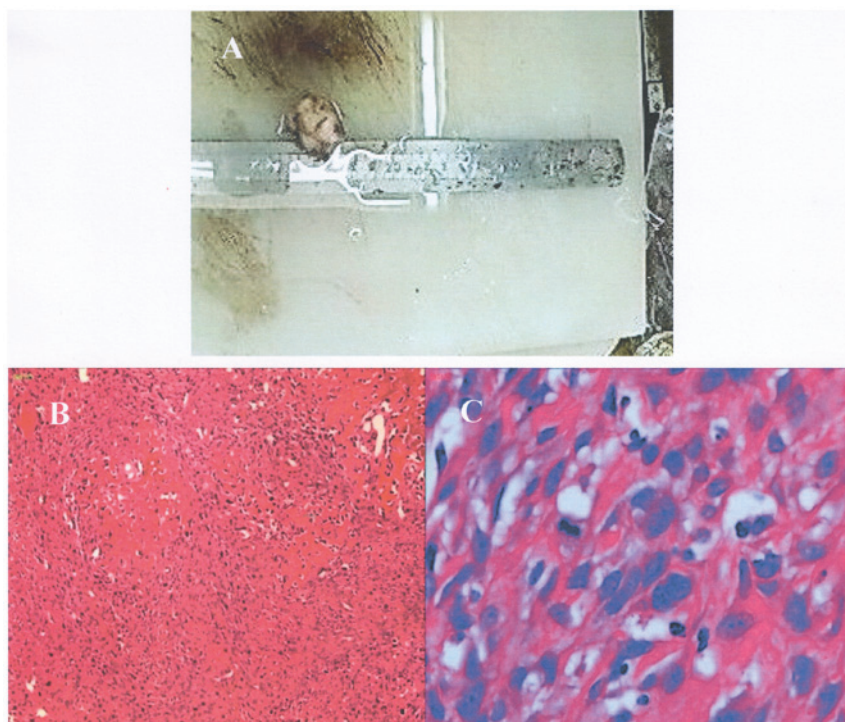


Figure 2. (A) A gray-white mass was resected, with a size of $\sim 4.0 \times 3.0 \times 3.0$ cm (magnification, $\times 100$). (B and C) Microscopy of the resected tumour with hematoxylin and eosin staining revealed that the mass consisted of spindle-like, small round cells, with nuclei that were hyperchromatic and pleomorphic, and neoplastic cartilage formation (magnification, $\times 400$).

of about $4.0 \times 3.0 \times 3.0$ cm was visible in the operation (Fig. 2A), and the tumour was incompletely removed as it closely related to the right jugular vein. On microscopy shows the resected

mass consists of spindle, small round cells, with the nuclei hyperchromatic and pleomorphism, and neoplastic cartilage formation is seen (Fig. 2B and C), postoperative pathological

Table I. Summary of the therapy received by the patient with extraskeletal osteosarcoma in right-hand neck subcutaneous tissue.

Therapy details	First surgery	Second surgery	Radiotherapy	Third surgery	Fourth surgery
Date of therapy	June 4, 2014	July 3, 2015	From August 3 to September 22, 2015	February 20, 2017	July 7, 2017
Therapeutic method	Local widely resection	Partial resection	SMART CTV1: 60.16Gy/1.88Gy/32f CTV2: 70.08Gy/2.19Gy/32f	Partial resection	Partial resection
Pretreatment diagnosis	Primary subcutaneous ESOS in right neck	Postoperative recurrence	Postoperative recurrence	Local recurrence	Local recurrence
Tumor size (CT or INOPF)	INOPF: 4.0x3.0x3.0 cm	CT: 2.9x1.9x1.7 cm	CT: 2.6x1.6x1.4 cm (Following radiotherapy)	CT: 8.8x6.0x5.4 cm	CT: 9.2x6.6x5.3 cm
Therapeutic effect	Incompletely removed	Partial resected	RECIST: SD. Acute radioactive skin injury	Excisions contains of multiple tissue fragments Following 3 months, the mass enlarged with trachea compression	INOPF: 10.0x6.0x6.0 cm Partial removed (the resected mass: 6.0x3.0x3.0 cm), with trachea compression relieved

SD, stable disease; RECIST 1.1, response evaluation criteria in solid tumors 1.1; INOPF, intraoperative findings; CT, computed tomography; CTV, clinical target volume; SMART, simultaneous modulated accelerated radiotherapy.

diagnosis was as ESOS. The patient was unwilling to undergo chemotherapy or local radiotherapy after the operation.

Second operation and radiotherapy. Ten months later, On June 29, 2015, the patient was admitted to hospital again for 'post-operative and recurrence' of the right cervical osteosarcoma (Fig. 3A and B). A partial resection of the right neck mass was performed on July 3, 2015 (the second operation), and the postoperative pathology report indicated that the osteosarcoma of the right neck was recurred. Four weeks later, the patient underwent postoperative simultaneous modulated accelerated radiotherapy (SMART). The prescribed dose of CTV1 and CTV2 was 60.16 Gy/32 fractions and 70.08 Gy/32 fractions respectively, both once daily. 6 weeks after the radiotherapy, CT were performed to assess RT effects (Fig. 3C and D) as stable disease (SD) according to the RECIST 1.1 criteria. During the period of RT, acute radioactive skin injury (level 2) occurred in the right neck skin (Fig. 3E and F) according to RTOG acute radiation injury classification criteria.

Third operation. The neck neoplasm to be founded increasing again from January 2017, with painful and obvious when swallowing, a mass was touched in the right neck, with mild tenderness and activity, CT showed recurrence (Fig. 4A and B). On February 20, 2017, the patient underwent the right neck neoplasm resection in condition of the resting compound anesthesia (the third operation). Postoperative pathological biopsy results showing (Fig. 4C and D): Neoplasm composed of spindle cells with nuclear atypia, nucleolus is clear, and multinucleated giant cells could be seen, nuclear fission is obvious, osteoid matrix is not obvious, and infringement of striated muscle tissue around them.

Fourth Operation and the follow-up. July 7, 2017, the patient underwent the partial resection for the mass enlarged once more with trachea compression, and damaged the skin. Partial mass with the range of about 6.0x3.0x3.0 cm was resected (Fig. 5). The patient is alive till now.

Discussion

Skeletal osteosarcoma (ESOS), also named as soft tissue osteosarcoma, is a rare malignant soft tissue sarcoma with histologic similarities to primary bone osteosarcoma but without attachment to the bone or periosteum, with malignant osteoid or bone (or both) formation and a uniform morphological sarcomatous tissue patterns (1). ESOS is a rare malignancy that the morbidity accounts for about 1 to 2% of all soft tissue sarcomas (1,7), and less than 4% of all osteosarcomas (7,8). Most of the ESOS occur in the upper and lower extremity, with the proportion of ~40.0- 67.5 (1,9) to ~85.7-88.7% (4,10), but very few occur in the head and neck, with the constituent ratio is ~2.5-3% (9,11) to ~5-7.3% (1,3). These tumors generally arise with a high incidence of the median age is ~57-60.7 years (1,10), which usually located in the deep soft tissues without attachment to skeletal bones but were firmly attached to the fascia (12). This case of primary ESOS occurs in subcutaneous on the right side of the neck is exceedingly rare, which underwent four times of the operation, followed by once postoperative radiotherapy, but relapse for several times.

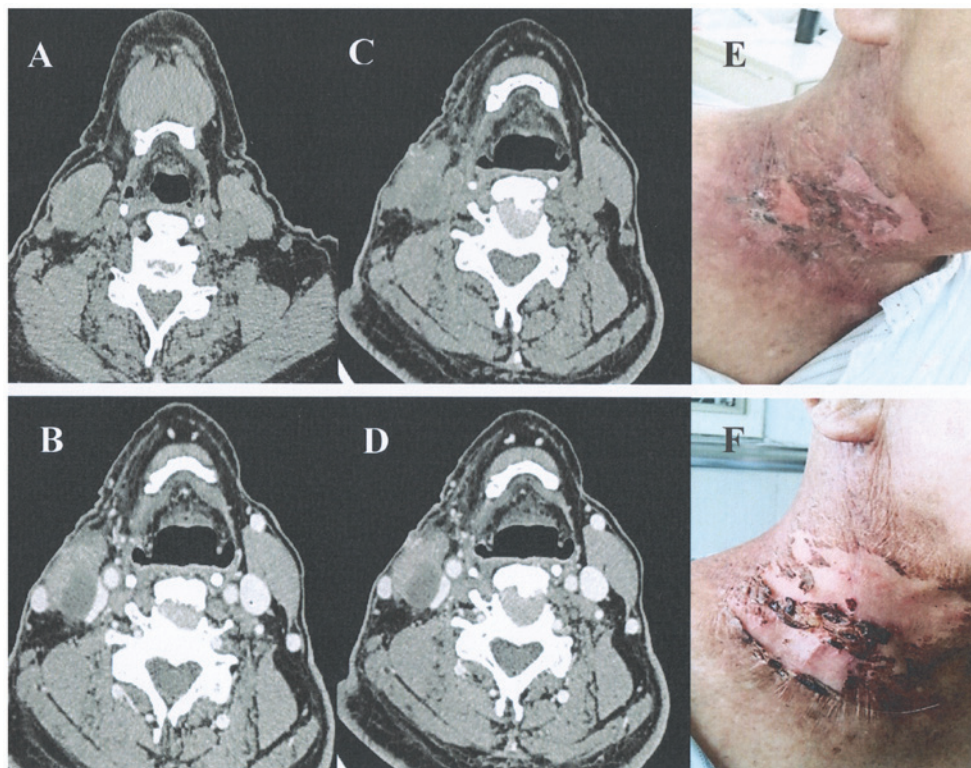


Figure 3. CT scan from June 29, 2015. (A) Unevenly distributed low density nodules were seen on the inside of the right sternocleidomastoid, with clear sternocleidomastoid boundaries, and flat compression of the right jugular vein. (B) Enhanced scanning: Arterial phase was slightly enhanced, and venous and delayed periods were further strengthened. (C) CT scan from November 10, 2015: Scan showing the medial low density nodules of the right sternocleidomastoid muscle were smaller than before and had decreased in density. (D) Enhanced scanning enhancement was not obvious. In terms of the Response Evaluation Criteria In Solid Tumors standard, it was 'Stable Disease'. (E) Acute radiation skin lesions (level 2) occurred in the right neck skin; however, (F) recovery was observed following local skin treatment. CT, computed tomography.

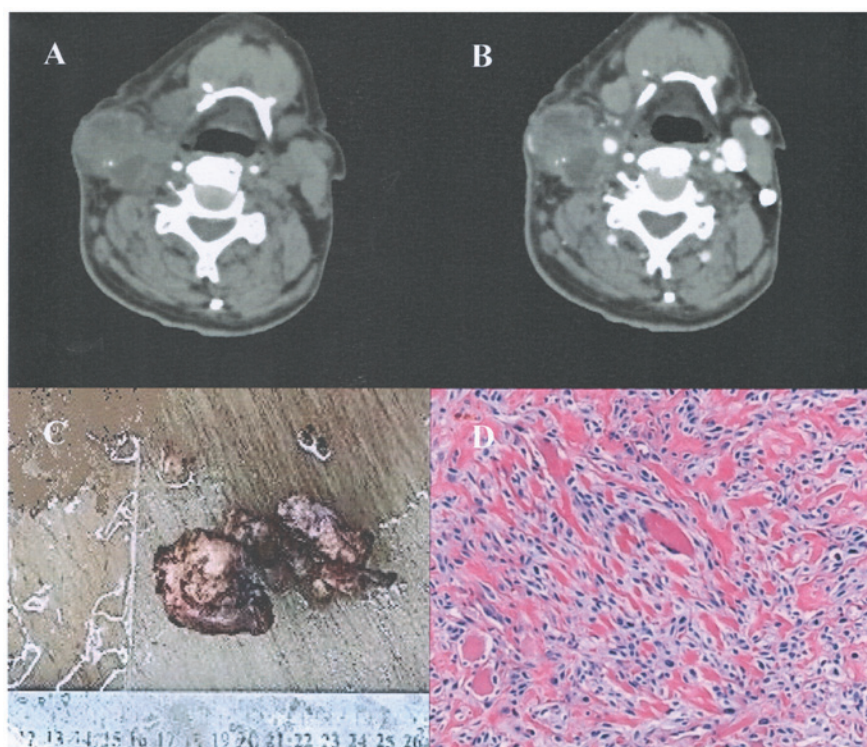


Figure 4. (A) CT scan showing an enlarged mass of $\sim 8.8 \times 6.0 \times 5.4$ cm, with an increased density on the right-hand side of the neck. (B) Contrast-enhanced CT revealed the mass was enhanced in homogeneity, with a fuzzy surrounding fat gap, adjacent skin thickening and a moderately enhanced nature. (C) Surgical excision contains multiple tissue fragments. (D) Hematoxylin and eosin staining (magnification, $\times 200$). The tumor was composed of spindle cells, nuclear heteromorphism, nucleolus clarity, multiple nuclear giant cells, nuclear fission, the osteoid matrix was not obvious, and the surrounding rhabdomyosis was infringed. CT, computed tomography.

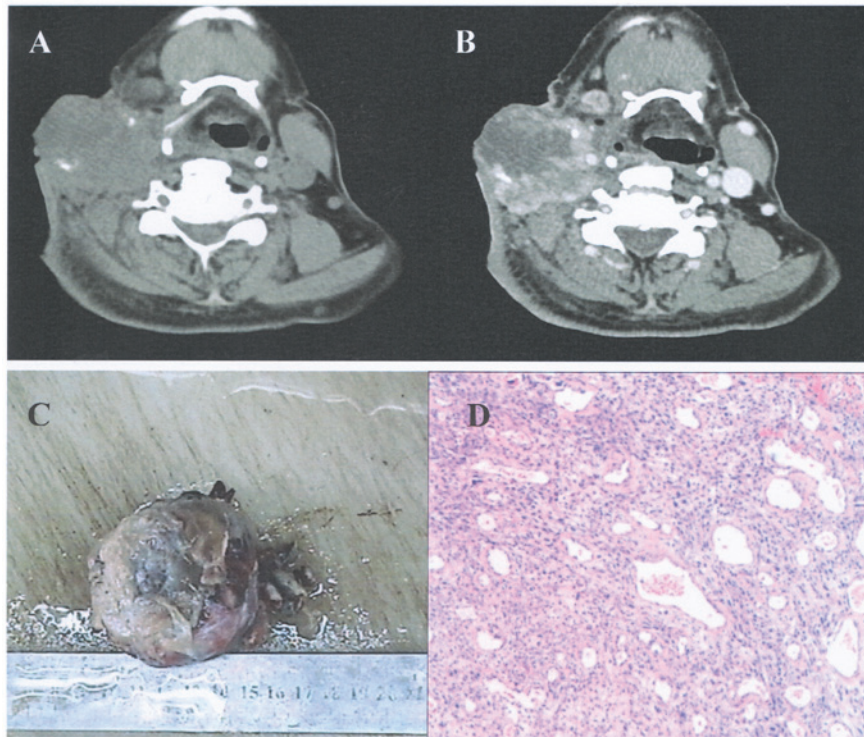


Figure 5. (A) CT scan showing large clumpy, low density soft tissue masses on the right-hand side of neck with the range of ~9.2x6.6x5.3 cm, with irregular speckle calcification on the inside of the mass; the mass was not clear with the sternocleidomastoid, and the right pharyngeal space disappeared. (B) Contrast-enhanced CT showing an inhomogeneous peripheral enhancement; no enhanced necrotic areas were seen in the center and the total vein of the right neck and the internal jugular vein were compressed. (C) The resected mass had a cauliflower-like, hard texture, and was (D) confirmed as relapsed extraskelatal osteosarcoma by pathology (Hemastoylin and eosin; magnification, x100). CT, computed tomography.

ESOS patients starting symptoms tend to be progressive enlargement of tumors and rarely causing pain or tenderness, the preoperative duration of symptoms ranged from 2 weeks to 25 years (median, 6 months) (12). But ESOS could firstly manifest as spontaneous tumor lysis syndrome which represents an oncological emergency must be treated as soon as possible (13). ESOS is a rare mesenchymal malignancy of soft tissue, histologically indistinguishable from primary osteosarcoma of bone. However, there are distinct differences in demographics, imaging features, prognosis, and management compared with osteogenic osteosarcoma (8), its correct diagnosis may depend on a combination of clinical, radiographic, and pathologic findings (8,12,14-16).

There are several treatment methods for ESOS, including surgery, radiation therapy, and chemotherapy (2-4,10,11), surgical resection is dominated, 85 to 98% (10,11), even all patients with localized disease were managed with surgical resection of the primary tumor (4), radical resections are effective for local control and have the best chance of cure for ESOS (8), 5-year OS and 5-year disease-free survival (DFS) was 51.4 and 43% respectively (10), but the proportion of patients treated alone with surgery was low (21.8%) (10), and its effect on distant metastasis is not so clear, multiagent chemotherapy may be help to reduce distant metastasis, a trend towards increased length of survival was found in patients who received chemotherapy compared to those who did not (16.4 months vs. 9.3 months) (2), the gemcitabine-docetaxel chemotherapy regimen was considered as well-tolerated and induced a long lasting partial response for ~14 months in the treatment of ESOS (17). Higher survival was observed

in patients who received perioperative chemotherapy with a trend in favour of multiagent osteosarcoma-type regimen which included doxorubicin, ifosfamide and cisplatin (10), and postoperative adjuvant external beam radiotherapy being considered to improve local control rate and preserve organ function (18,19), and especially the patients who with tumour >5 cm and R0 margins seems to benefit more from RT (10), and there is a tendency to extend 5-y DFS in patients who underwent postoperative adjuvant RT compared with surgery alone (66 vs. 42%, $P=0.38$) (11), though RT was not associated with a lower disease-related mortality rate or a longer event-free survival (4). However, the available data are contradictory with regard to the use of chemotherapy and radiotherapy regimens in the management of ESOS, radiographic response rates and pathologic complete response rates to doxorubicin-based systemic therapy are low (3), no significant association of disease-specific or event-free survival was found with the addition of radiation, chemotherapy, or both to surgery, radiation and chemotherapeutic treatment were not associated with a lower incidence of death due to disease or a longer event-free survival (4). Currently, a multimodality approach is used to treat extra skeletal osteosarcoma, which entails incorporation of multidrug chemotherapy and /or radiotherapy along with the surgery to get the best outcome in terms of disease specific survival and local relapse free survival (10). In fact, there are many factors influence the treatment effects and clinical outcomes of ESOS, including tumor size, tumor location, pathology classification and grade, clinical stage, surgical margin, choice of chemotherapy drugs, age (1,4,7,9,11,20), expression of oncogenes (21,22), and so on.

In this case of ESOS, lesion located in subcutaneous on the right side of the neck, in the posterior of the sternocleidomastoid, with the adjacent sternocleidomastoid and the right internal jugular vein were displaced, thus, the tumour was incompletely removed. The postoperative chemotherapy and local radiotherapy seem to be necessary (2,10,11,16,17), but the patient refused the postoperative radiation and chemotherapy, with the result of the local recurrence after about nine months of the first operation. In the case, the patient voluntarily received local radiotherapy after the second operation, and DFS is about 15 months. Third resection performed when relapsed again, second course of radiotherapy was not considered for having had a history of local radiotherapy and an obvious skin injury, but the patients still refused to chemotherapy, 5 months later, the patient underwent another operation for relapsed once more.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

JSZ participated in the conception and design of the case report and wrote the manuscript. GW and YL evaluated the patient, participated in the radiotherapy procedures and were major contributors in writing the manuscript. ZHW performed the surgical management procedures and reviewed the manuscript. GDC conducted the surgical management procedures. HW participated in radiotherapy and wrote the manuscript. TCZ assisted with the treatment of radiotherapy and reviewed the manuscript. All authors have read and approved the final draft.

Ethics approval and consent to participate

The patient provided written informed consent for participation in the present study.

Consent for publication

The patient provided written informed consent for the publication of any associated data and images in this case report.

Competing interests

The authors declare that they have no competing interests.

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