CASE REPORT

Anterior abdominal wall extraosseous osteosarcoma, occurring 40 years after para-aortic irradiation

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SUMMARY

Extraskeletal osteosarcomas (OSs) are highly malignant soft tissue tumours associated with a poor prognosis. Only a few records of these rare aggressive neoplasms have been reported in the literature.

We describe the case of a 49-year-old man, who presented to our tertiary care centre with a painful isolated lump around the umbilicus. After surgical biopsy, imaging and subsequent pathological analysis, the swelling was diagnosed to be a localised extraskeletal OS. He received previous radiation as treatment for testicular seminoma 40 years ago, which has been in remission ever since. He also happens to have testicular hydrocele since 10 years. He was subjected to resection and free flap reconstruction complicated by lower anterior abdominal wall haematoma and large pseudoaneurysm of the left femoral artery. Patient completed 60 Gy of adjuvant electron beam irradiation for close margins and is scheduled for adjuvant chemotherapy. We describe a brief account of his illness.

BACKGROUND

Soft tissue osteosarcomas (OSs) are rare malignant mesenchymal neoplasms, which characteristically produce osteoid, bone or cartilage in soft tissues with either minimal skeletal and periosteal attachment or completely without it.^{1,2} These account for 1–2% of all soft tissue sarcomas and 2–4% of all OSs. There is a male preponderance with peak incidence in the sixth decade, but it has also been recorded in the paediatric age group. No racial preferences have been reported. Common sites of occurrence in the order of probability are: thighs, buttocks, upper extremity, retroperitoneum or any other soft tissue site, including pleura, uterus and breast, and presenting as large (mean tumour size 9 cm) painful masses usually post trauma. X-ray or radiation therapy exposure has been documented in 4–13% of cases with a latent period of 2–40 years, while other predisposing factors include genetic chromosomal defects, increased incidence of chondromas and external injury. Data on their management are scarce and originate from case reports or case series.

In this case, the tumour recurred 40 years after primary radiation therapy to mid abdomen, which makes it unique and interesting. The prognosis of this neoplasm is poor with an aggressive natural history, so the more data we can gather about it, the better for future clinical references and aid.

CASE PRESENTATION

We report a rare case of extraosseous extraskeletal osteosarcoma (EOO) diagnosed and managed at SHIFA Cancer Centre, SHIFA International Hospital, Islamabad, Pakistan. A 49-year-old man with Eastern Cooperative Oncology Group (ECOG) performance status of zero, no comorbidities and no known family history of malignancy presented with a solitary, painful anterior abdominal swelling which grew in size over 7 months. He gave a history of receiving 3 weeks of dog leg irradiation to the para-aortic and pelvic lymph nodes after being diagnosed with early stage left testicular seminoma 40 years ago, for which he is in remission until now. He also carries a right testicular hydrocele since 10 years and an artificial left eye after a prior surgery. The patient felt an anterior abdominal mass (extra-peritoneal) around the umbilicus, around 3×4 cm in size since December 2015 which grew with time to be felt as a 9 cm mass at diagnosis.

INVESTIGATIONS

Pre-op CT of chest, abdomen and pelvis—figure 1A reveals lower anterior abdominal soft tissue mass in subcutaneous tissue overlying the rectus abdominus muscle. (B) Radiation treatment portal is shown in red, over the grafted tissue with 5 cm margins all around the preoperative fused tumour image.

Histopathology—figure 2—H&E stained slide at 10X magnification showing a malignant neoplasm arranged in solid nests and singly. Figure 3: H&E stained slide at 20X magnification shows a spindle cell proliferation with brisk mitotic activity. Figure 4: H&E stained slide at 40X magnification of cells shows nuclear atypia and pleomorphism and there is patchy osteoid in between the tumour cells.

Abdominal wall mass, excision with margin clearance; extraskeletal OS, tumour size 10×8.5×2.5 cm, all resection margins free from tumour, closest deep margin 3 mm, French Federation of Cancer Centers Sarcoma Group (FNCLCC) system histological grade 3.

Immunohistochemistry

Anti-smooth muscle actin patchy positive, Desmin negative, CKAE1/AE3 negative and S100 focal positive. Immunohistochemistry was of little value as it has no diagnostic role in OS.

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Figure 1 (A) Pre-op CT Image showing anterior abdominal soft tissue mass (red) in subcutaneous tissue overlying the rectus abdominus muscle. (B) Radiation treatment portal is shown in red, over the grafted tissue with 5 cm margins all around the preoperative fused tumour image.

TREATMENT

Patient underwent incisional biopsy in an outside medical facility revealing EOO and had delayed wound healing for 5 months. He eventually had resection reconstruction in late July 2016. Histopathology revealed EOO, tumour size $10 \times 8.5 \times 2.5$ cm, resection margins free, closest margin 3 mm, FNCLCC grade III and necrosis 40%, while metastatic workup, including a high resolution computerised tomography (HRCT) chest, was negative. His disease was staged as pT2bN0M0. His recovery remained quite eventful with development of a large mixed density lower anterior abdominal wall haematoma, while CT scan revealed a large pseudoaneurysm arising from left common femoral artery at the level of inguinal ligament with surrounding fat stranding and enlarged obturator internus muscle. Patient has completed 60 Gy of adjuvant electron beam irradiation over 30 days for close margins.

OUTCOME AND FOLLOW-UP

Patient tolerated radiation therapy quite well, with erythema grade II and tightness felt in the graft, which resolved after regular topical application of al-hydrin gel over a month. He is scheduled for adjuvant intravenous chemotherapy, that is, cisplatin and adriamycin at 3-week interval (total six cycles).

DISCUSSION

Extrasosseous OS is a rare variant of OS which occurs in soft tissues.³ These are aggressive compared with conventional OSs.⁴ Wilson reported the first case of extrasosseous OS in 1941.⁵ Histologically, all morphological variants can be seen, and immunohistochemistry stains can help in differentiating from other soft tissue sarcomas.⁶ The exact aetiology is unknown and ionising radiation has been postulated.⁷ Myositis ossificans has also been implicated as a possible cause and may lead to development of OS development in the soft tissue.^{8,9}

In a report of 37 patients, the median age was 55 (range 13–81 years) and 57% were men. Eighty-nine per cent of patients had OS in a soft tissue site, and 11% had OS of hard palate, ethmoid sinus and breast, while 86% of patients had high-grade tumours and 73% had stage III disease. In 14% of cases, the history of previous radiotherapy is a known risk factor for these sarcomas as a secondary malignancy. At 45 months' median follow-up, 16% had local and 30% had distant recurrences as first event, respectively. Poor overall survival was observed in advanced stage ($p < 0.001$), the absence of surgery ($p < 0.001$), large primary size ($T > 10$ cm, $p = 0.002$) and age ($p = 0.002$) in univariate analysis and large tumour size ($T > 10$ cm, $p = 0.005$) in multivariate analysis. Patients are usually managed with trimodality treatment which includes neoadjuvant radiotherapy or chemoradiotherapy followed by surgery or adjuvant radiotherapy or chemotherapy. Radiation

Figure 2 H&E stained slide at 10X magnification showing a malignant neoplasm arranged in solid nests and singly.

Figure 3 H&E stained slide at 20X magnification shows a spindle cell proliferation with brisk mitotic activity.

Figure 4 H&E stained slide at 40X magnification of cells shows nuclear atypia and pleomorphism and there is patchy osteoid in between the tumour cells.

doses of 41.4–50 Gy in neoadjuvant setting have been used and a dose up to 70 Gy in adjuvant setting has been used. Cisplatin, doxorubicin, ifosfamide, mitomycin C and methotrexate are used in various combinations in adjuvant therapy and gemcitabine-based chemotherapy is used as a salvage.^{10 11} In a study of 40 patients with high-grade EOO, all recurred within 3 years. There was a male predominance (male to female ratio 1.9:1) with lower limbs being the most commonly involved region (68%). By univariate analysis of Kaplan-Meier survival curves, the patients with chondroblastic tumours progressed far better than those with predominant osteoblastic tumours ($p=0.03$).¹¹ In an analysis of 12 patients with EOO, seven of whom received chemotherapy and four, radiation therapy, a trend towards increased length of survival in patients who received chemotherapy compared with those who did not was observed (16.4 months vs 9.3 months, $p=0.16$).¹²

Radiotherapy alone is kept for palliation and/or salvage therapy. Large tumour size was prognostic.¹² Recurrences are believed to occur mostly within 2 years after surgery, highlighting the need for adjuvant treatment, that is, chemotherapy and radiotherapy.¹³ Imaging, for example, local plain conventional radiograph, CT or MRI scan of the soft tissue may be essential to rule out any continuity of the tumour with the bone, while staging HRCT chest rules out lung metastases. A wide local excision with a wide margin (at least 5 cm) of normal tissues should be attempted.¹⁴ Patients with an extremity EOO can be treated with limb salvage procedures, and where not possible, amputation may be recommended.^{15 16}

More than 80–90% of patients develop local recurrences and metastasis to the lungs and bones. The time period between surgical removal of the primary neoplasm and recurrence is between 2 months and 10 years.¹⁷ M.D. Anderson

Cancer Center (1960–1999) reviewed 60 patients with EOO who responded poorly to chemotherapy with risk of relapse of 19%. In 30 of these patients with localised disease, the 5-year actuarial local recurrence-free, distant recurrence-free, event-free and disease-specific survival rates were 82%, 64%, 47% and 46%, respectively.¹⁵

Learning points

- ▶ Rare entity.
- ▶ Reported as first case in this region to best of our knowledge.
- ▶ Late complication of curative radiotherapy in a cured germ cell tumour.
- ▶ Occurred after a latent period of 40 years.
- ▶ Patient is re-irradiated encompassing almost the same site.

Contributors MF, AQ and MF: manuscript write-up. NM: diagnosis.

Competing interests None declared.

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