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Case study

A case report of long-term survival of metastatic extraskeletal myxoid chondrosarcoma treated with surgery and hypofractionated radiotherapy

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Abstract

We describe the case of a patient with a 10-year history of metastatic extraskeletal myxoid chondrosarcoma (EMC), who underwent repeated surgical excision and ten courses of hypofractionated radiotherapy to locally recurrent or metastatic disease. We review the literature on EMC's and propose that surgery and radiotherapy can be used to control disease progression and palliate symptoms for extended periods of time with acceptable toxicity profiles.

Key words: extraskeletal myxoid chondrosarcoma; metastasis; radiation therapy; spinal cord radiation tolerance

INTRODUCTION

Extraskeletal myxoid chondrosarcoma (EMC) is a rare type of soft tissue sarcoma that is most commonly found in the lower extremities and characterised by a broad morphologic appearance. EMC do share certain histological features such as the presence of primitive chondroblastic tissue and genetic abnormalities such as the t(9;22)(q22;q12·2) translocation.[1,2] One of the largest case series of 87 patients with EMC came from the Memorial Sloan Kettering Cancer Center (MSKCC).[3] In this series, patients presenting with localised disease who received definitive treatment with surgical resection had a median disease survival time of 4·7 years.[3] A multi-institutional case series of 42 patients from Japan demonstrated similar outcomes, in which wide local excision of localised EMC led to a disease-free survival rate of 45% at 5 years.[4]

The MSKCC case series[3] also showed that of patients treated with curative intent, 37% will develop local recurrence and 26% will develop metastatic disease, most commonly in the lungs. Once metastasis is detected, survival is shortened to a median of 17·8 months. Despite these outcomes, this case series did not find any benefit with adjunctive treatment. Neoadjuvant, intraoperative or postoperative radiotherapy administered for 22 patients was not associated with a decrease in local recurrence, although there likely was adverse selection bias in the group selected for radiotherapy. In addition, 21 patients received 39 courses of chemotherapy but no patients achieved either a partial or complete radiological response by RECIST criteria.

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Here, we describe the case of a patient with a 10-year history of metastatic EMC who underwent repeated resection and radiotherapy, showing that palliative surgery and hypofractionated radiation can control disease progression, and may have contributed to the prolonged survival of this patient.

CASE REPORT

A chart review was conducted in accordance with institutional policies of the case of Mr D. G., a then 41-year-old gentleman with good baseline health who presented at the beginning of 2002 with a 1-year history of worsening right knee pain. Mr D. G. underwent a magnetic resonance imaging (MRI) scan that revealed a 12 cm soft tissue mass centred in the right adductor magnus muscle with extension to the right distal femur and popliteal fossa. Biopsy of this lesion revealed myxoid chondrosarcoma.

Table 1 chronologically outlines the clinical details of his disease. In brief, Mr D. G. underwent resection of the primary tumour in the right thigh in April 2002. A 0·7 and 0·5 cm lung nodule were seen on initial staging but were too small to be definitively characterised. In October 2003, the previously seen lung nodules grew in size and additional lesions were visualised. He also developed symptomatic chest wall recurrence and underwent thoracotomy and resection of one of the lesions that confirmed metastatic EMC. He then presented with a thoracic spine recurrence in 2004, for which he underwent excision and spine fusion followed by radiation therapy to T10–L3. Between 2008 and 2013, he had multiple courses of radiation therapy to recurrent or metastatic lesions at various sites including the lung, chest wall and spine. Overall, he had a favourable response to these radiation treatments, including excellent pain relief and complete radiographic response at several sites (Figure 1). Owing to the widespread systemic disease, he also underwent one course of pemetrexed chemotherapy in 2008, which was discontinued after two cycles because of disease progression.

Mr D. G. developed a local recurrence in the right femur in September 2012 and underwent radical resection of the right femur and the placement of a mega-prosthesis. This was followed by additional radiation therapy to the right leg. In July 2013, he developed back pain and was found on MRI to have a recurrence in levels T7–T9 of the spine. He underwent a biopsy of this lesion that revealed bone fragments without evidence of malignancy. Owing to high clinical suspicion of recurrence, severe pain and potential for cord compression, he was offered empiric radiation therapy to this area.

At that time, Mr D. G. had already received nine courses of radiation therapy with overlapping field borders. The most concerning area was the spinal cord at the level of the T9/T10 intervertebral disk. This area had received 30 Gy when T10–L3 was treated in January 2005 in addition to lesser doses contributed by other courses of radiation to chest wall or lung metastasis. Many of the treatments took place in the era of 2D conventional simulation. Therefore, it was not possible to obtain the exact spinal cord dose. In addition, the patient received differing doses per fraction with intervals of several years between certain treatments making radiobiological estimate of dose calculations difficult.

We conservatively estimated that the spinal cord at the T9–T10 interspace has received a dose of 45–50 Gy_2 (2 Gy per fraction equivalents) from prior radiation. Therefore, we chose to give an additional 12 Gy in 3 Gy per fraction to T7–T9 followed by an additional boost of 18 Gy with blocking of the T9/T10 interspace. The maximal dose to the spine at the field junction area in T-spine was estimated to be ~65 Gy in 2 Gy per fraction equivalent. Mr D. G. experienced no acute toxicities and had excellent pain relief during treatment.

At last follow-up on 19 November 2013, Mr D. G. reports no pain while on moderate doses of narcotic pain medication. However, he does require the assistance of a walker for ambulation. This is owing to decreased strength in his right leg that occurred after he underwent radical resection of his right femur in November 2011, which was followed by two additional surgeries to clear out infection and help with wound healing. These complications are at least partially due to prior radiation (50 Gy/10 fractions) to this area.

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Table 1. *Summary of treatment and response*

Date	Clinical status	Treatment	Response to therapy	Estimated spinal cord dose
February 2002	Posterior right knee pain for 1 year. Diagnosis of EMC of the right thigh measuring $12 \times 7 \times 6$ cm. Sub centimetre lung nodules on chest CT		—	
April 2002	Initial surgery	Resection of the mass and right distal femur and replacement with a metal distal femoral prosthesis and revision knee implant	—	
October 2003	Chest pain and lung lesions on CT	Thoracotomy and excision of metastatic lung nodules followed by excision of right chest wall lesion	—	
October 2004	Left chest wall pain	Wide resection of left tenth rib metastasis	Moderate pain relief	
December 2004	Metastasis to T10 causing back pain and radiculopathy	Thoracotomy, anterior corpectomy with spinal cord decompression, anterior spinal fusion T11–L1	Moderate pain relief	
January 2005	Postoperative radiation	30 Gy in 10 fx's to T10–L3 (AP/PA technique using 16 MV photons)	Moderate pain relief	Estimated 36 Gy_2 to T9/T10
June 2005	Two growing lung nodules in the right posterior lung and left lower lung	Both lesions received 40 Gy in 10 fx's using conformal arcs using 6 MV photons with SBRT technique	Partial radiographic response to therapy	Max cord dose 26·4 to T6–T8Estimated 14 Gy_2 to T9/T10
June 2006	Back pain with lytic lesions seen in L4–L5 and sacrum	30 Gy/10 fx's to L4–L5 sacrum	Excellent pain relief	Negligible dose to thoracic spine
February 2008	Recurrent chest wall and lung lesions	Pemetrexed at 500 mg/m^2 for two cycles from June to July 2008	Disease progression	
August 2008	Progressive nodules after chemotherapy in the right paratracheal node, right chest wall mass, left lower chest wall mass	40 Gy in 10 fx's to all three lesions using 6 MV photons	Partial radiographic response	Estimated 9·6 Gy to T5–T6 Negligible dose to T9/T10
November 2009	Lump in the right leg near the original resection scar	50 Gy in 10 fx's to right thigh using SBRT technique with CBCT guidance	Complete clinical response	Negligible dose to T9/T10
July 2011	Growing masses in the right medial thigh and left flank	35 Gy in 10 fx's to right groin and left flank	Partial clinical response	Negligible dose to thoracic spine
August 2012	Large, growing left clavicle mass	36 Gy/9 fx to left clavicle using 3D-CRT	Complete clinical response	Negligible dose to T9/T10
September 2012	Right hip pain due to locally recurrent tumour	Radical resection of the right femur, including the proximal shaft and distal femur		
November 2012	Postoperative radiation	35 Gy in 10 fx's to right hip		Negligible dose to thoracic spine
April 2013	Symptomatic progression of masses in the left chest wall on CT	45 Gy in 5 fx's to left chest wall using SBRT	Excellent pain relief	Max cord dose 6·9 Gy at approximately T7
July 2013	Back pain with new lesions from T7–T9 on MRI	12 Gy in 4 fx's to T7–T9 followed by boost of 18 Gy in 6 fx's to superior extent of T7–T9 avoiding the T9 to T10 junction	Excellent pain relief	12 Gy at T9/T10 interspace

fx, fractions; Gy_2, dose in 2 Gy/fx equivalents; CT, computed tomography; AP/PA, anterior/posterior opposing beams; MV, megavoltage; SBRT, stereotactic body radiation therapy; CBCT, cone beam computed tomography; 3D-CRT, 3D-conformal radiotherapy; MRI, magnetic resonance imaging.

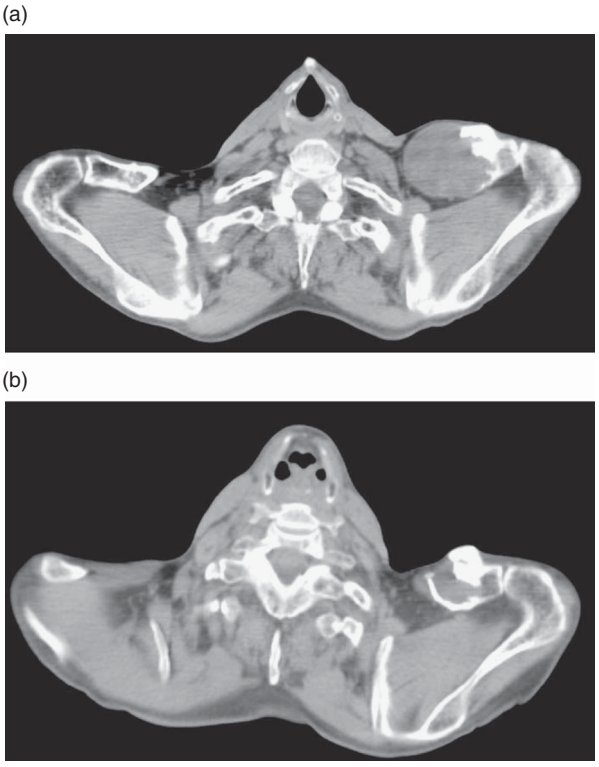

Figure 1. Computed tomography scan on 27 August 2012 shows large soft tissue mass arising in the left supraclavicular fossa with destruction of the left clavicle. The lesion was treated with 36 Gy in 9 fx's finishing on 17 September 2012. Follow-up imaging 7 months later on 11 April 2013 shows complete radiographic response to treatment.

DISCUSSION

We report on a case of metastatic EMC treated by multiple surgical resections, hypofractionated radiotherapy and two cycles of pemetrexed chemotherapy. Our patient initially presented with what was thought to be localised disease and underwent resection aimed at cure without additional therapy. He subsequently developed both locally recurrent and metastatic disease that frequently caused him pain and functional decline. He was aggressively treated with surgical resection and radiotherapy that significantly reduced his pain and improved his quality of life. These treatments may have also contributed to his prolonged survival of over 10 years with metastatic disease, which far exceeds the median survival of 17·8 month reported in a large retrospective series.[3]

Interestingly, prior clinical experience has not demonstrated a clear benefit with the use of adjunctive radiation in resected EMCs[3] and radiobiological research have shown that human chondrosarcoma lines may have intrinsic radiation resistance owing to a deficiency in cell cycle regulators that would normally inhibit cell division after DNA damage from ionising radiation.[5] To overcome possible radiation resistance, we chose to deliver radiotherapy for our patient in 3–5 Gy per fraction, which is larger than the 1·8–2 Gy per fraction delivered in conventional fractionation for carcinomas. As our experience shows, this hypofractionated radiation can yield partial and even complete radiographic response after treatment. This is consistent with the experience of others who have noted that hypofractionated radiotherapy can overcome intrinsic radioresistance in other tumour types such as melanoma.[6] Our patient did receive two cycles of pemetrexed chemotherapy that was discontinued because of disease progression. This is similar to findings reported by Drilon, in which 21 patients underwent 39 courses of chemotherapy with no patients demonstrating any response.[3]

In planning treatment for this patient's most recent recurrence at T7–T9, we took into account the fact that he had already received 45–50 Gy_2 to his spinal cord at the T9/T10 interspace. To avoid cord injuries, intensity modulated radiotherapy was applied to minimise radiation doses to the cord. Based on QUANTEC data, a dose of 60 Gy_2 to the full cross-section of the cord is associated with a 6% risk of myelopathy.[7] However, spinal cord tolerance is known to increase by at least 25% after 6 months.[7] This meant that our dose of 65 Gy_2 to the cord at T9/T10 is likely associated with a small chance of myelopathy. Given the patient's excellent response to prior radiation and the almost certain likelihood of myelopathy from tumour progression, we felt the benefits justified the risks. However, the patient was extensively counselled during the consent process regarding the possibility of myelopathy. To date, the patient has not shown any signs or symptoms of radiation-induced myelopathy.

CONCLUSION

We showed in this case report that repeated surgical resection and hypofractionated radiotherapy can achieve excellent control of

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metastatic and recurrent disease and improve quality of life in a patient with EMC. In addition, these aggressive treatments may have contributed to his unexpected survival of over 10 years after being diagnosed with metastatic EMC.

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