

Case Report

Recurrent leiomyosarcoma with de-differentiation to chondrosarcoma and osteosarcoma: a case report

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ABSTRACT

Leiomyosarcoma are a rare type of tumour of smooth muscle that can be found in the retroperitoneum. There is a paucity of reported data around dedifferentiation of leiomyosarcoma. Our case report describes de-differentiation of recurrent leiomyosarcoma into osteosarcoma and chondrosarcoma in a patient who had a local recurrence of his leiomyosarcoma. The recurrence is on a background of intermediate grade leiomyosarcoma of the retroperitoneum and he underwent his original resection in 2019 and included a right nephrectomy and right hemicolectomy. Our patient is currently undergoing radiotherapy and we will continue ongoing follow up for his progress.

Keywords: Leiomyosarcoma, Retroperitoneum, Chondrosarcoma, Osteosarcoma

INTRODUCTION

Retroperitoneal sarcomas arise from mesenchymal cells and account for approximately 10% of all soft tissue sarcomas, and less than 1% of all malignant tumours.^{1,2} Leiomyosarcoma are a subtype of sarcoma, often originating from the abdomen or the uterus showing smooth muscle differentiation.^{1,3} Histologically leiomyosarcomas are characterised by morphological and immunohistochemical evidence of smooth muscle differentiation.¹

Complete resection of retroperitoneal sarcomas is the standard treatment modality, however they present a unique surgical challenge. There is a lack of fascial planes in the retroperitoneal region and they often present late, are in close proximity or have direct attachments to critical local structures including the aorta, vena cava, spine and other neurovascular structures.⁴ Due to these factors, even an aggressive surgical approach can result in positive margins, with 20% of reported cases having positive

margins.^{5,6} Recurrence is also high, with rates of 40-80% reported in literature.^{7,8}

We describe a man with a recurrence of a leiomyosarcoma showing osteosarcomatous and chondrosarcomatous de-differentiation.

CASE REPORT

A 69-year-old man developed a recurrence of his leiomyosarcoma nine months from his original sarcoma resection. He was a previously well man, with a history of prostate adenocarcinoma that was in remission. He was a non-smoker, and had minimal alcohol intake.

He originally underwent a laparotomy in 2019 for an en-block resection of a retroperitoneal sarcoma including a right nephrectomy and right hemicolectomy. A number of immunohistochemical stains were performed on the specimen with the following pattern: CD34, BCL2 and desmin positive. Beta catenin and smooth muscle actin positive in blood vessels only. STAT6, CD99, S100,

SOX10, CD117, DOG1, EMA, SMA, myosin, calponin, caldesmon and MUC4 negative. This was favoured to be an intermediate grade retroperitoneal leiomyosarcoma. His margins at this time were clear, with the closest margin reported as 6 mm at the retroperitoneal margin and 8mm at the inferior margin. Post operatively there was a complication that included an anastomotic leak and a retroperitoneal collection.

In August 2020, a follow up fluorodeoxyglucose-positron emission tomography with computed tomography (FDG-PT-CT) found a recurrence of his retroperitoneal sarcoma with extension posterior to the liver. The fat plane between the tumour and ileocolic anastomosis was obliterated, with no erosion into the 12th rib. There was no evidence of abdominopelvic lymphadenopathy or distant metastases. Follow up magnetic resonance imaging (MRI) confirmed these findings, with the tumour centred on the right lateral abdominal musculature, with involvement of the right iliopsoas muscle, segment six of liver, and suspicion for involvement of the ileocolic anastomosis (Figure 1).

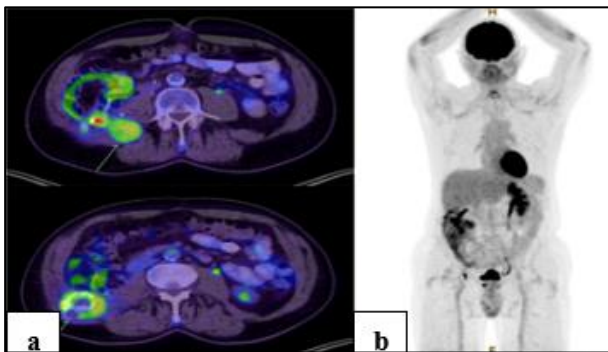


Figure 1: (a) FDG- PT- CT demonstrating a recurrence of his retroperitoneal sarcoma with extension posterior to the liver, obliterated fat plane between the fat plane and the ileocolic anastomosis, with no erosion into the 12th rib, with no evidence of abdominopelvic lymphadenopathy or distant metastases; and (b) PET only view.

In September 2020, he underwent a second en bloc resection of the dumbbell shaped lesion in a joint case of the upper gastrointestinal surgical team and the plastics and reconstructive surgery team. The sarcoma intra-operatively was more extensive than the imaging findings suggested. The superficial component involved the lateral abdominal side wall (external, internal oblique muscle and transversus abdominis), segment VI of the liver and the 11th and 12th ribs, as well as his previous ileocolic anastomosis. The deep component involved psoas major, iliacus, quadratus lumborum, and femoral nerve lateral to but not involving transversus abdominis.

A further gallbladder resection was done for gallstones, and not tumour involvement. The margins were clear by 0.3 mm on the transverse spinous process and 1 mm on the diaphragmatic margin. Given the close margins the

patient's case was discussed at the local sarcoma multidisciplinary meeting and deemed not to be for further surgery at this time, but a decision was made to offer the patient radiotherapy to prevent further recurrence (Figure 2).

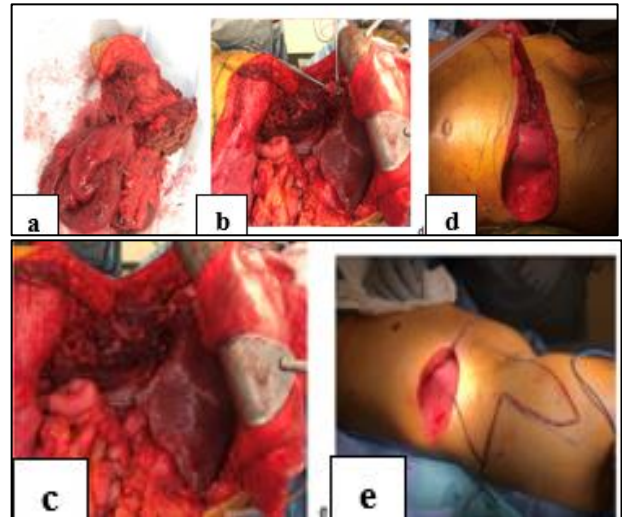


Figure 2: (a) Excised leiomyosarcoma specimen - involved psoas major, iliacus, quadratus lumborum, and femoral nerve lateral to but not involving transversus abdominis; (b) and (c) resection of leiomyosarcoma – cavity and resection bed demonstrating remaining liver, bowel and lateral abdominal musculature; (d) and (e) skin defect – closed with tissue flap repair by the plastics and reconstructive team.

On histology, the tumour was high grade, multinodular with varied morphology. It showed bland spindle cell areas without specific differentiation as well as areas with heterologous differentiation in the form of osteosarcoma and chondrosarcoma. Staining was positive for SMA (patchy) and BCL2. Repeat desmin was negative, as was S100, GFAP, CD34, caldesmon. H3K27me3 showed retained nuclear staining and MDM2 FISH was not amplified, excluding malignant peripheral nerve sheath tumour and de-differentiated liposarcoma respectively. Some areas of the tumour had a similar appearance to the previously diagnosed leiomyosarcoma although this wasn't supported with immunohistochemistry. In addition to showing osteosarcomatous and chondrosarcomatous differentiation, much of the tumour showed higher grade features than the previous resection. The case was reviewed to an expert soft tissue pathologist who agreed with the diagnosis of de-differentiated leiomyosarcoma (Figure 3).

Post-operatively the patient has been progressing well. There was a small wound collection that required drainage. The patient successfully underwent rehabilitation to aid in regaining strength and the ability to walk post resection of the involved femoral nerve. A 3 month post-operative FDG-PT-CT scan demonstrated some local activity

thought to be related to post-surgical changes of an extensive surgical site.

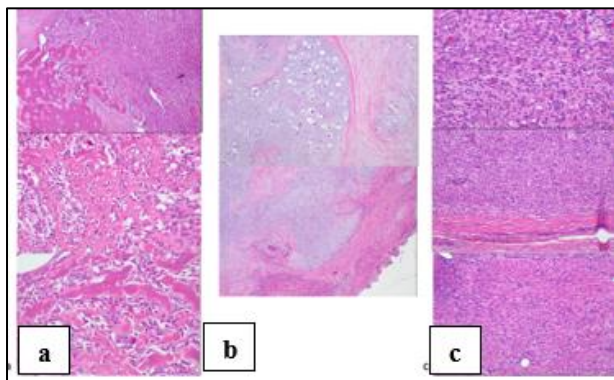


Figure 3: Histopathology slides demonstrating (a) malignant osteoid formation (osteosarcoma); (b) malignant cartilage (chondrosarcoma); and (c) non-descript spindle cell component (similar to smooth muscle tumour previously).

DISCUSSION

Although there have been occasional reports, there is a paucity of literature describing de-differentiation in sarcomas, particularly in leiomyosarcomas.⁹⁻¹¹ There are some reports of pleomorphic leiomyosarcomas, and a previously reported case series of dedifferentiation.^{9,10} A pleomorphic leiomyosarcoma variably expresses smooth muscle markers, while that of dedifferentiated leiomyosarcoma does not express any smooth muscle markers.⁹ Reports of de-differentiated liposarcomas have previously been reported in literature.¹¹⁻¹⁴ Within a case series report by Binh et al reporting mostly on dedifferentiated liposarcoma, there was a case initially diagnosed as a “mesenchymoma” with an altered diagnosis of de-differentiated liposarcoma with heterologous leiomyosarcomatous and chondrosarcomatous components.¹⁵ Perhaps most similar to our case report, in another case series by Chen et al described a case of de-differentiated leiomyosarcoma with osteosarcomatous differentiation and a case with both metaplastic cartilage and bone formation in the retroperitoneum.¹⁶

The tissue specimens of our case were sent for further expert analysis due to the unusual nature. The desmin in our case report was strongly positive in our initial tumour, and negative within the specimen of the recurrence. Further stains were conducted on the tumour to rule out carcinosarcoma of primary kidney or adrenal origin and these were negative.

Unfortunately for our patient prognosis for recurrences of leiomyosarcoma remains poor. Recurrence rates have been reported between 40-80%, and account for 75% of sarcoma deaths for those with retroperitoneal sarcomas.^{7,8} Along with the tumour grade, a recurrence will have a significant effect on survival outcomes.^{6,7} While a

complete surgical resection is the best chance for a cure for sarcomas, there is some consideration of using radiotherapy as an adjunct. There are some difficulties with this including the size of the radiation fields, complications of radiation to radiosensitive viscera including small bowel and stomach.¹⁷ The role of other therapies, such as chemotherapy and molecular targeted agents is still not clear.² Some early aggregate evidence of postoperative adjuvant radiotherapy suggests there may be better survival and local control compared with surgery only resections.^{17,18}

Our case demonstrated an aggressive high-grade sarcoma, with a relatively short time between the original resection and resection of the recurrence, as well as variation between imaging findings and operative findings suggesting a rapid tumour growth. In conjunction with a very narrow tumour margin reaching the limits of operative oncological resection in our multidisciplinary meeting it was decided to offer the patient a trial of adjuvant radiotherapy. Early surveillance for detection of recurrence is recommended, and we will be monitoring this patient closely for evidence of further recurrence post radiotherapy.²

CONCLUSION

Leiomyosarcoma are a rare type of tumour of smooth muscle that can be found in the retroperitoneum. While there is a paucity of reported data around dedifferentiation of leiomyosarcoma, our case report adds to two other previously described cases reporting de-differentiation of leiomyosarcoma into osteosarcoma and/or chondrosarcoma. Some evidence suggests that radiotherapy, assessed in the neoadjuvant setting, may reduce the rates of sarcoma recurrence. Our patient is currently undergoing radiotherapy and we will continue ongoing follow up for his progress. Not a lot is known on how to treat de-differentiated leiomyosarcoma to osteosarcoma and chondrosarcoma, therefore it is important to publish this case report so as to contribute to the overall understanding of this rare disease.

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Ethical approval: Not required

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