



## Malignant melanoma of soft parts with osteoclast-rich giant cells: A rare tumour of the jejunum

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### CASE REPORT

Please cite this paper as: Mallick S, Singh L, Rajan K, Sharma, MC, Bansl VK, Dinda AK. Malignant melanoma of soft parts with osteoclast-rich giant cells: A rare tumour of the jejunum. AMJ 2014, 7, 4, 181-184. <http://doi.org/10.21767/AMJ.2014.1970>

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### ABSTRACT

Malignant melanoma of soft parts (MMSP), first described by Franz M. Enzinger, is a rare tumour of unknown cell origin. We describe a case of a 45-year-old male who presented with a one-year history of abdominal pain, weakness, and anaemia. Computerised tomography enteroclysis showed a mass in the jejunum that was suggestive of a gastrointestinal stromal tumour. An ulceroinfiltrative lesion measuring 6.5 x 4 x 2cm was identified. Microscopy revealed typical features of MMSP with numerous osteoclasts-like giant cells. The diverse histomorphology and immunohistochemical characteristics of this case involving a rare tumour at a rare site is presented.

#### Key Words

Malignant melanoma of soft parts, jejunum, osteoclastic giant cells.

#### What this study adds:

##### 1. What is known about this subject?

Malignant melanoma of soft parts (MMSP) is a rare soft tissue neoplasm that occurs mostly in the extremities. Gastrointestinal MMSP is extremely rare.

##### 2. What is the key finding of this report?

Our case is being presented due to its rarity and histomorphological differentiation, which must be recognised to differentiate it from GIST and poorly differentiated carcinomas. Due to the high risk of recurrence and distal metastasis, a close follow-up and screening of the patient is necessary.

##### 3. What are the implications for future practice?

The most common mesenchymal tumour of the small intestine is a gastrointestinal stromal tumour (GIST). MMSP in this location is very rare, and this case of osteoclastic-giant cell rich MMSP is also extremely rare. Other more common tumours like leiomyosarcoma, epitheloid GIST, and malignant peripheral nerve sheath tumour should be considered as differential diagnoses.

#### Background

Malignant melanoma of soft parts (MMSP) or the clear cell sarcoma (CCS) is a rare tumour of unknown cell origin, and was first described by Franz M. Enzinger.<sup>1,2</sup> The tumours are usually found around tendons or aponeuroses in the extremities. Only a few cases have been described in intra-abdominal organs. Ekfors et al. first reported the occurrence of MMSP in the gastrointestinal tract.<sup>3</sup> Age and sex distribution remain unknown due to the rarity of this lesion. Microscopically it mimics the epitheloid variant of gastrointestinal stromal tumour (GIST). The histogenesis of the tumour is poorly understood. Only finger countable cases have been reported in the literature. The characteristic cytogenetic finding of MMSP is translocation t (12; 22) (q13; q12), which helps in differentiating these tumours from close mimickers.<sup>4</sup> Here we describe a case MMSP of the jejunum with numerous osteoclast-rich giant cells.

#### Case details

A 45-year-old male presented with a one-year history of a painful abdomen, weakness, and easy fatigability. There was no history of haematemesis, malena, jaundice, abdominal distention, vomiting, or fever. No evidence of

recurrent infection was found. On general physical examination, there was pallor. Previous medical history was unremarkable. Haemogram revealed haemoglobin of 50g/L (reference; 120–140g/L). Abdominal examination did not reveal any organomegaly or palpable lump. An abdomino-pelvic ultrasonogram, upper gastrointestinal endoscopy, and colonoscopy were within normal limits. Enteroscopy showed a large ulcerated growth seen at the mid-jejunum. Computerised tomography enteroclysis showed long segment aneurismal dilatation of the jejunum with thick enhancing mass and enlarged mesenteric lymph nodes. The provisional diagnosis of a lymphoma or GIST was made.

Diagnostic laparoscopy showed no ascites, peritoneal, and omental deposits, or liver metastasis. A mass was seen at mid-jejunum involving the mesentery. Intra-operatively the mass was present in the jejunum; 60cm distal to the duodeno-jejunal junction, and extended up to the root of mesentery. Following serial ligation of the mesenteric vessels, resection of the involved jejunum with the mass was done with proximal 10cm and distal 5cm margin.

**Pathological features:** Grossly, a 4.4 x 4.3cm, solid, poorly circumscribed tumour was seen which appeared to infiltrate transmurally along with ulceration of the overlying mucosa. On cut section, the tumour showed grey to yellow gelatinous areas and haemorrhage (Figures 1a and 1b).

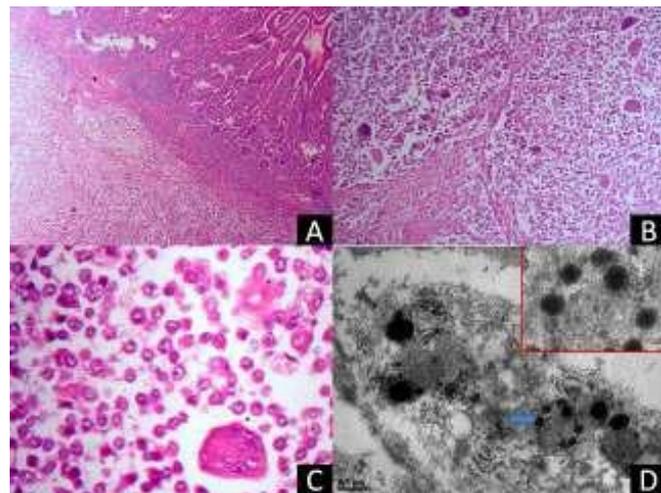
**Figure 1: (a) Gross photograph shows a growth mainly in serosa; (b) Cut surface shows an ulceroproliferative growth with transmural infiltration**



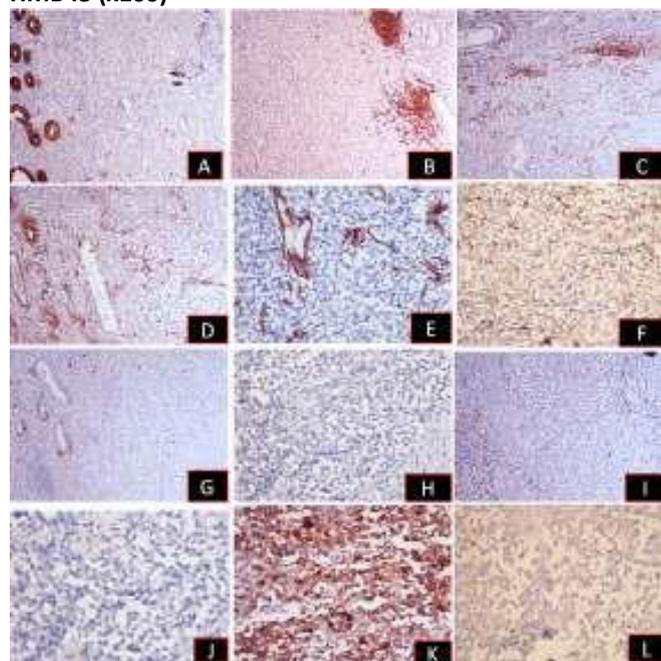
Haematoxylin and eosin (H&E) stained tissue sections from the mass showed a normal jejunal mucosa with tumour in the submucosa. Tumour cells were arranged in lobules/nests separated by fibrovascular septae. Individual tumour cells were round with a moderate amount of cytoplasm, large vesicular nuclei with prominent nucleoli in a few of them. Nuclear pleomorphism with sparse mitotic figures were seen. Numerous osteoclast-like multinucleated giant cells were noted scattered in between the tumour cells (Figures 2a, 2b, and 2c). Immunohistochemically the tumour cells and the giant cells showed diffuse positivity for S-100 (Dako). All other markers such as pan cytokeratin, CD20, CD3, epithelial membrane antigen, smooth muscle actin, CD68,

chromogranin, synaptophysin, CD117, DOG1, and HMB45 were negative (Figure 3).

**Figure 2 (a, b): Microphotograph showing normal jejunal mucosa with tumour in the submucosa; Tumour cells arranged in lobules/nests separated by fibrovascular septae (H&Ex40, x100); (c) Individual tumour cells: Round with moderate amount of cytoplasm and large vesicular nuclei, Prominent nucleoli in a few cells. Numerous multinucleated giant cells (H&Ex200); (d) Scanning electron microscopy showing premelanosomes (arrow)**



**Figure 3: Microphotograph of immunohistochemistry showing positive for S-100 (K) and negative for the rest of the markers. (a) Pan cytokeratin (x100); (b) CD20 (x100); (c) CD3 (x100); (d) epithelial membrane antigen (x100); (e) smooth muscle actin (x100); (f) CD68 (x100); (g) chromogranin (x100); (h) synaptophysin (x100); (i) CD117 (x100); (j) Dog1 (x100); (k) S100 (x100); and (l) HMB45 (x100)**





## Discussion

Mesenchymal tumours comprise a very significant proportion of small intestinal malignancies, accounting for 14 per cent of all cases, the majority of which are GISTs and leiomyosarcomas.<sup>5</sup> Ekfors et al., in 1993, were the first to report the occurrence of MMSP in the duodenum.<sup>3</sup> The rarity of this tumour can be judged by the fact that since then only 30 cases have been reported, of which Zambrano et al. described the largest series comprising six cases.<sup>6</sup>

The exact histogenesis of the tumour is not known. On the basis of morphology, Enzinger first termed it as clear cell sarcoma of the tendon sheath and aponeuroses.<sup>1</sup> Later on, due to the ultra-structural demonstration of premelanosome in these cells by Hoffman et al., Enzinger renamed the tumour as malignant melanoma of soft parts (MMSP).<sup>1,7</sup> They argued that the tumour cells also resembled melanoma or a nevus cell. The tumour is most commonly seen in the upper and lower extremities, with a few cases reported in the face. Gastrointestinal occurrences are very rare. The ileum is the most common site; other reported sites include the stomach, colon, and duodenum.<sup>8,9</sup>

In contrast to tumours in the soft parts, tumours in the gastrointestinal tract show both morphological and cytogenetic variations. Although the first morphological variation of the presence of numerous giant cells was noted by Alper and Beckwith, the entity osteoclast-rich giant cell tumour was first described later by Zambrano et al. in 2003.<sup>6</sup> The most common cytogenetic abnormality is t (12; 22) (q13; q12) translocation, which causes the fusion of EWSR1–ATF1 genes. Four types of fusion transcripts have been identified, of which fusions between exon 8 of EWSR1 and exon 4 of ATF1 is the most common. Another variant of fusion of EWSR1–CREB secondary to translocation t (2:22) was demonstrated by Antonescu et al.<sup>11,12</sup>

Recently, the MMSP of the gastrointestinal tract has been divided into four categories:<sup>13</sup>

- 1) Small bowel tumours that are identical to MMSP in all morphological and immunohistochemical aspects (S–100, HMB45, and or all other melanocytic marker), t (11:22) translocation resulting EWS–ATF1 fusion gene.
- 2) Tumours identical to the above but which lack the melanocytic marker.
- 3) Tumours similar to those in category 2 that feature a scattering of osteoclast-like multinucleated giant cells.
- 4) Tumours resembling cutaneous melanomas but with a genetic signature of MMSP.

Our case belongs to category 3. However, later Kosemehmetoglu et al. morphologically classified MMSP into

two groups: gastrointestinal stromal tumours (CCSLGT), which contain the osteoclast-like cell, and soft tissue type CCS without giant cells.<sup>14</sup>

Although the tumours most commonly occur in the third to fifth decade of life, a single case in a child (10 years old) has also been reported.<sup>9,15</sup> Its erstwhile name—“clear cell sarcoma”—is due to the typical histological findings of large cells with clear cytoplasm and prominent nucleoli. The tumour shows an organoid and trabecular pattern of arrangement. Unlike soft tissue CCS, the tumours of gastrointestinal tract shows brisk mitosis and necrosis.

Histologically, the closest differential diagnosis is malignant giant cell tumours, leiomyosarcoma, GIST containing osteoclast-like multinucleated giant cells, and, less commonly, malignant peripheral nerve sheath tumours and PEComas. S–100 positivity, the absence of all other immunohistochemical markers, and the presence of giant cells aid in the diagnosis. No marker can differentiate MMSP from malignant melanoma; the confirmation of diagnosis can only be done by cytogenetic studies.

The intestinal MMSPs show a more aggressive course than their soft tissue counterparts. Most of the cases had lymph node metastases, as was seen in our case. The most common site of metastasis in intestinal MMSPs was the liver, in contrast with soft tissue MMSP, which showed a predilection for lung metastasis.<sup>14</sup> The difference is probably due to vascular drainage. The literature shows that liver metastasis occurred in most of the cases in the later course of the disease. The exact prognostic factor is not known due to the limited number of cases. A tumour size > 5 cm, and necrosis irrespective of tumour size are thought to be poor prognostic factors.<sup>15</sup> As reviewed by Kosemehmetoglu et al., all 12 patients with osteoclast-rich tumours died due to visceral metastasis in less than 36 months; in comparison, the clear cell sarcoma of soft parts had better prognosis of five-year survival of 54 per cent.<sup>14,16</sup> Complete excision of these tumours is the mainstay treatment, along with radiotherapy. The role of chemotherapy is not known.

## Conclusion

Our case is being presented due to its rarity and histomorphological differentiation, which must be recognised to differentiate it from GIST and poorly differentiated carcinomas. Due to high risk of recurrence and distal metastasis, a close follow-up and ongoing screening of the patient is necessary



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## PEER REVIEW

Not commissioned. Externally peer reviewed.

## CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

## PATIENT CONSENT

The authors Mallick S, Singh L, Ranjan K, Sharma MC, Bansl VK, Dinda AK, declare that:

1. They have obtained written, informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees.