Clear cell sarcoma-like tumour of the ileum

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Abstract

Clear cell sarcoma-like tumour (CCSLT) of the gastrointestinal tract are rare malignant tumours and derive their name from their morphological resemblance to clear cell sarcoma (CSS) of soft tissue. We report a case of an 83-year old lady with a CCSLT in the ileum. Microscopically, the tumour was composed of uniform spindle to epithelioid cells, organized in nests. In addition, scattered intervening osteoclast-like giant cells were also noted. Melanin pigment deposition was not a feature. The tumour cells were positive for S100, SOX-10, CD56 and synaptophysin (focal) and negative for HMB45, Melan-A, MiTF, epithelial markers, desmin, caldesmon, smooth muscle actin (SMA), CD117, DOG1, CD34 and chromogranin. Fluorescence *in situ* hybridization (FISH) for *EWSR1* displayed a split signal indicating a chromosomal translocation. This was further confirmed by RT-PCR analysis which demonstrated *EWS/CREB1* translocation: t(2;22). The overall features confirmed a diagnosis of CCSLT of the gastrointestinal tract.

Recognition of these tumours is important, particularly given the morphological resemblance to conventional CCS. As such, CCSLT should be suspected in spindled to epithelioid intramural tumours of the gastrointestinal tract with S100 positivity and showing no other specific melanocytic differentiation.

Keywords clear cell sarcoma; clear cell sarcoma-like tumours; *EWS/CREB1* translocation

Introduction

Clear cell sarcoma-like tumours (CCSLT) of the gastrointestinal tract are extremely rare malignant tumours, first described in 2003 by Zambrano et al.,[1] with less than 50 cases having been previously described.[2] CCSLTs share a morphological overlap with a spectrum of tumours, chiefly clear cell sarcoma of soft tissue (CCS) with which it also shares a common genetic alteration.[1–6] Here we present a case of CCSLT arising in the ileum, describing the pathological features, discussing the differential diagnosis and precise nomenclature of these lesions.

Case report

An 83-year old lady initially presented with obstructive symptoms including lower abdominal pain and vomiting. Her symptoms settled after the administration of antibiotics and she was subsequently discharged. She re-presented, an abdominal mass was palpated on this admission and a computed tomography scan (CT) scan was performed, which revealed mass in the region of the ileum. On the basis of the above findings surgical excision of the mass was performed. Macroscopic examination of the specimen showed a solid, firm, lobulated mass measuring 6.5 × 4.5 × 2.5 cm.

Microscopic examination showed a multinodular, infiltrative intramural lesion (the bulk of the tumour lies between the submucosa and the muscularis propria) (Figure 1) with focal surface mucosal ulceration and extension into serosal fat. It was composed of relatively monotonous epithelioid and plump spindle shaped cells disposed in sheets with a striking nested pattern (Figure 2). The cells showed characteristic lightly eosinophilic to clear cytoplasm and moderate nuclear pleomorphism (Figure 3). The nuclear chromatin was dispersed small but clearly discernible nucleoli were noted as were occasional pseudo-inclusions and nuclear vacuolization. The mitotic count in the briskest areas was 8 per 10 high power fields. Only punctate foci of coagulative necrosis were evident. Near the surface, associated with areas of mucosal ulceration, were foreign body giant cells. However, interspersed among the tumour cells were very occasional osteoclast-like giant cells. (Figure 4) together with a light scattering of lymphocytes and plasma cells. Focally, areas of cystic degeneration were noted but pseudo-alveolar, pseudo-papillary or rosette patterns were not observed. No melanin pigment was seen. One of eight lymph nodes contained metastatic tumour (Figure 5).

Immunohistochemistry: The tumour cells were strongly and diffusely positive for S-100 (Figure 6a), SOX-10 (Figure 6b), CD56 (Figure 6c), vimentin, and focally for synaptophysin (Figure 6d).

Epithelial markers, desmin, caldesmon, smooth muscle actin, CD117, DOG1, CD34, chromogranin, HMB-45, Melan-A, tyrosinase, micro-ophthalmic transcription factor (MiTF) and CD99 were all negative. Fluorescence *in situ* hybridization (FISH) for Ewing's Sarcoma RNA-binding breakpoint 1 (EWSR1) displayed a split signal indicating a chromosomal translocation. RT-PCR analysis demonstrated EWS/CREB1 translocation: t(2;22).

Based on the morphological and immunohistochemical features together with the molecular confirmation of a t(2;22) translocation, a diagnosis of Clear cell sarcoma-like tumor

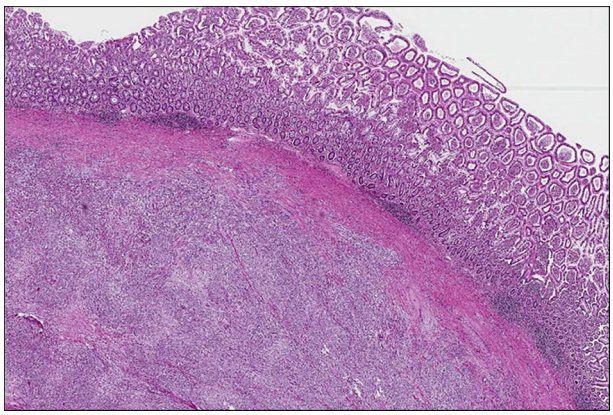

Figure 1 Scanning magnification of the tumour showing an intramural tumour predominantly centred between submucosa and muscularis propria. (H&E ×20).

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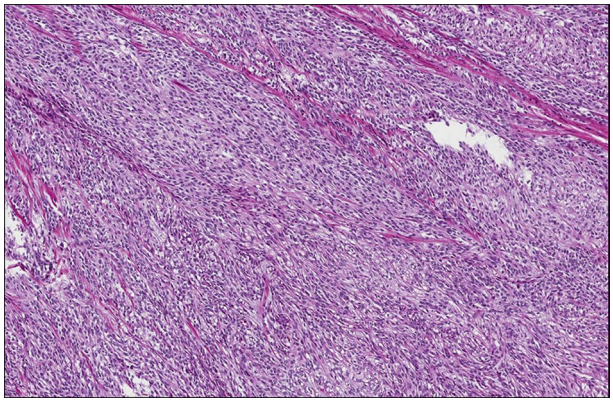

Figure 2 The tumour is composed of uniform epithelial to spindle shaped cells, largely organized in nests. (H&E ×100).

(CCSLT) of the ileum ("malignant Gastrointestinal Neuroectodermal Tumor") was made.

Discussion

CCSLT of the gastrointestinal tract is named for its resemblance to clear cell sarcoma (CCS) ("malignant melanoma of soft parts") of soft tissue (aponeuroses and tendons).[5] Morphologically, the differential diagnosis of CCSLT of the gastrointestinal tract can be

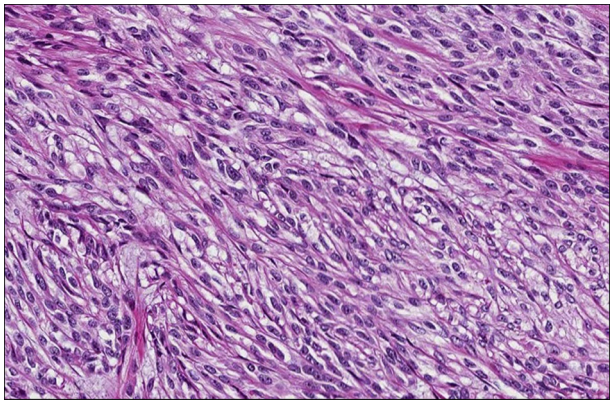

Figure 3 The cells demonstrate the characteristic lightly eosinophilic to clear cytoplasm and moderate nuclear pleomorphism. (H&E ×200).

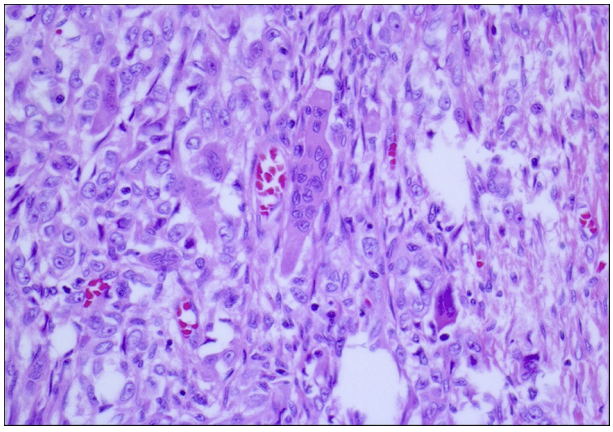

Figure 4 The striking feature in this tumour is the presence of scattered intervening osteoclast-like giant cells (H&E ×400).

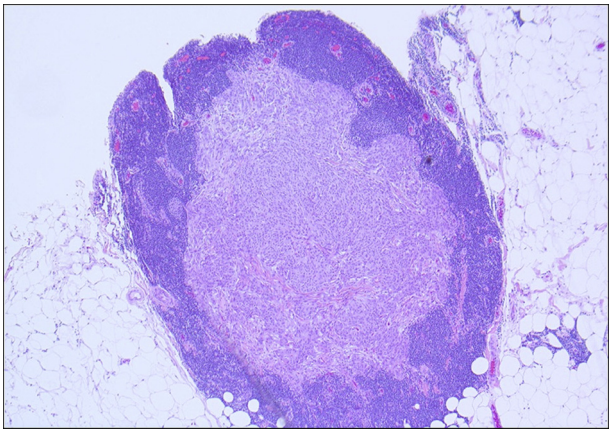

Figure 5 One lymph node shows a metastatic deposit of tumour, a common eventuality in these tumours (H&E ×40).

challenging and includes a broad range of tumours (Table 1),[2,3] principally CCS. While there is great morphologic and indeed, molecular mimicry, CCSLT differs from CCS by lacking full immunophenotypic and ultrastructural evidence of melanocytic differentiation.[1–3] In other words, CCS of soft tissue is positive for HMB-45, Melan-A, MiTF and tyrosinase but CCSLT is negative despite looking the same/very similar morphologically. The basic phenotype of both tumours is the same: epithelioid, plump spindle shaped cells. However, CCS is meant to have "wreath-like" giant cells while CCSLT has osteoclast-like giant cells (not present in all cases though).[1,2,4,7,8] Extensive necrosis and high-mitotic rates are usual in CCSLT.

It is also important to remember that true CCS (identical to its soft tissue counterpart) can also occur in the gastrointestinal tract, albeit extremely rarely.[9–11] CCSLT occurs in the gastrointestinal tract much more commonly that true CCS; both tumours being rare. Parenthetically, CCS of soft tissue differs from malignant melanoma molecularly: the latter shows *BRAF* mutations and not the CCS translocations (see later).

CCSLT tends to occur in young patients of either gender (mean age: 35 years), although a wide age range has been encountered (10–81 years).[2] It has a predilection for the small bowel (ileum and jejunum) but cases in the stomach and colon have also been described.[2] Like most intestinal tumours, intestinal obstruction, abdominal mass and pain are the commonest presenting symptoms. Clinical the tumour pursues an aggressive course and most of the reported cases (including this case) have metastases to lymph nodes and/or liver at the time of presentation. Median survival is of the magnitude of 18.5 months and surgery is the mainstay of treatment.[2]

In addition, to the morphologic overlap CCSLT and CCS of soft tissue share similar molecular arrangements. *EWSRI-ATF1* t(12;22) and *EWSR1-CREB1* t(2;22) translocations occur in CCSLT and CCS.[2–6] These molecular alterations are not seen in melanoma, which is characterized by *BRAF* mutations. Similarly, BRAF mutations are not detected in CCSLT and CCS. It is thought that *EWSR1-CREB1* translocation is commoner in CCSLT and *EWSRI-ATF1* in CCS, but a recent publication has shown that the majority of CCSLT of the GIT harboured *EWSRI-ATF1* translocations. A subset of CCSLT cases harbour yet to be identified fusion partners with *EWSR1*.[3]

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