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# Gastrointestinal clear cell sarcoma-like tumour of the ascending colon

**A Gahanbani Ardakani, DJ Boyle, C Elton**

Royal Free London NHS Foundation Trust, UK

**ABSTRACT**

INTRODUCTION A clear cell sarcoma-like gastrointestinal tumour (CCSLGT) is a rare malignant soft tissue sarcoma. In the literature, they are sometimes referred to as malignant gastrointestinal neuroectodermal tumours, clear cell sarcomas or osteoclast rich tumours of the gastrointestinal tract.

CASE HISTORY We present a case of a CCSLGT arising from the ascending colon of a previously well 22-year-old man presenting with abdominal pain and anaemia. Computed tomography of the abdomen and pelvis showed a 7cm irregular mass in the right flank that seemed to emerge from the proximal transverse colon. A laparoscopic right hemicolectomy was undertaken to remove the mass. Microscopic pathological examination of the specimen revealed sections of spindle to oval cells with monomorphic nuclei and scant cytoplasm. The cells were arranged in a striking perivascular growth pattern with microcystic breakdown and pseudopapillary formation. Immunohistochemistry analysis showed that the tumour cells removed expressed S100 protein, and were negative for smooth muscle actin, desmin, CD34, CD117, DOG1, HMB-45 and MNF116. Additionally, cytogenetic testing identified *EWSR1* gene rearrangement, which was observed by interphase fluorescence in situ hybridisation.

CONCLUSIONS A complex tumour, a CCSLGT can be thought of in simple terms as a gastrointestinal tract tumour that is S100 protein positive, osteoclast rich, HMB-45 negative and compromises a t(12;22)(q13;q12) gene translocation. These simplified CCSLGT characteristics seem to be described and classified under different aliases in the literature, which makes it difficult to accurately predict the appropriate diagnostic and therapeutic modality required to provide the best clinical care. Given that this case report describes the fourth CCSLGT of primary colonic origins, it may aid future targeted therapies as well as offering epidemiological evidence on prevalence and prognosis.

**KEYWORDS**

Clear cell sarcoma – Colon – Malignant gastrointestinal neuroectodermal tumour – Gastrointestinal stromal tumour – S100 – Clear cell sarcoma-like tumour of the gastrointestinal tract – Osteoclast rich – *EWSR1*

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**CORRESPONDENCE TO**

**Amir Gahanbani Ardakani**, E: amir.ardakani@nhs.net

A clear cell sarcoma-like gastrointestinal tumour (CCSLGT) is a rare malignant neoplasm that arises in the wall of the stomach, or the small or large bowel, and primarily affects children and young adults.[1–4] They are highly aggressive tumours that commonly reoccur with widespread metastatic nodal and visceral disease, even after treatment.[1] These tumours were originally thought to be related to clear cell sarcomas (CCSs) of tendons and aponeurosis. However, it has now been recognised that they have distinctive microscopic, histological, genetic and immunophenotypic components that differentiate them from conventional CCSs.[1,3,5]

To date, the majority of reported cases have involved the stomach and small intestine, with only three previous potential instances of primary colonic CCSLGTs reported in the literature.[3,6] We present a case of a confirmed CCSLGT affecting the ascending colon.

## Case history

A previously well 22-year-old man was referred initially with a 1-year history of worsening abdominal pain that was intermittent in nature, accompanied by weight loss and fatigue. Clinical examination was unremarkable (except for generalised abdominal tenderness) and exclusive of peritonism. Routine blood tests revealed a haemoglobin level of 5.2g/dl, and upper gastrointestinal endoscopy and abdominal ultrasonography were both reported as normal. Computed tomography (CT) of the abdomen and pelvis showed a large 7cm irregular mass in the right flank, which appeared to arise from the proximal transverse colon, accompanied by small volume ascites. A colonoscopy was performed, which confirmed the CT findings and enabled this lesion to be biopsied. There was no evidence of metastatic disease on staging CT of the chest.

A subsequent laparoscopic right hemicolectomy to remove the lesion was undertaken. Macroscopically, the specimen was 200mm of colon and 50mm of terminal ileum with a 75mm polypoidal tumour arising from the ascending colon.

Microscopic pathological examination of the specimen showed sections of spindle to oval cells with monomorphic nuclei and scant cytoplasm. The cells were arranged in a perivascular growth pattern with microcystic breakdown and pseudopapillary formation. Mitotic activity was deemed brisk (>20 per 10 high power fields in areas) and regions of necrosis were also observed. The tumour was transmural, extending from the submucosa to the subserosal layer. One of the lymph nodes adjacent to the tumour had been almost totally replaced by tumour. The remaining 46 lymph nodes showed marked sinusoidal dilation. Immunohistochemistry analysis indicated that the tumour cells expressed S100 protein, and were negative for smooth muscle actin, desmin, CD34, CD117, DOG1, HMB-45 and MNF116. Cytogenetic testing identified *EWSR1* gene rearrangement, which was observed by interphase fluorescence in situ hybridisation. The above findings were consistent with an ascending colon CCSLGT.

The patient left in good condition after approximately three weeks in hospital. A referral was made to a regional sarcoma centre multidisciplinary team that concluded there was no indication for adjuvant treatment at present. Instead, a programme of regular active surveillance with CT was agreed.

## Discussion

Since Zambrano *et al* proposed the idea of CCSLGTs being acknowledged as a new, previously unrecognised entity in 2003, approximately 40 case reports of tumours reminiscent of CCSs arising from the gastrointestinal system have been described.[4,6] However, only 16 of these reports describe neoplasms that correlated with the accepted morphological, structural and immunohistochemical features of a 'true' CCSLGT. A CCSLGT has features very similar to those of a CCS but with no specific evidence of melanocytic differentiation. It is widely accepted that CCSLGTs express the S100 protein and the SOX10 protein, and they can be characterised genetically by *EWSR1* gene rearrangements. These tumours tend to lack the melanocyte specific markers including HMB-45, melan A, tyrosinase and microphthalmia associated transcription factor.[6]

In the more recent literature, there is evidence that these tumours may arise from primitive cells of the neural crest, with features of neural differentiation, and there may be scope to appropriately rename these tumours malignant gastrointestinal neuroectodermal tumours (GNETs). On the other hand, the true aetiology of CCSLGTs remains unknown and this makes it difficult to reach a consensus with regard to management.[1]

Macroscopically, these tumours can range in size from 1.8cm to 15cm and often show transmural involvement of the bowel wall. They typically extend into the serosa and are accompanied occasionally by mucosal ulceration.[5,7] Microscopically, unlike CCSs, CCSLGTs lack well formed nests of eosinophilic cytoplasm; instead, they consist of small or inapparent nucleoli arranged in sheets and papillary or alveolar architectures. CCSLGTs consist of relatively monomorphic ovoid or epithelioid cells and have variable numbers of CD68 positive osteoclast-like giant cells.[1–4] Mitotic activity in these tumours is characteristically brisk, accompanied by typical areas of focal necrosis.[1,6,8]

Tumours of this nature tend to present in young to middle aged patients with a median age of approximately 40 years although cases with patients aged 17–77 years have been reported.[5,6] There seems to be an equal distribution among the sexes with presenting symptoms similar to those of any other gastrointestinal tumours: bowel obstruction, abdominal pain, abdominal mass, diarrhoea, fever, anaemia or gastrointestinal bleeding.[5,6,9,10] CCSLGTs are mostly aggressive and overall, they have a poor prognosis. They tend to metastasise to the liver as well as to regional lymph nodes.[11] The most common site for CCSLGTs is the small intestine, with the stomach and the colon more rarely affected.[6]

## Conclusions

A complex tumour, a CCSLGT can be thought of in simple terms as a gastrointestinal tract tumour that is S100 protein positive, osteoclast rich, HMB-45 negative and compromises a t(12;22)(q13;q12) gene translocation.[7,12] Of the 40 potential cases described so far, this is the fourth with a CCSLGT of primary colonic origin. Our case suitably highlights the importance of using histological, immunohistochemical and molecular methods to make the diagnosis of CCSLGT.

Authors seem to report these tumours under different aliases including CCS, GNET and CCSLGT. These different titles may be essentially describing the same tumour body arising from the gastrointestinal tract, with matching microscopic, histological, genetic and immunophenotypic components. It may be possible to establish a new tumour entity, titled appropriately, by collating and systematically reviewing cases similar to the one described here. This may prove beneficial when providing overall clinical care to our patients as well as providing epidemiological information on prevalence and prognosis.

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