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Case Report

Gastrointestinal clear cell sarcoma-like tumour [CCSLGT] in an elderly patient – A rare case report

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ABSTRACT

Clear Cell Sarcoma Like tumor of Gastrointestinal Tract (CCSLGT) is a rare malignant neoplasm described in stomach, small intestine, and large intestine, with a high predilection for small intestine. It has its own unique histology, immune-phenotype, clinical behavior, and molecular characteristics which distinguishes it from other sarcomas/carcinomas in gastrointestinal system. Due to its rarity, only limited studies have been performed in the literature. Moreover, its histogenesis is uncertain till now. A rare case of CCSLGT which occurred in ileum of an elderly woman has been presented here with a short review of its histogenesis.

1. Introduction

Clear Cell Sarcoma Like tumor of Gastrointestinal Tract (CCSLGT) is a rare malignant neoplasm described in stomach, small intestine, and large intestine, with a high predilection for small intestine.[1] Most of the tumors present with abdominal pain or bowel obstruction. The entity CCSLGT is evolving recently with unique histology, immune-phenotype, and clinical behavior, although it shares common cytogenetic features with Clear cell sarcoma of extremities.[1] Recently an alternate designation of GNET (Malignant Gastrointestinal Neuro-Ectodermal tumor) has been proposed for CCSLGT. We present a case of CCSGLT in an elderly female patient, with a note on its histogenesis.

2. Case History

A 65-year-old woman presented to the emergency clinic with history of loose stools, vomiting and abdominal pain for 15 days. Upper GI Endoscopy and Colonoscopy were unremarkable. CT Abdomen revealed a circumferential growth in ileum, which was resected through exploratory Laparotomy. Gross specimen measured 20 cm length of small intestine, with external surface showing mild congestion and a constriction at one focus. On cut section, the constricted focus showed an elevated circumscribed solid firm grey-white growth, measuring 3.5X2.0 cm, noted in the lumen. The adjacent mucosa showed normal appearance. On microscopic examination, an infiltrative neoplasm was noted predominantly in the submucosa and muscularis propria while superficial mucosa showed features of ulceration. Tumor cells were uniform, round to ovoid, arranged in alveolar, pseudo-papillary and nested pattern; with individual cells exhibiting pleomorphic nuclei, small to indistinct nucleoli and pale eosinophilic to clear cytoplasm. Also, noted are scattered osteoclast-like giant cells in sections. Eight lymph nodes were resected out of which five showed tumor deposits. An Immuno-histochemical study was performed with a panel of markers comprising Cytokeratin, Epithelial Membrane antigen (EMA), S-100, CD 117, Melan A, HMB 45, Synaptophysin, Chromogranin, Desmin, Smooth Muscle

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Actin(SMA), Myogenin, Myo D1, CD 56 & CD 57, LCA and Ki-67 antigen. The tumor areas were strongly and diffusely positive for S-100, CD 57 and moderately positive for CD 56, EMA showing positivity in few cells and Ki-67 index of 35%, while all the other markers were negative.

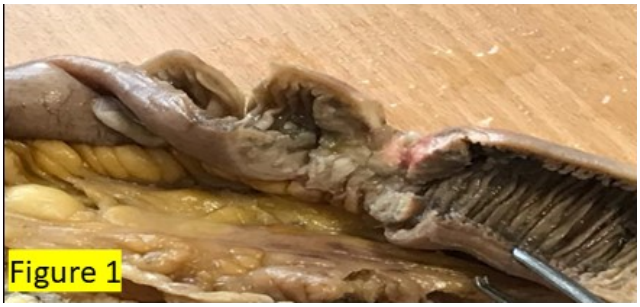

Fig. 1: Gross image of small intestine showing an ulcerative growth in its lumen

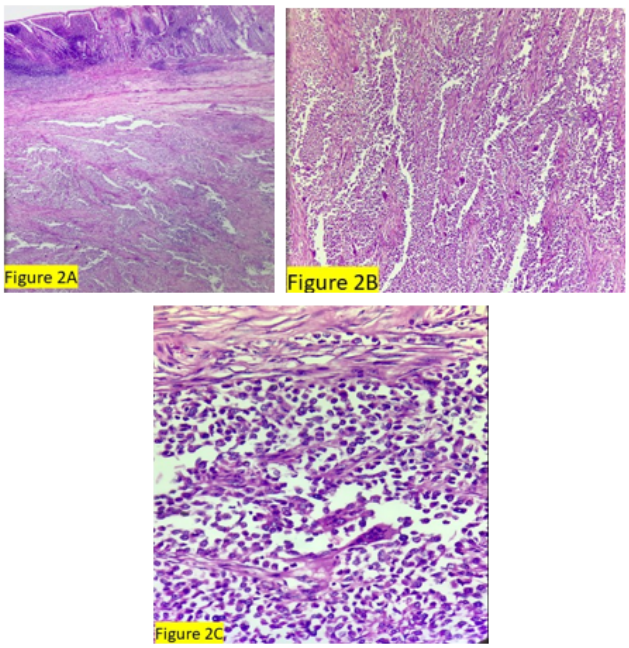

Fig. 2: A: Gross image of small intestine showing an ulcerative growth in its lumen; **B:** Microphotograph showing an infiltrating tumour in submucosa of ileum with occasional osteoclast type giant cells. [H&E,10X]; **C:** Microphotograph showing an infiltrating tumour composed of clear cells in alveolar pattern admixed with occasional osteoclast type giant cells. [H&E, 40X]

3. Discussion

CCSLGT is a rare malignant neoplasm with aggressive features usually noted in small intestine. Few case studies have reported CCSLGT in age range from 17 to 77 years; with a mean age group of approximately 40 years.[2]

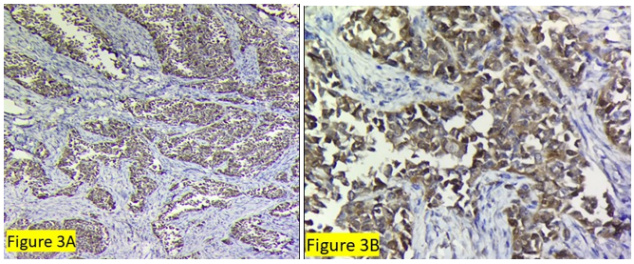

Fig. 3: A: Microphotograph showing an infiltrating tumour composed of clear cells stained with S-100 immunostain [IHC, 10X]; **B:** Microphotograph showing an infiltrating tumour composed of clear cells stained with S-100 immunostain [IHC, 40X]

Clinically CCSLGT can be mistaken for carcinomas as they do present with lymph node metastasis. The tumor cells which are arranged in pseudo-papillary, sheet, alveolar and nested patterns show strong positivity for S100 while multinucleated osteoclast-like giant cells observed in these tumors express strong positivity for CD 68.

Giants in the discipline of Pathology have wondered about the histogenesis of this very rare tumor for decades. Dr Enzinger, in 1965 identified few tumors which happened to occur in young adult women in foot and knee, bearing close approximation to tendons and aponeuroses.[3] These tumors showed nests or aggregates of round to spindle pale staining cells with prominent nucleoli and tendency for metastases and recurrence. Some of the tumour cells stained positive for Fontana reaction, albeit the morphology was not favoring a melanin producing tumour. He proposed a new term called CCSTA [Clear cell sarcoma of Tendons and Aponeuroses], but with uncertain histogenesis.

Later in 1983, Dr Enzinger and Dr Chung reinterpreted the same set of tumors as melanoma of soft parts, as the cells were staining positive to S-100, in addition to Fontana stain. They also documented the ultrastructural positivity of premelanosomes and thought these cells originated from neural crest cells. They said these tumours were akin to Melanoma, albeit not a true malignant melanoma.[3]

Sandberg et al, identified e t(12;22)(q13;q12) chromosomal translocation, leading to the formation of the EWS-ATF1 fusion transcript in CCSTA.[4] This gave an insight for a sarcoma type transcript rather than a melanomatous type. This was followed by a report by Zambrano et al, where they found 6 cases of Clear cell sarcoma like tumours in Gastrointestinal tract, one of the tumours showing molecular transcript like CCSTA.[5] Friedricks et al, also noted a similar case in small bowel with clear cells in alveolar pattern, admixed with few osteoclast-like giant cells, exhibiting t(12;22)(q13;q12) translocation, and proposed a new terminology for the same as Gastrointestinal clear cell sarcoma with osteoclast-like giant cells.[6]

Recent literatures state although CCSLGT is similar to Clear cell sarcoma of soft parts, they do not express melanocyte markers such as HMB 45 and Melan A not BRAF mutations. Molecular analysis reveals 50% of the tumors exhibit t(2:22)(q33;q12) translocation resulting in EWSR1-CREB1 or rest of the tumors exhibit t(12:22)(q13;12) involving EWSR1-ATF1.[7–10]

Differential diagnosis of Alveolar RMS, Epithelioid GIST and Carcinoma of small bowel can be sorted out with negative staining for MyoD1, CD 117 and cytokeratin respectively. Study by Stockman et al state that the cell of origin of CCSLGT as neural crest cells in Gastrointestinal tract, paving the way for consideration of the novel nomenclature of these neoplasms as Gastrointestinal Neuro-Ectodermal Tumors (GNETs).[2]

4. Conclusion

CCSLGT is a rare tumour of small intestine which may simulate a carcinoma, but microscopy reveals a sarcomatous nature. Immunohistochemical and molecular analyses are required for confirmation. CCSLGT should be considered as a differential in evaluating a tumour showing clear cells admixed with osteoclast-like giant cells.

5. Source of Funding

None.

6. Conflict of Interest

None.

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