Primary CIC-rearranged Gastric sarcoma: A rare diagnosis.

Saroj Dhungana[1], Binay Thakur[1], Nikesh Bhandari[1], Shashank Shrestha[1], Ashish Kharel[1], Deewash Neupane[1]

[1]Department of Surgical Oncology; BP Koirala Memorial Cancer Hospital, Bharatpur, Nepal

Abstract

Gastric sarcoma is rare, accounting for 1-3% of all gastric neoplasms. WHO has published a new classification of soft tissue tumors and a group of undifferentiated round cell sarcomas, including CIC-rearranged sarcoma has been added. CIC-rearranged sarcoma has not been reported till date. We report a case of CIC-rearranged gastric sarcoma which was managed with chemotherapy and multivisceral resection.

Keywords: sarcoma, round cell sarcoma, CIS, gastrectomy

Introduction

Gastric sarcomas are one of the uncommon Ggastrointestinal (GI) malignancies. Because of its rare occurrences, atypical and delayed presentation, these tumors are still a diagnostic challenge. Sarcomas consist of large subsets of tumors. One among them being undifferentiated round cell tumor which includes CIC - rearranged sarcoma.[1] CIC rearranged sarcomas are one of the rarest sarcomas to occur. To date less than 200 cases are reported and none involving the stomach.[2] We report a case of CIC - rearranged sarcoma of the stomach.

Case Report

Forty-five years female presented with the complaints of progressive abdominal pain pronounced at left upper quadrant with mobile lump along with dark colored stool since one month one year back in another hospital. Gastroscopy suggested antral mass and histopathological examination (HPE) with immunohistochemistry (IHC) revealed gastric sarcoma. Computed tomography (CT) showed gastric mass with transverse colonic and adjacent small bowel infiltration. She received two cycles of chemotherapy (cyclophosphamide, vincristine and doxorubicin). She was referred to our center for further management.

Re-evaluation showed, 15 X 15 cm extending from epigastric region to infraumbilical

Correspondence
Dr. Saroj Dhungana
Department of Surgical Oncology (Thoracic unit), BP Koirala Memorial Cancer Hospital, Bharatpur, Nepal.
Email: sarose.dhungana@gmail.com. Phone: +977-9856014120

region with static disease on CT and gastroscopy (Fig. 1).

Exploratory laparotomy with distal subtotal distal gastrectomy with resection of transverse colon and jejunum was done 9 months back. Intraoperative findings showed 15*15*10cm mass arising from posterior wall of distal stomach invading transverse mesocolon and jejunum along with few peri gastric lymphadenopathies with no ascites, liver and peritoneal metastases. HPE and IHC revealed undifferentiated spindle cell sarcoma of stomach, ypT4aN1M0 with tumor free margins.

Fig. 1. After 2 cycles of chemotherapy.

Afterwards, she received 6 cycles of Epirubicin+Ifosfamide based chemotherapy. After completion of chemotherapy, she was re-evaluated. Gastroscopy and CT (Fig. 2) suggested anastomotic recurrence.

The Laparotomy was performed 2 months ago. There was solid mass of 6 x 4 cm over previous gastrojejunostomy with invasion of pancreatic body, tail and splenic flexure of colon. Intraoperatively, 2x2 cm few solid – cystic masses at the mesocolon. Multi-visceral resection (resection of gastrojejunostomy, segmental colonic resection and spleen preserving distal pancreatectomy) was performed (Fig. 3).

Fig. 2. Recurrent disease.

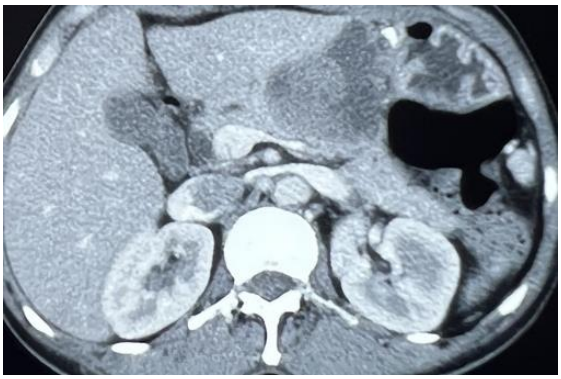
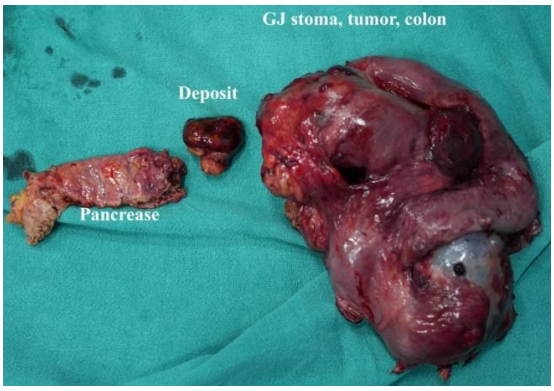


Fig. 3. Multivisceral resection



Discussion

The first gastric sarcoma was reported by Bruck, in 1847, and the first operation was performed by Virchow, in 1887. Gastric sarcomas constitute 1 to 3% of all gastric neoplasms.[3] Histologically, the gastric sarcomas can be classified as fibro-, myo-, lympho-, and myxosarcoma. Fibrosarcoma originates in the submucosa; myosarcoma in the muscularis; lymphosarcoma in the lymph nodes of the submucosa; however subserous origin of these sarcomas is less known.[4]

Though previously classified under Ewing like sarcoma, the 2020 WHO classification of soft tissue tumors puts CIC-rearranged sarcomas under broad group of

undifferentiated sarcoma, and it belongs to the subgroup of undifferentiated round cell sarcoma of bone and soft tissues along with Ewing sarcoma, Round cell sarcoma with EWSR–non-ETS fusions and sarcoma with BCOR genetic alterations.[1] CIC sarcoma represents a rare disease, accounting for less than 1% of all sarcomas.

To date, there have been fewer than 200 documented cases. Out of these, 88 cases have sufficient clinical and pathological data. The ages ranged from 8 to 69 years, with an average of 30.7 years and a median of 29.5 years. In terms of gender distribution, there were 41 males (46.6%) and 47 females (53.4%). The most prevalent primary locations were the soft tissues of the limbs (48.9% out of 88 cases), followed by the soft tissues of the trunk (39.8% out of 88 cases) and parenchymal organs (7.9% out of 88 cases).[2]

They have primitive small round-cell morphology and rearrangement of the CIC gene, which is located on chromosome 19q13.2 and is commonly fused to the DUX4 gene on chromosome 4q35.2 or 10q26.3.[5,6,7] Although alternative fusion partners such as the FOXO4 gene have recently been identified in some tumors the partner genes in some CIC-rearranged undifferentiated round-cell sarcomas remain unknown.[8]

As mentioned above, literature review shows soft tissue to be the most common location (90%). Cases originating in visceral organs make up around 10% of the total.[9] Extremely uncommon instances have been documented within deep-seated organs like the gastrointestinal tract, kidney, and brain.

Clinical features and imaging features of CIC-rearranged sarcoma of the stomach are similar to any other GI malignancy. In IHC, CD99 and WT1 expression is one of the most important features which help them to differentiate from other sarcomas. Nuclear EST variant transcription factor 4 gene (ETV4) and Wilms tumor suppressor gene (WT1) expression is seen in more than 90% of CIC-rearranged sarcomas.[10]

Surgery remains the only effective treatment of CIC-rearranged sarcoma. Surgical treatment should be aimed at complete removal of the tumor with at least a 2-cm margin. Systematic lymphadenectomy is not indicated. Usual management for localised disease is surgical resection, chemotherapy with Ewing-based regimens, and adjuvant radiation, after which 55% develop metastases at a median time to progression of 10.5 months. In advanced disease, durable systemic therapy responses occur infrequently with a median duration of systemic treatment response of 2.1 months. Radiotherapy to the primary site is used frequently in localised and advanced disease.[11]

Patients with CIC-rearranged tumors follow an aggressive clinical course with a high metastatic rate, mainly to the lung. The 5-year OS is 43% in all affected patients and 49% for the patients who presented with localized disease at diagnosis.[12] It has a median OS of 16.3 months.[11]

In a thorough search of literature, we could not find a single reported case of CIC-rearranged gastric sarcoma. In our case, IHC was done thrice, and a conclusive result was achieved only after the second surgery. It emphasizes the diagnostic difficulties. Our

case highlights certain peculiarities of CIC-rearranged gastric sarcoma: ineffectiveness of chemotherapy and pattern of recurrence, which is local. Till other reports become available, radical surgery seems to be the only curative method of treatment.

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