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GASTRIC GERM CELL TUMORS IN CHILDREN: RARE TUMOR WITH DIVERSE CLINICAL PRESENTATIONS

Surgery

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ABSTRACT

To retrospectively review the cases of gastric germ cell tumors (GCT), treated at our centre in the last 4 years (2014-2018)

Methods All cases of gastric GCT diagnosed and treated at our institute in the last 4 years were retrospectively reviewed. The demographic profiles of the patients, clinic-pathological features and follow-up data were recorded.

Results Four cases of gastric GCT were diagnosed and treated at our institute in the past 4 years. All our cases were boys. Their ages ranged from 4 days to 8 years. Out of the 4 cases, 3 were teratoma (2 mature, 1 immature) and 1 was yolk sac tumor (YST). On follow-up, all patients were asymptomatic with no evidence of recurrence. All cases differed in their age at presentation and clinical symptoms.

Case 1 A 4 day old new-born presented with massive abdominal distension, respiratory distress and poor feeding. Surgical exploration revealed a huge lump arising from the greater curvature of the stomach and was completely excised. Histopathology confirmed the diagnosis of immature teratoma.

Case 2 One year old male presented to the emergency with history of malaena and hematemesis of 2 weeks duration. Upper gastrointestinal (GI) endoscopy with computed tomography (CT) of the abdomen showed an ulcerated, bilobed mass across the greater curvature of the stomach having an intra-gastric and an extra-gastric component. Complete surgical excision with repair of the stomach was performed. Histopathology confirmed mature teratoma.

Case 3 An eight year old boy presented with history of pain in left upper abdomen of 2 months duration. CT abdomen revealed a large heterogeneous mass with fluid, soft tissue, bone and fat attenuation mixed with chunky calcifications, in relation to the greater curvature of stomach. Surgical excision revealed mature teratoma.

Case 4 A 3 year old boy presented with recurrent episodes of malaena and anaemia of 2 months duration. Upper GI endoscopy revealed deep excavated ulcer on the lesser curvature of stomach. CT abdomen revealed large heterogeneously enhancing soft tissue mass lesion on the lessercurvature of stomach with multiple liver and omental metastasis. Serum alpha-fetoprotein (AFP) was 21000 ng/ml. Trucut biopsy from the mass was suggestive of YST. Following 3 courses of chemotherapy, sleeve gastrectomy with excision of the mass with omentectomy with biopsy of the liver nodules was done. Histopathology revealed only necrotic tissue with no evidence of residual malignancy.

Conclusion Gastric GCT is an exceptionally rare embryonic neoplasm, which can have diverse clinical presentation depending on the age and site of involvement. With recent advances in imaging, an accurate pre-operative diagnosis is possible. Gastric GCT have an excellent prognosis if treated promptly and complete surgical excision is usually curative.

KEYWORDS

Gastric germ cell tumors; teratoma; mature; immature; yolk sac tumor

INTRODUCTION

Gastric germ cell tumors (GCT) are very rare. Primary gastric teratomas constitute less than 1% of all teratomas in children [1]. A literature search revealed only around 115 reported cases of gastric teratoma in children [2]. Because of the rarity of gastric teratoma, there are relatively few studies examining optimal management and long-term outcome of these tumors [2-4]. In fact, the literature discussing the management of gastric teratomas consists mainly of case reports. Gastric yolk sac tumors (YST) are even rarer. Only seven cases of pure YST of the stomach, with a median age of 65 years, and five cases of YST combined with adenocarcinoma have been reported [5]. Herein, we report our experience with treating primary gastric GCT at our institution and review the existing literature. All 4 cases of gastric GCT described herein differed from each other in terms of age at presentation and clinical symptoms.

METHODS

A retrospective review of the medical records and pathology reports of all patients with primary gastric GCT treated at our institute from 2014 to 2018 were reviewed. Patients were included if they had a germ cell tumor involving the stomach. Tumors secondarily involving the stomach are not included in this series. Pathologic specimens were reviewed in all cases. The data collected included the age at presentation, sex, chief complaints, diagnostic investigations, clinical management, operative findings, histologic diagnosis, complications, and long-term outcome.

RESULTS

Four cases of gastric GCT were diagnosed and treated at our institute in the past 4 years. All our cases were boys. Their ages ranged from 4 days to 8 years. Out of the 4 cases, 3 were teratoma (2 mature, 1 immature) and 1 was yolk sac tumor (YST). On follow-up, all patients were asymptomatic with no evidence of recurrence. All cases differed in their age at presentation and clinical symptoms.

TABLE 1: Summary of clinico-pathological features of gastric germ cell tumors (AFP: alpha-fetoprotein)

Case No.	Age, Sex	Clinical presentation	Serum AFP level (ng/ml)	Tumor location	Surgery	Histopathology	Follow-up
1.	10 days, male	Abdominal distension, Poor feeding, Palpable lump	11050	Posterior wall of stomach, extending into retroperitoneum	Excision of mass and repair of stomach	Immature teratoma	24 months, asymptomatic

2.	1 year, male	Upper GI bleed, Anaemia, Palpable lump	9.7	Greater curvature of the stomach, extending to the fundus	Excision of mass and repair of stomach	Mature teratoma	36 months, asymptomatic
3.	8 years, male	Pain abdomen, Palpable lump	0.87	Fundus	Excision of mass and repair of stomach	Mature teratoma	30 months, asymptomatic
4.	3 years, male	Upper GI bleed, Anaemia, Palpable lump	21000	Lesser curvature of stomach, liver and omental nodules	Excision of mass and repair of stomach, omentectomy, biopsy of liver nodules	Yolk sac tumor	18 months, asymptomatic, no recurrence

Case 1

A 10 day old new-born male presented to the emergency with massive abdominal distension, respiratory distress and poor feeding. The baby was born at term by caesarean section following prolonged labour. The antenatal period was uneventful and an antenatal ultrasound scan in 3rd trimester was reported as normal. On examination, the baby was sick looking with mild dehydration. Respiration was laboured with reduced air entry in bilateral basal lung fields. Abdominal examination revealed a large, hard, fixed, lobulated mass with variegated consistency occupying the entire abdomen. The overlying skin was stretched and shiny with distended veins (Fig. 1a).

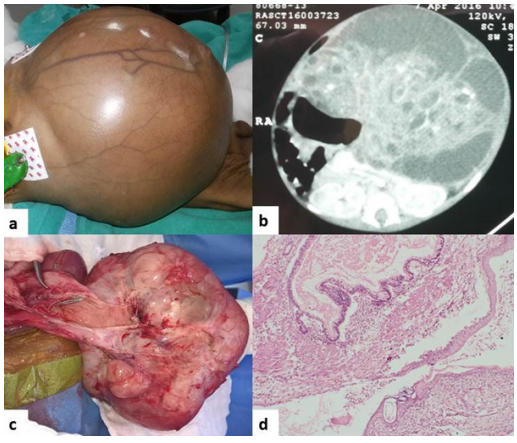

Fig. 1a: Hard, fixed, lobulated mass occupying the entire abdomen with visible veins, **1b:** CT abdomen showing a well-defined, heterogeneously enhancing lesion in the retroperitoneum with displacement of abdominal viscera to the right, **1c:** Intra-operative photograph showing large mass arising from posterior wall of stomach, **1d:** Photo micrograph showing tumor with heterologous elements of all three germ layers including pilosebaceous units and hair follicles, mature squamous epithelium, gastrointestinal epithelium and glands with areas of immature neuro-epithelial elements

Computed tomography (CT) of abdomen showed a large, well defined, heterogeneously enhancing lesion in the retroperitoneum, 12x15x18 cm in size, with displacement of bowel loops, pancreas, stomach and vessels to the right side (Fig. 1b). The lesion showed dense calcification and areas of cystic changes. Serum alpha-fetoprotein (AFP) was normal for age. Based on the clinical presentation and investigations, a provisional diagnosis of retroperitoneal neuroblastoma was made.

Due to the rapidly increasing size of the mass causing respiratory distress and poor feeding, surgical exploration was planned. Laparotomy revealed a 17x15x12 cm hard, fixed, irregular mass occupying the entire abdomen with displacement and compression of abdominal viscera to the right (Fig. 1c). Mass was densely adherent to the parietal wall with neovascularisation. Mass was arising from the posterior wall of the stomach, extending into retroperitoneum. Sleeve of posterior wall of the stomach excised in toto with the tumor and the stomach repaired in two layers. Post-operative period was uneventful.

Microscopic examination of sections from the mass showed a tumor with heterologous elements of all three germ layers including pilosebaceous units and hair follicles, mature squamous epithelium along with large areas of keratin, glial tissue, choroid plexus, mature cartilage, muscles and loose connective stroma comprising of spindle shaped cells, gastrointestinal epithelium and glands. Foci of calcification were also seen. Areas of immature neuroepithelial elements were also present (Fig. 1d). The final diagnosis was an immature teratoma. The patient is asymptomatic with no evidence of recurrence at 24 months follow up.

Case 2

One year old boy presented to the emergency with history of malaena of 2 months duration and hematemesis since 1 week. There was no history of abdominal pain, vomiting, fever or jaundice. The boy was born at term by vaginal delivery with no adverse perinatal events. On examination, the patient was pale and had tachycardia. Abdominal palpation revealed a firm, non-tender mass of size 5 x 4 cm in the epigastrium and left hypochondrium which moved with respiration. Initial haemoglobin level was 6 g/dl. Renal function tests, liver function tests and coagulation profile were normal. CT scan of abdomen revealed a well-defined, heterogenous mass on the greater curvature of stomach having an intra-gastric and an extra-gastric component with calcifications and fat density (Fig. 2a).

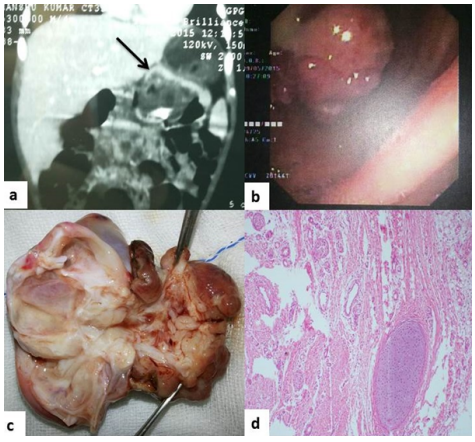

Fig. 2a: CT abdomen showing a well-defined, heterogenous mass (arrow) on the greater curvature of stomach having an intra-gastric and an extra-gastric component with calcifications and fat density, **2b:** Upper GI endoscopy showing a large polypoidal mass on the greater curvature of stomach, **2c:** Cut section of the specimen showing a variegated mass with areas of bone and cartilage, **2d:** Photo micrograph showing tumor composed of areas of cartilage and smooth muscle

Upper gastro-intestinal (GI) endoscopy showed a large polypoidal mass on the greater curvature of stomach, about 2-3 cm distal to the gastro-esophageal junction, with lobulations and haemorrhagic areas over it (Fig. 2b). Serum AFP was 9.7 ng/ml.

Laparotomy revealed a variegated mass of size approximately 6 x 4 cm in the upper portion of the stomach; larger part of the lesion was exophytic and a small portion of the lesion was intra-gastric. The mass was completely excised with a sleeve of the stomach wall and the stomach was repaired in 2 layers. Patient recovered uneventfully from surgery. Histopathology showed a tumor composed of mature ectodermal, entodermal and mesodermal elements like squamous epithelium with pilosebaceous units, hair follicles, intestinal mucosa, smooth muscle, cartilage, nerve bundles, glial tissue, ganglion cells, fat, cuboidal epithelium, bone and ciliated pseudostratified epithelium (Fig. 2c, 2d). No immature elements were seen. The final diagnosis was mature teratoma. The patient is asymptomatic at 2 year follow up.

Case 3

An 8 year old boy presented to us with history of pain in the left subcostal region of three months duration. There was no history of vomiting, hematemesis, malaena, fever or jaundice. General physical

examination was unremarkable. Abdominal palpation revealed a firm, non-tender mass occupying the epigastrium, left hypochondrium and left lumbar regions. The margins of the mass were well defined and it moved with respiration. Laboratory investigations including hemogram, renal function tests, liver function tests and coagulation profile were normal. Serum AFP was 0.87 ng/ml. CT abdomen revealed a large heterogeneous mass with fluid, soft tissue, bone and fat attenuation mixed with chunky calcifications, in relation to the greater curvature of stomach, displacing the small and large bowel loops inferiorly, suggesting the possibility of a gastric teratoma (Fig. 3a).

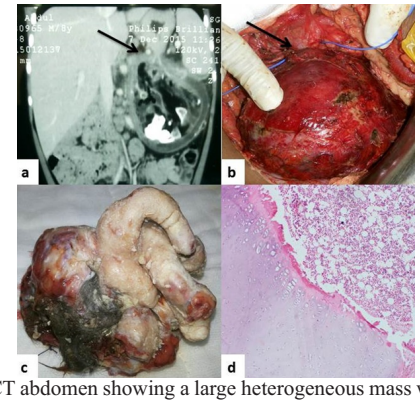

Fig. 3a: CT abdomen showing a large heterogeneous mass with fluid, soft tissue, bone and fat attenuation mixed with chunky calcifications, in relation to the greater curvature of stomach (arrow), **3b:** Intra-operative photograph showing a large mass communicating with the stomach (arrow), **3c:** Cut surface of the mass showing areas of bone, cartilage, fat and hair, **3d:** Photo micrograph showing tumor composed of bone, cartilage and bone marrow components

Laparotomy revealed a large intra-peritoneal mass, approximately 12x10x10 cm, which was hard, fixed, irregular and was communicating with the stomach at fundus on the postero-superior aspect (Fig. 3b). There was no intra-gastric component. The mass was excised completely including a sleeve of stomach wall and the stomach was repaired in 2 layers. Post-operative period was uneventful and the patient was discharged home on 7th post-operative day. Cut surface of the mass on gross examination showed areas of bone, cartilage, fat, hair and haemorrhage (Fig. 3c). Microscopy of sections from the mass showed heterogenous solid cystic neoplasm composed of derivatives of all three germ cell layers. Different areas of the lesion show stratified squamous epithelium with developing pilosebacious units, hair follicles, cartillage, bone, mature adiopse tissue, bronchial epithelium, muscle, lymphoid follicles and focal collection of ganglion cells (Fig. 3d). Immature components were not seen. The final diagnosis was a mature teratoma. The patient is asymptomatic with no evidence of recurrence at 30 months follow up.

Case 4

A 3 year old boy presented to us with recurrent episodes of malaena and anaemia of 2 months duration. He also had progressive abdominal distension and low grade fever. A hard mass was palpable in the epigastrium, measuring 7x8 cm with ill-defined margins. Upper GI endoscopy revealed deep excavated ulcer with necrotic slough at base and surrounding thick hyperemic folds on the lesser curvature, 4cm from gastro-esophageal (GE) junction (Fig. 4 a).

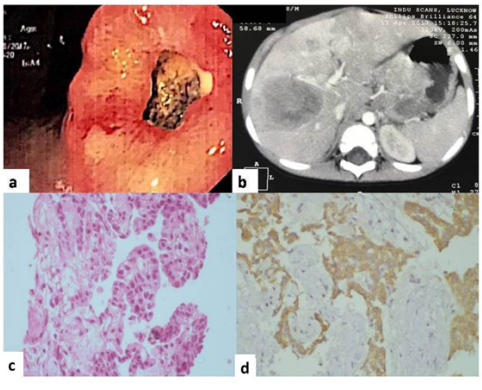

Fig. 4a: Upper GI endoscopy picture showing deep excavated ulcer and surrounding thick hyperemic folds on the lesser curvature of stomach, **4b**: CT abdomen showing large heterogeneously enhancing mass lesion on the lesser curvature of stomach with multiple liver metastasis, **4c:** Photo micrograph showing tumor disposed in broken papillae and cords along with loose connective tissue. The tumor cells show round hyperchromatic nuclei, inconspicuous nucleoli and moderate amount of cytoplasm, **4d:** Immuno-histochemistry showing tumor cells with strong cytoplasmic positivity for AFP and cytokeratin.

Computed tomography (CT) scan of abdomen revealed large heterogeneously enhancing soft tissue attenuation mass lesion in the lesser sac with indistinct fat planes with the lesser curvature of stomach (Fig. 4 b). Nodular inhomogenously enhancing lesions were seen in the omentum. Multiple small to moderate sized, oval & rounded, peripherally enhancing lesions were seen in both lobes of liver, suggestive of metastasis. Serum alpha-fetoprotein (AFP) was 21000 ng/ml. Trucut biopsy from the mass was suggestive of YST (Fig. 4c, 4d).

Patient was started on 3 weekly chemotherapy based on cisplatin, etoposide and bleomycin (PEB). Following 3 courses of PEB, CT revealed significant reduction in size of the mass and liver nodules. AFP was 10.1 ng/ml. Laparotomy revealed mass on the lesser curvature of the stomach of size 5 x 4 cm near the GE junction. There were multiple fibrotic omental nodules and nodules in both lobes of the liver. Sleeve gastrectomy with excision of the mass with omentectomy with biopsy of the liver nodules with sampling of peri gastric lymph nodes was done. Post-operative course was uneventful. Histopathology of the specimen and biopsies revealed only necrotic tissue with no evidence of residual malignancy. 3 month follow up CT revealed no residual mass with AFP of 3 ng/ml.

DISCUSSION

Teratomas are the most frequently occurring germ cell tumors in children. Teratomas presenting in the heart, liver and stomach are rare, accounting for less than 1% of cases [6]. Unlike other childhood teratomas which show a marked female preponderance, gastric teratomas occur mainly in boys [3]. All our cases were male. This tumor usually occurs in children less than 1 year of age, especially neonates. However, few cases have been reported in older children [7]. Our oldest patient was eight years old at the time of diagnosis.

The clinical features of gastric GCT depends upon the site of origin, size, and endogastric component. The usual clinical features are abdominal distension, palpable mass, vomiting and constipation. A palpable mass is reported in 75% of patients and only abdominal distension in 56% [8]. All our patients had a palpable abdominal lump. In case of intramural extension the patients may present with hematemesis or melena as the intramural component can ulcerate and haemorrhage, as seen in 2 cases in our series. Larger gastric GCT can cause premature labor, dystocia and respiratory distress in the newborn because of their size. The newborn who presented to us had massive abdominal distension and laboured breathing with history of prolonged labour. Very rarely, gastric GCT can present acutely with rupture or gastric perforation [9]. Gastric GCT usually arise posteriorly from the region of the greater curvature or the posterior wall and grow centrifugally [8]. Occasionally, they may arise from the lesser curvature of stomach, antrum or fundus, as seen in one of our cases. Commonly they grow in a purely exogastric fashion (> 60%), with 30% showing endogastric growth and very few showing both endo- and exogastric components [10].

Gastric GCT are usually benign and can be classified into mature and immature teratomas. Immature gastric teratomas are rare. There are approximately a dozen cases of immature gastric teratoma reported so far [11]. Gastric yolk sac tumors (YST) are even rarer. Only seven cases of pure YST of the stomach, with a median age of 65 years, and five cases of YST combined with adenocarcinoma have been reported [5,12]. Thorough sampling of these tumors is very important as prevalence of microscopic foci of a yolk sac tumor, happens to be directly related to its malignant potential. It also happens to be the only valid predictor of recurrence rather than the grade of the tumor [2]. Serum AFP level is a useful marker in these cases for detecting recurrence, presence of residual tumors or malignant transformation.

In most of the cases the preoperative diagnosis of gastric GCT is difficult. Abdominal radiograph, ultrasonography, CT/MRI (Magnetic Resonance Imaging) and endoscopy are important diagnostic tools. Plain films usually reveal a soft tissue mass with associated irregular

areas of calcifications. USG demonstrate a heterogeneous mass with mixed echogenicity. CT scan demonstrates a mass with solid and cystic components and internal calcifications and fat. CT scan is the modality of choice. When combined with intravenous and oral contrasts, it can detect the origin of the tumour, its relation with gastrointestinal tract and major blood vessels, presence of bones and calcifications, tumour extent and presence of metastasis. Other modalities like barium meal and upper GI endoscopy have a role in the diagnosis of a bleeding gastric teratoma with an intramural component. Upper GI endoscopy showed an intra-mural mass in 2 cases in our series.

Treatment for gastric GCT is complete surgical excision. Total excision and primary repair of the gastric wall is the treatment of choice [2, 3, 4, 7]. Partial, subtotal, and total gastrectomies have been performed as dictated by the extent of stomach involvement [13]. The prognosis following surgical excision of a mature gastric teratoma has been shown to be excellent [2, 3, 4, 7]. Chemotherapy is recommended for malignant GCT of stomach [5]. Regular and long term follow up with serum AFP and abdominal imaging is strongly recommended, especially in cases of immature teratoma.

CONCLUSION

Gastric GCT is an exceptionally rare embryonic neoplasm, which can have diverse clinical presentation depending on the age and site of involvement. With recent advances in imaging, an accurate pre-operative diagnosis is possible. Gastric GCT have an excellent prognosis if treated promptly and complete surgical excision is usually curative.

Conflict of interest: Nil

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