Case Report

SYNCHRONOUS ADENOCARCINOMA AND GASTROINTESTINAL STROMAL TUMOUR (GIST) OF THE STOMACH
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Abstract:
Gastrointestinal stromal tumours are rare mesenchymal neoplasms of gastrointestinal tract with a malignant potential and unpredictable behavior and stomach is the commonest location involved. However coexistence of gastric carcinoma and GIST is very rare. A 32-year-old male patient who presented with upper abdominal dyspeptic symptoms, was evaluated with Upper GI Endoscopy which revealed an ulcerated lesion in the antral part of the stomach. Biopsy was taken and histopathological examination revealed the lesion as poorly differentiated adenocarcinoma. Distal radical gastrectomy revealed another 3 cm of submucosal mass of GIST along with the existing adenocarcinoma.

Key wards: Gastrointestinal stromal tumour (GIST), Adenocarcinoma, Synchronous tumour, Gastric neoplasm

Introduction:
Gastrointestinal stromal tumours are rare mesenchymal neoplasms of gastrointestinal tract with an incidence of 1.5 per 100,000 patients per year¹,² typically described in adults with a peak incidence in the sixth and seventh decades³. Adenocarcinoma is the most common histological type gastric tumor. It may coexist with another synchronous tumor of different histological type in a different part of stomach. Gastric carcinoma may coexist most commonly with lymphoma and less commonly with carcinoid and GIST⁴. We report a very rare combination of synchronous distal adenocarcinoma with GIST in the stomach.

Case Report:
A 32-year-old farmer, from Doshmina, Patuakhali was admitted at Shaheed Suhrawardy Medical College Hospital on 05th May, 2013 with the complaints of 08 months duration of upper abdominal dyspeptic symptoms (vague upper abdominal pain, postprandial distension/discomfort and nausea). He gave a history of 3 episodes of melena during last 5 weeks with significant weight loss for the last 6 months. He was a smoker taking 20 sticks/day for 10 years. On examination he was found malnourished and severely anaemic, non-icteric, with no peripheral lymphadenopathy. Abdominal examination revealed no abdominal lump, hepatomegaly, or ascitis. Digital rectal examination revealed nothing abnormal.

His Hb% was 7.5 mg/dl, with a raised ESR (45 mmin 1st hour). Endoscopy of upper GIT revealed an ulcerated lesion in the antral part of the stomach; biopsy was taken, and histopathology revealed poorly differentiated adenocarcinoma. CT scan of abdomen
showed a well defined rounded hypodense shadow at distal stomach; no metastatic features were identified. After adequate preparation and optimization of the patient, he underwent Laparotomy on 13th May, 2013. On laparotomy, a rounded well circumscribed (5×8 cm) mass was found in the antral part of the stomach, there was no hepatic metastases, ascites or peritoneal seedling. Distal radical gastrectomy was done. The resected specimen was cut open and two lesions were identified; an ulcerated lesion at the antral part of stomach and another well circumscribed mass lesion at body of stomach 3-4cm proximal to the ulcerated lesion (Fig. 1 and 2). Two lesions were well marked and sent for histopathology. Histopathology of the ulcerative lesion revealed early gastric carcinoma (signet ring cell type) (Fig. 3) and the tumour of the body was low risk category GIST (Fig. 4); immunohistochemistry showed positive staining for CD117.

Fig.-1: Per operative photograph of tumour of the stomach

Fig.-2: Photograph of resected specimen showing both ulcerative lesion and tumour

Fig.-3: Microscopic view of gastric adenocarcinoma (H and E stain)

Fig.-4: Microscopic view of GIST (H and E stain)

Discussion:
Gastrointestinal stromal tumors (GISTs) are rare mesenchymal neoplasms of the digestive tract. Synchronous occurrence of a gastrointestinal stromal tumour with a tumor of different histogenesis is very rare and has been documented in the literature mainly in case reports. There are only a few previous reports of simultaneous adenocarcinoma and GIST in the stomach.5,6

The clinical presentation of GIST is characterized by GI bleeding, abdominal pain, weight loss, anaemia, a palpable mass.7 The etiology may be represented by mutations in the Kit gene or PDGFRA (platelet derived growth factor receptor alpha) gene and the origin of
GIST is considered to be the interstitial cells of Cajal. The most common location for GIST is the stomach (52-60%), followed by small intestine (20%-30%) and colorectum (10%)\(^9\). However, when GIST is submucosal or subserosal, the gastric mucosa may not be invaded and endoscopic biopsy may be inconclusive.

In most of the reported cases of synchronous adenocarcinoma and GIST, biopsy fragment showed adenocarcinoma and GIST were detected only following laparotomy and examination of the resected specimen. In our case, distal radical gastrectomy was performed for distal gastric adenocarcinoma and a small GIST was found incidentally on histopathological examination of the specimen. Yan-Jun Lie et al found that incidental GIST coexisted most commonly with oesophageal (1.13%) and gastric tumours (0.53%), less with colorectal tumours (0.03%) and has a high prevalence in males\(^10\). The simultaneous finding of epithelial and stromal gastric tumors raises the question of whether such an occurrence is a simple incidental association or the two lesions are connected by a causal relationship. Various hypotheses have been proposed regarding the simultaneous development of GIST and adenocarcinoma. A possible explanation for the synchronous occurrence of these two entities is represented by metallothioneins (MT), proteins with an increased affinity for heavy metal ions, coded by a family of 10 functional genes in human. The expression of these metalloproteins has been associated with protection against DNA damage, apoptosis, cell survival, angiogenesis and oxidative stress\(^11\). Soo et al observed the nuclear expression of MT as determined by immunohistochemistry in all the GIST. Knowing that MT is correlated with cell proliferation, there is a possibility that MT may be involved in GIST proliferation\(^12\).

The possibility of gene mutations might underlie tumour predisposition harboring a double gastric neoplasia cannot be theoretically discarded. Evidence of familial disease was derived in only one case\(^13\). At present, however no data are available to support such a hypothesis. An interesting hypothesis is that a single carcinogenic agent may interact with the neighboring tissue inducing the development of tumor of different histotype in the same organ\(^13\).

**Conclusion:**

Coexistence of gastric carcinoma and GIST is rare and proven relationship of this synchronous development has not been established. High clinical suspicion during laparotomy is required to detect GIST because they are asymptomatic and is an incidental finding most of the time. Surgical excision is the mainstay of therapy and further research is needed for explaining the simultaneous tumor development.

**References**

1. Theodosopoulos T, Dellaportas D, Psychogiou V, et al. Synchronous gastric adenocarcinoma and gastrointestinal stromal tumour (GIST) of the stomach: a case report. World J Surg Oncol 2011;9:60.
2. Casali PG, Blay JY; ESMO/CONTICANET/ EUROBONE Consensus Panel of Experts. Gastrointestinal stromal tumours ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010; 21 Suppl 5:98-102.
3. Miranda ME, Alberti LR, Tatsuo ES, Picarro C, Rausch M. Gastrointestinal stromal tumor of the stomach in a child with a 3-year follow-up period—Case report. Int J Surg 2011; 2:114–117.
4. Goteri G, Ranaldi R, Rezai B, Baccarini MG, Bearzi I. Synchronous mucosa-associated lymphoid tissue lymphoma and adenocarcinoma of the stomach. Am J Surg Pathol 1997; 21: 505-9.
5. Katsoulis IE, Bossi M, Richman PJ, Livingstone JI. Collision of adenocarcinoma and gastrointestinal stromal tumour (GIST) in the stomach: Report of a case. Int Semin Surg Oncol 2007;4:2.
6. Bircan S, Candir O, Aydin S, Baspinar S, Buldum M, Kapucuoglu M, et al. Synchronous primary adenocarcinoma and gastrointestinal stromal tumour in the stomach: A report of two cases. Turk J Gastroenterol 2004;15:187-91.
7. Rabin I, Chikman B, Lavy R, et al. Gastrointestinal stromal tumors: a 19 year experience. Isr Med Assoc J 2009;11:98-102.
8. Kang YN, Jung HR, Hwang I. Clinicopathological and immunohistochemical features of gastrointestinal stromal tumors. Cancer Res Treat 2010;42:135-43.
9. Corless CL, Fletcher JA, Heinrich MC. Biology of gastrointestinal stromal tumors. J Clin Oncol 2004;22:3813–25.

10. Liu YJ, Yang Z, Hao LS, Xia L, Jia QB, Wu XT. Synchronous incidental gastrointestinal stromal and epithelial malignant tumors. World J Gastroenterol 2009; 15: 2027–31.

11. Cherian MG, Jayasurya A, Bay BH. Metallothioneins in human tumors and potential roles in carcinogenesis. Mutat Res 2003; 533: 201-9.

12. Soo ET, Ng CT, Yip GW, et al. Differential expression of metallothionein in gastrointestinal stromal tumors and gastric carcinomas. Anat Rec (Hoboken) 2011;294:267-72.

13. Maiorana A, Fante R, Maria Cesinaro A, Andriana Fano R. Synchronous occurrence of epithelial and stromal tumours in the stomach: A report of 6 cases. Arch Pathol Lab Med 2000; 124: 682-6.