A Tale of Two Sisters: Two Pediatric Cases within a Familial Cluster of Hereditary Diffuse Gastric Carcinoma

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BACKGROUND/AIM

- Hereditary Diffuse Gastric Cancer (HDGC) is a familial form of poorly differentiated signet ring cell carcinoma (SRCC)
- Caused by an autosomal dominant mutation in the CDH1/E-cadherin gene mediating cell adhesion
- Early stages of SRCC can be exceptionally difficult to diagnose as there are characteristically widespread submucosal foci beneath an intact surface epithelium
- Carriers are advised to undergo prophylactic gastrectomy due to the high mortality associated with invasive HDGC
- Carriers also have an increased risk of lobular breast carcinoma, cleft lip/palate, and colorectal adenocarcinoma.

CASE

- A 15-year-old female with no significant past medical history presented to clinic with a 4-month history of generalized abdominal pain with no specific aggravating/relieving factors.
- Family history was significant for a paternal great-aunt who reportedly died from gastric cancer at age 28 .
- EGD revealed diffuse mild inflammation in the stomach with normal appearing rugae without ulceration or masses and normal proximal duodenum.
- Biopsy of the antrum revealed poorly differentiated signet ring cell carcinoma.
- The patient subsequently underwent a curative laparoscopic roux-en-Y esophagojejunostomy, jejunojejunostomy with exploratory laparoscopy.
- Analysis of the stomach revealed 156 foci of SRCC confined to the lamina propria with the final proximal and distal surgical margins negative for the tumor by microscopy.
- Based upon the unusual occurrence of SRCC in a young female, the patient and her family underwent genetic testing, revealing a pathologic mutation in the CDH1/E-cadherin gene in the patient, her 10-year-old sister, and the father.
- Screening EGD in the 10-year-old sister and the father also revealed SRCC confined to the lamina propria.

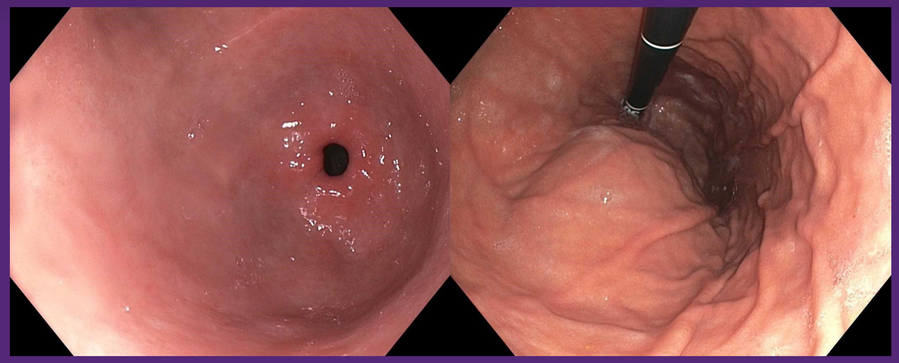

Image 1 – EGD revealed diffuse mild inflammation of the stomach with normal appearing rugae without ulceration or masses

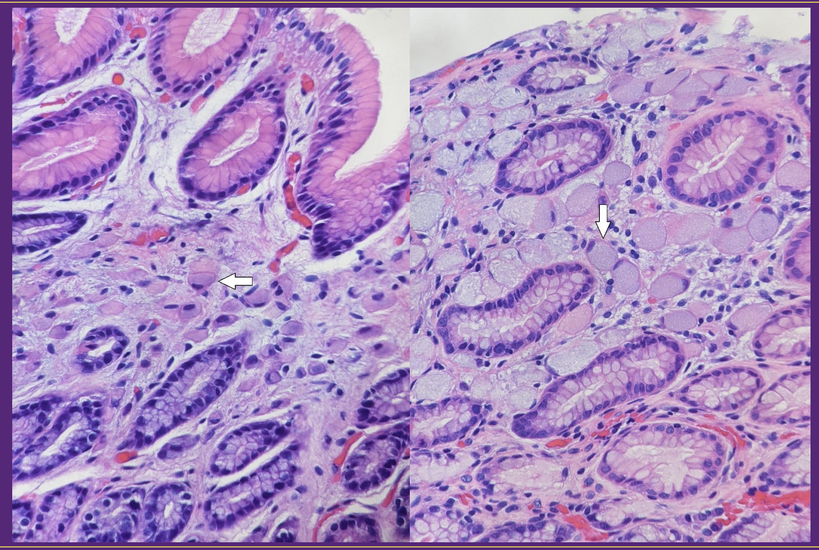

Image 2 – Biopsy from gastric antrum demonstrating poorly differentiated signet ring cell carcinoma present in the lamina propria.

CONCLUSIONS

- Worldwide, approximately 990,000 people are diagnosed with gastric cancer, of which about 738,000 die from this condition yearly.
- Gastric carcinoma primarily affects patients between the ages of 50 and 70 years of age and is uncommon before the 5th decade of life.
- Early-onset gastric cancer (EOGC) is defined as gastric cancer occurring at the age of 45 years old or younger.
- Gastric carcinoma is exceedingly rare in the pediatric population, which may lend to delayed diagnosis.
- HDGC should be considered when a patient presents with gastrointestinal symptoms and has a positive family history of gastric cancer among 1st and 2nd degree relatives, particularly if a relative was diagnosed before the age of 50.
- HDGC may exhibit indolence for decades even after invading the lamina propria. The molecular mechanisms that initiate the transition from indolent to invasive behavior are unknown and require more research.
- Early identification and treatment of gastric signet-ring cell carcinoma is imperative for a more favorable prognosis.

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