Somatic Mutation of CDH1 Leading to Diffuse Gastric Cancer

Rees Checketts OMS-III, Katrina Roop DO, Jay Roop DO

THE UNIVERSITY of NORTH TEXAS HEALTH SCIENCE CENTER at FORT WORTH

INTRODUCTION

Hereditary Diffuse Gastric Cancer (HDGC) is a serious cancer impacting both patients and their family members. As such, a thorough work-up including molecular pathophysiology is warranted in patients and close family members.

ABSTRACT

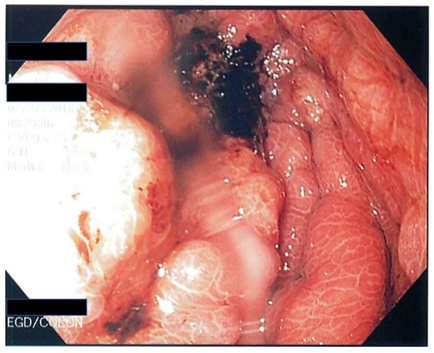
HDGC is an autosomal dominant disease[1] with 80% penetrance at 80 years of age[2]. It develops when a mutation causes a loss of function of e-cadherin leading to loss of cell-to-cell adherence[3]. Because of its poor prognosis, inheritance pattern, and high penetrance, family members with a mutation are recommended to undergo prophylactic gastrectomy[1]. Somatic mutations leading to HDGC are increasingly being identified, providing relief from unnecessary surgery and secondary effects.

CASE REPORT

Subjective
- This is a 68-year-old male with a two-month history of early satiety, loss of appetite, and unintentional weight loss
- Denied nausea, vomiting, diarrhea, constipation, and abdominal pain

Subjective (cont'd)
- History of gastritis, and colonic polyposis (CP), and treated H. pylori infection and peptic ulcer disease
- No hospitalizations. Six colonoscopies for monitoring of CP
- Social history includes a 50 pack-year smoking history, 3-4 alcoholic drinks per day, no drug use, the owner of an energy company without identified exposure
- Worked in a building with known disturbed asbestos
- Has an identical twin brother who remains unaffected. Both have possible combat exposure to Agent Orange.

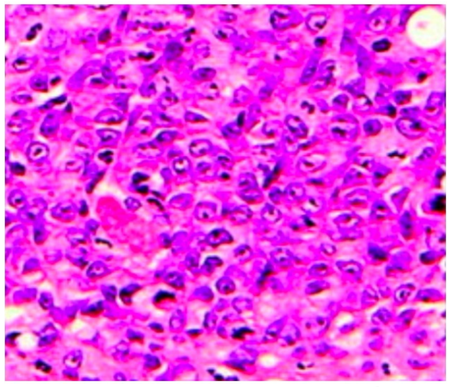
Objective
- Diagnosis of Signet Ring Cell Carcinoma (SRCC) with metastasis to peritoneum made with biopsy
- Early and repeat imaging (two CT scans and an MRI) showed no metastasis until 12 months post diagnosis
- Patient received palliative chemotherapy initially but ultimately only tolerated 5-Fluorouracil
- Molecular pathology confirmed somatic variant alone of CDH1 p.P625_A62Bdel



Picture taken during EGD and biopsy demonstrating thickened folds, inflammation, and appearance of diffuse wall infiltration.

DISCUSSION

Cases are increasingly being identified of somatic mutations of CDH1[4]. Information regarding risk factors is limited to EBV infection[5-7]. Further research is needed to understand risks and associations between the somatic development of this cancer. Identifying those mutations as affecting e-cadherin and/or leading to DGC germline or somatic, needs be an essential part of work-up and treatment for these cancers.



Histopathology of SRCC on biopsy[8].

REFERENCES

1.Luo W, Fedda F, Lynch P, Tan D. CDH1 Gene and Hereditary Diffuse Gastric Cancer Syndrome: Molecular and Histological Alterations and Implications for Diagnosis And Treatment. *Front Pharmacol*. 2018;9:1421.
2.Melo Pezo X, Medrano Samamé H, Torres Rosas E. [Hereditary diffuse gastric cancer]. *Rev Gastroenterol Peru*. 2015;35(1):73–78.
3.Humar B, Blair V, Charlton A, More H, Martin I, Guilford P. E-cadherin deficiency initiates gastric signet-ring cell carcinoma in mice and man. *Cancer Res*. 2009;69(5):2050-2056.
4.Choi S, Jang J, Heo YJ, et al. CDH1 mutations in gastric cancers are not associated with family history. *Pathol Res Pract*. 2020;216(5):152941.
5.Guilford P, Humar B, Blair V. Hereditary diffuse gastric cancer: translation of CDH1 germline mutations into clinical practice. Gastric Cancer. 2010;13(1):1-10.
6.Usui G, Matsusaka K, Mano Y, et al. DNA Methylation and Genetic Aberrations in Gastric Cancer. Digestion. 2021;102(1):25- 32.
7.Bustos-Carpinteyro AR, Oliveira C, Sousa A, et al. CDH1 somatic alterations in Mexican patients with diffuse and mixed sporadic gastric cancer. BMC Cancer. 2019;19(1):69.
8.Photo taken from https://cancerres.aacrjournals.org/content/69/5/2050 on 4/3/2021.

1.Luo W, Fedda F, Lynch P, Tan D. CDH1 Gene and Hereditary Diffuse Gastric Cancer Syndrome: Molecular and Histological Alterations and Implications for Diagnosis And Treatment. *Front Pharmacol*. 2018;9:1421.

2.Melo Pezo X, Medrano Samamé H, Torres Rosas E. [Hereditary diffuse gastric cancer]. *Rev Gastroenterol Peru*. 2015;35(1):73–78.

3.Humar B, Blair V, Charlton A, More H, Martin I, Guilford P. E-cadherin deficiency initiates gastric signet-ring cell carcinoma in mice and man. *Cancer Res*. 2009;69(5):2050-2056.

4. Choi S, Jang J, Heo YJ, et al. CDH1 mutations in gastric cancers are not associated with family history. *Pathol Res Pract*. 2020;216(5):152941.