

# A Case of Hereditary Diffuse Gastric Cancer

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## Background

- Hereditary diffuse gastric cancer (HDGC) is an autosomal dominant disorder associated with pathogenic germline variants in the cadherin 1 (CDH1) or alpha-1 catenin (CTNNA1) genes.
- Carriers have an increased risk of cancer<sup>1</sup>
  - 80% risk of developing gastric cancer (average age ~38).
  - 60% lifetime risk of developing lobular breast cancer.
- Our patient was diagnosed with CDH1+ HDGC based on genetic testing and upper endoscopy.

## Case Presentation

An asymptomatic 50-year-old Bangladeshi female presented for surveillance colonoscopy given a strong family history of colon cancer and stomach cancer (Fig. 4). Prior upper endoscopy was normal and colonoscopy showed two tubular adenomas measuring 7-8 mm.

- Referred to a genetic counsellor due to concern for hereditary syndrome. An Ambry Colonext Panel with RNA Analysis was performed and returned positive for pathogenic heterozygous c.1137G >A mutation in the CDH1 gene.
- Opted for surveillance instead of prophylactic gastrectomy. An upper endoscopy was performed showing few, minute pale regions on close inspection, but no masses, ulcerations or other features suggestive of malignancy (Figs. 1, 2, 3).
- Per Cambridge protocol<sup>2</sup>, 34 biopsies were collected. One gastric body biopsy returned positive for gastric adenocarcinoma with signet ring cell features and weak E-Cadherin expression.
- Cross sectional imaging was negative for metastatic disease.
- Met with oncology and surgery teams and underwent laparotomy with total gastrectomy and Roux-en-Y esophagojejunostomy.
- Gastrectomy biopsy confirmed a single microscopic focus of diffuse adenocarcinoma.

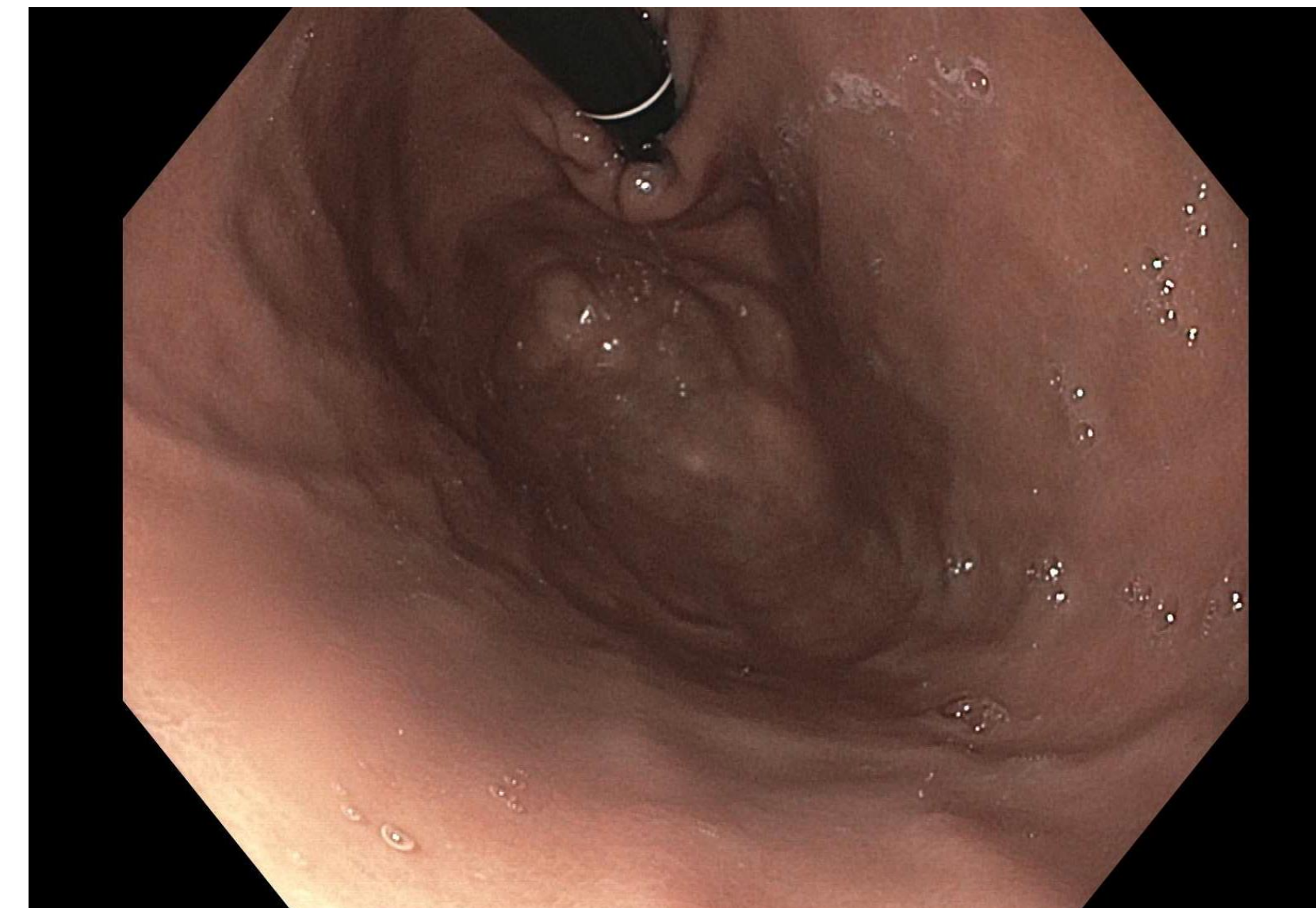


Figure 1: Gastric fundus.

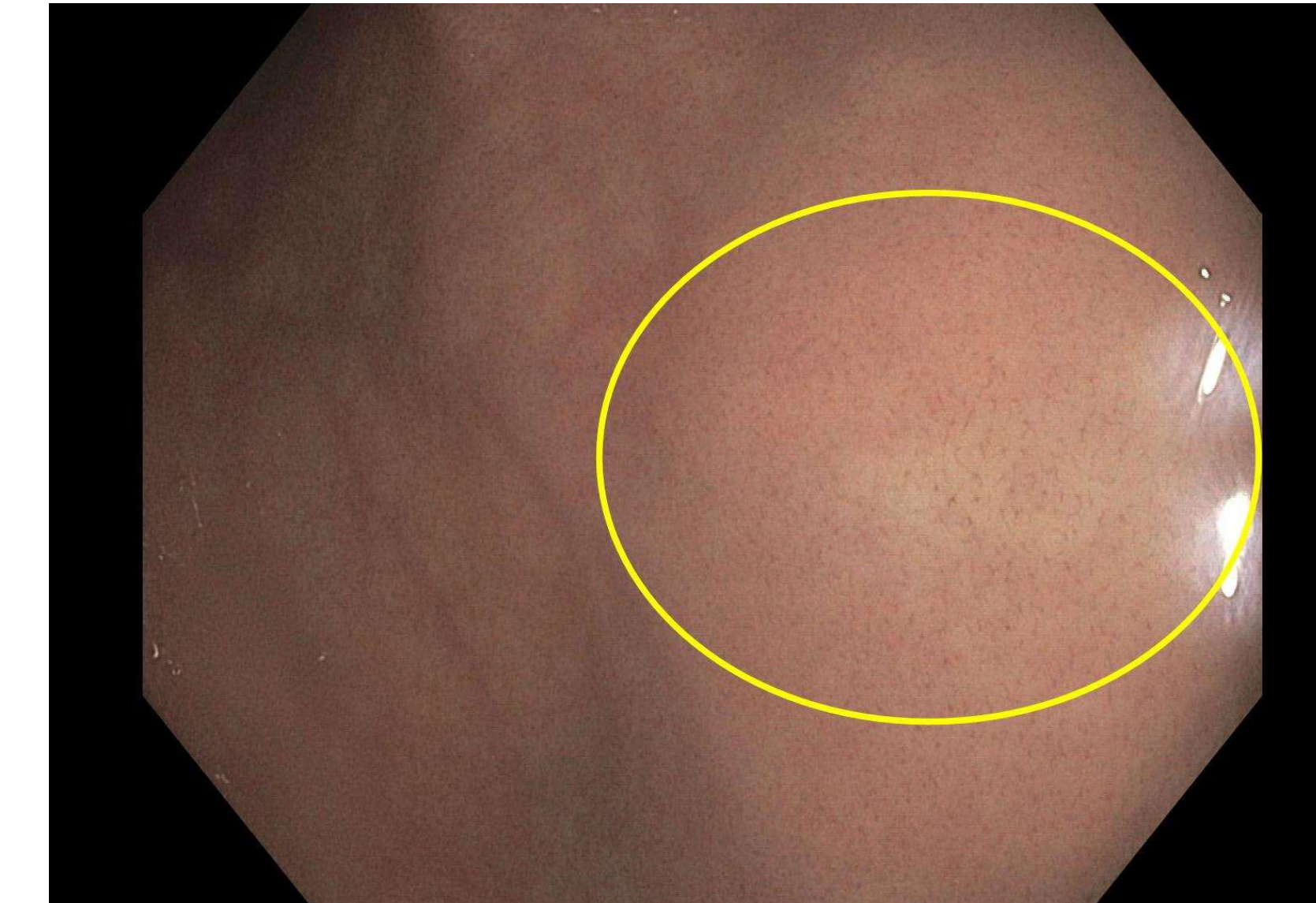


Figure 2: Gastric fundus, pale spot (circled).

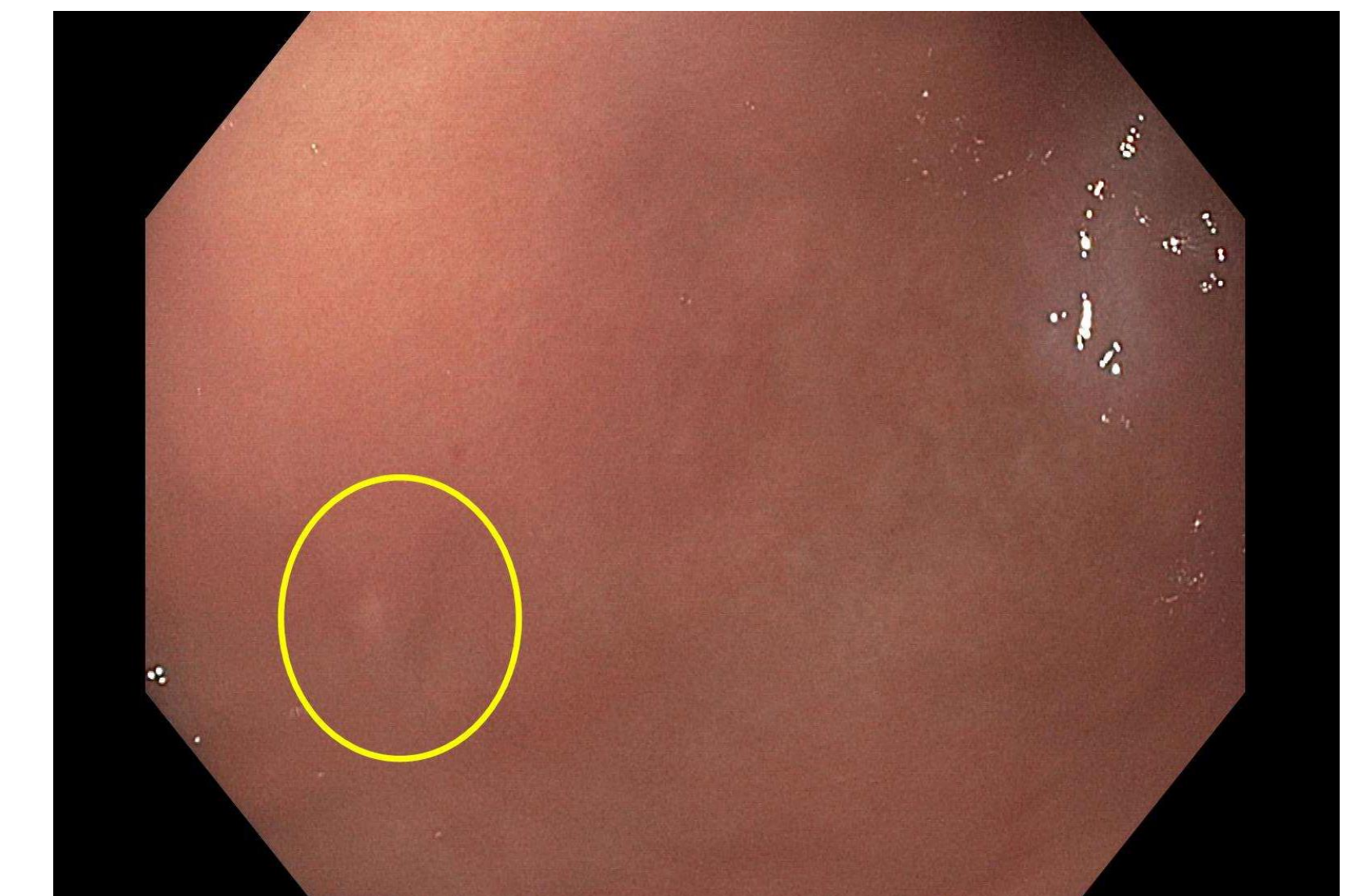


Figure 3: Gastric body, pale spot (circled).

## Discussion

- Diagnosis of HDGC-associated signet ring cancers is especially difficult because they are only visible on direct mucosal evaluation late in the disease process.
- Recommendations<sup>1</sup>
  - Genetic testing.
  - Prophylactic gastrectomy, as early as age 20, regardless of endoscopic findings. Patients denying surgery can be offered annual endoscopy with the understanding that frequent surveillance has not been proven to be effective in early gastric cancer detection in HDGC. During endoscopy, any visible lesion should be biopsied and a minimum of 30 biopsies are recommended to include all five anatomic gastric zones.
  - H. pylori should be screened for and treated.
  - Referral to a breast surgeon, annual surveillance or bilateral risk-reducing mastectomy can be considered.

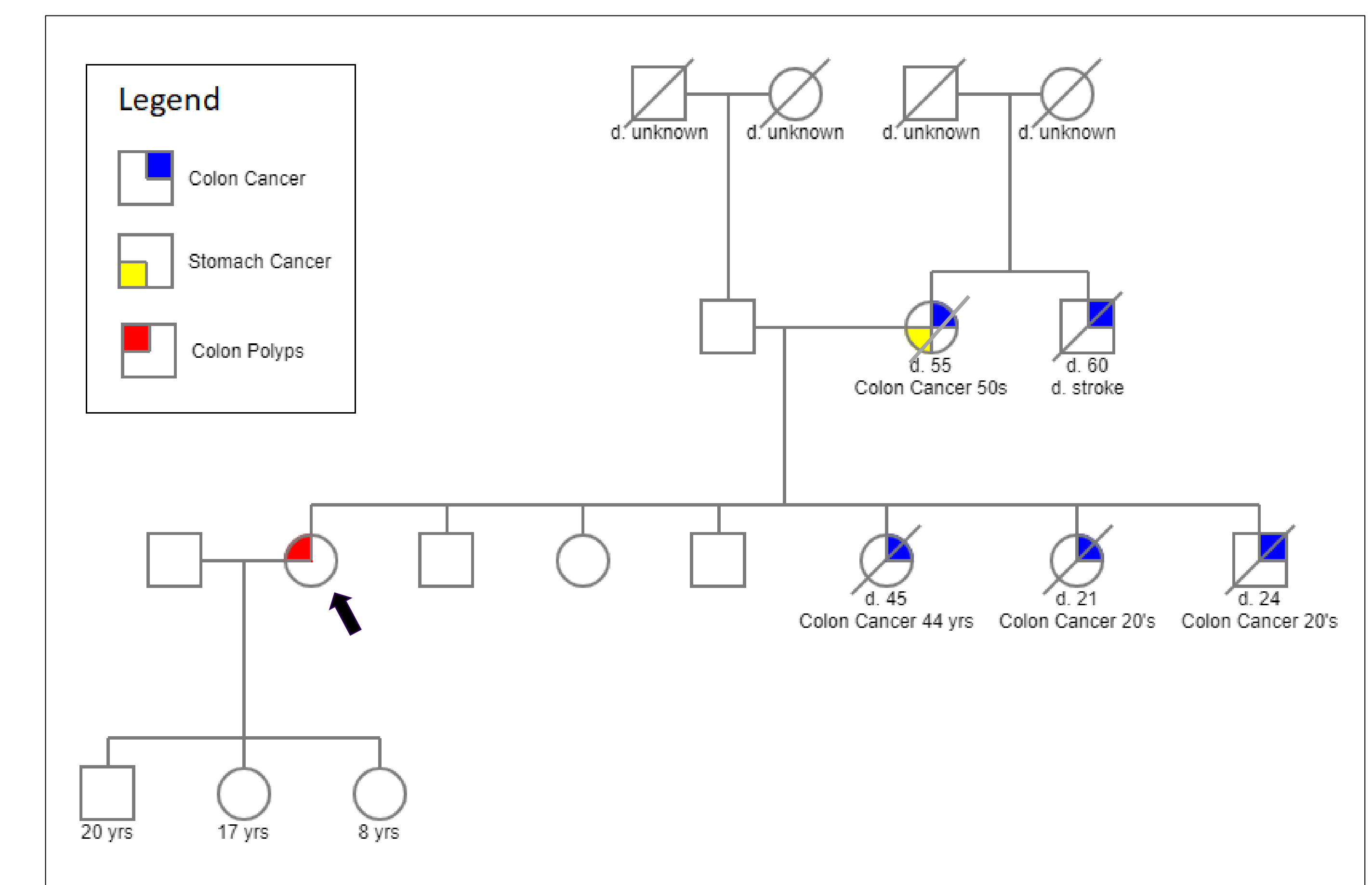


Figure 4: Pedigree for our patient (denoted by arrow) demonstrating family history of colon cancer and stomach cancer.

## References

1. Kaurah P and Huntsman DG. Hereditary Diffuse Gastric Cancer. 2002 Nov 4 [Updated 2018 Mar 22]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022.
2. van der Post RS et al.. Hereditary diffuse gastric cancer: Updated clinical guidelines with an emphasis on germline CDH1 mutation carriers. J Med Genet. 2015;52:361-374.