All Roads Lead to SMAD4: Hypertrophic Gastropathy in Association With A SMAD4 Mutation

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Introduction

- Juvenile Polyposis Syndrome (JPS) and Ménétrier Disease (MD) can both cause protein-losing gastropathies with similar histological features.
- Rarely has JPS been documented to present as hypertrophic gastric folds.
- We report the diagnostic challenge of a case of hypertrophic gastropathy in a patient with a germline SMAD4 mutation.

Case Report

- A 39-year-old male with history of hypertension presented to the ED with symptomatic anemia. He reported fatigue, exertional dyspnea, and no GI symptoms.
- Family history included paternal JPS and a benign gastric mass.
- Initial workup included diagnostic EGD and colonoscopy.
- Colonoscopy discovered nine sessile polyps (inflammatory and hyperplastic).
- EGD showed severe gastritis and diffusely thickened gastric folds.
- Biopsies of gastric tissue showed cystically dilated foveolar glands and edematous, inflamed lamina propria.
- Histological findings were later confirmed via full-thickness tissue resection. Also noted was a demarcation of tissue in the antrum with normal mucosa distally. Testing for CMV and H. Pylori was negative. Genetic testing revealed a SMAD4 gene mutation of unknown significance.

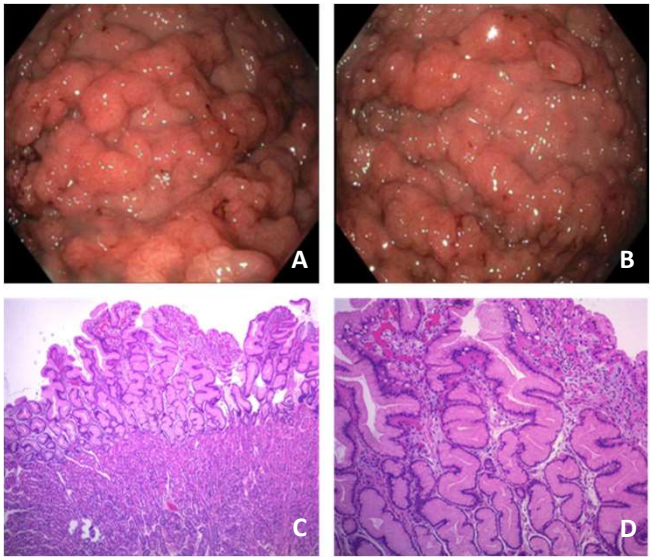

Figure A: Endoscopic view of gastric body, first EGD (10x)
Figure B: Endoscopic View of gastric body, follow-up EGD (10x)
Figure C: Gastric mucosa demonstrating foveolar hyperplasia with cystically dilated foveolar glands and edematous, mildly inflamed lamina propria (H&E Stain) (40x)
Figure D: Gastric mucosa demonstrating foveolar hyperplasia with cystically dilated foveolar glands and edematous, mildly inflamed lamina propria (H&E Stain) (100x)

Conclusion

- After review of the patient's family history and clinical course, we believe this may have been a misdiagnosed case of JPS rather than MD.
- Highlighted within this case report is the novelty of gastric rugal hypertrophy due to JPS, and importance of considering mimickers of MD when suspicion for this rare gastropathy arises.

Case Report (continued)

- In light of the clinical findings, MD was the leading diagnostic theory. Cetuximab was planned as a therapeutic option.
- Several weeks later, prior to treatment, the patient developed atypical Hemolytic Uremic Syndrome and succumbed to his condition.

Discussion

- Juvenile Polyposis Syndrome and Ménétrier Disease present similarly histologically and clinically.
- Disease origins vary, with MD theorized to be acquired secondarily to CMV or H. Pylori infections while JPS is likely due to germline mutations. [1]
- SMAD4 is a germline mutation found in up to 50% of JPS cases. [1]
- The significance of SMAD4 lies in it's role as a regulator of GI tract development and homeostasis.
- Surgical resection is the mainstay of treatment for diffuse JPS as well as MD.
- Medical management results are inconclusive, with Cetuximab showing promise for MD.

References

- Huh WJ, Coffey RJ, Washington MK. Ménétrier's Disease: Its Mimickers and Pathogenesis. J Pathol Transl Med. 2016;50(1):10-16.