CASE REPORT

Menetrier's Disease with Squamous Metaplasia in a Child with Long Term Disease Evolution: A Case Review

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Abstract:

Menetrier's Disease is a hypertrophied gastropathy rarely encountered in pediatric population presenting with protein loss. It has acute and self-limiting disease course in children. In our patient the disease had long duration of progression lasting over 3 years. Eight year old boy had presented with failure to thrive and hypoproteinemia. Endoscopically he found to have thickened gastric folds from which biopsy was taken. Histopathological examination showed typical microscopic features of Menetrier's disease with squamous metaplasia. The squamous metaplasia seen associated with Menetrier's disease has not been noticed before in a child. Clinical suspicion along with endoscopic biopsy and histopathological study is essential in diagnosis.

Keywords: Menetrier's Disease, Pediatric, Squamous Metaplasia

Introduction:

Menetrier's disease is rare hypertrophic gastropathy first described by Pierre Menetrier in 1988 commonly present with protein loss and hypochlorhydria [1]. It is a disease of adult and rarely been reported in children. Clinically pediatric patients present with hypoalbuminemia and edema secondary to protein loss through the abnormal gastric mucosa. It usually has a self-limited benign course in children responding to the symptomatic measures in most of the cases. This article aims discussing a case of pediatric Menetrier's disease with squamous metaplasia with long standing disease evolution which is unusual in children with emphasis on its clinical, endoscopic, and pathological aspects and approach to its treatment.

Case Report:

Eight-year-old male child presented with failure to thrive and weight loss, pain in abdomen, loose motions, and generalised weakness since past 3 years. On examination the child was pale, averagely built and poorly nourished. He was treated with multiple treatment modalities by different clinicians in 3 years of disease course. Laboratory investigations revealed haemoglobin – 6.4 g%, total leucocyte count- 4900/cmm and microcytic hypochromic type of anaemia. Erythrocyte sedimentation rate was raised to 40 mm at the end of 1 hour. Child had hypoproteinemia with hypoalbuminemia with total protein – 4.5 g/dl, albumin- 2.0 g/dl and globulin- 2.5 g/dl. Serology testing for HIV1/2, HCV and HBs Ag was negative. Ultrasound examination of abdomen was normal. His gastroscopy revealed oedematous, thickened gastric folds with focal whitish patchy areas (Fig. 1), clinically thought as Zollinger Ellison syndrome, Menetrier's disease, or Sarcoidosis. Urea test was negative.

Endoscopic biopsy was done from thickened mucosal folds in stomach revealed marked foveolar hyperplasia with tortuous corkscrew glands with focal squamous metaplasia (Fig.2).

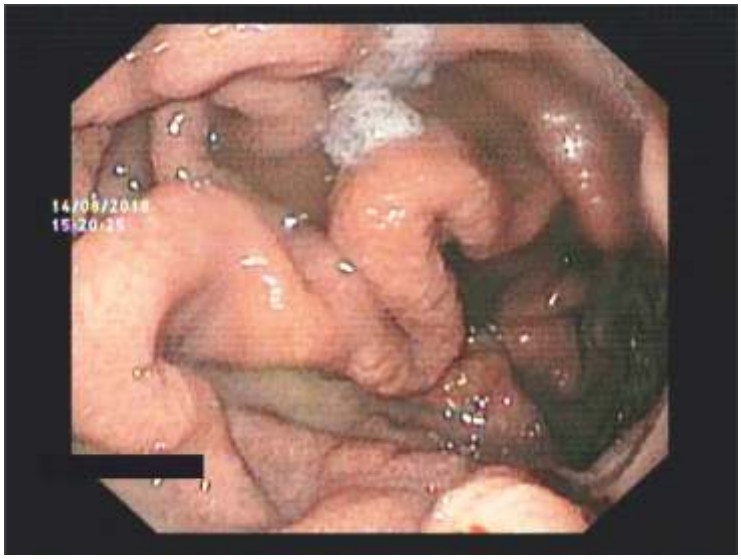

Fig. 1: Gastroscopy showing Oedematous and Thickened Gastric Folds with Focal Whitish Patchy Areas

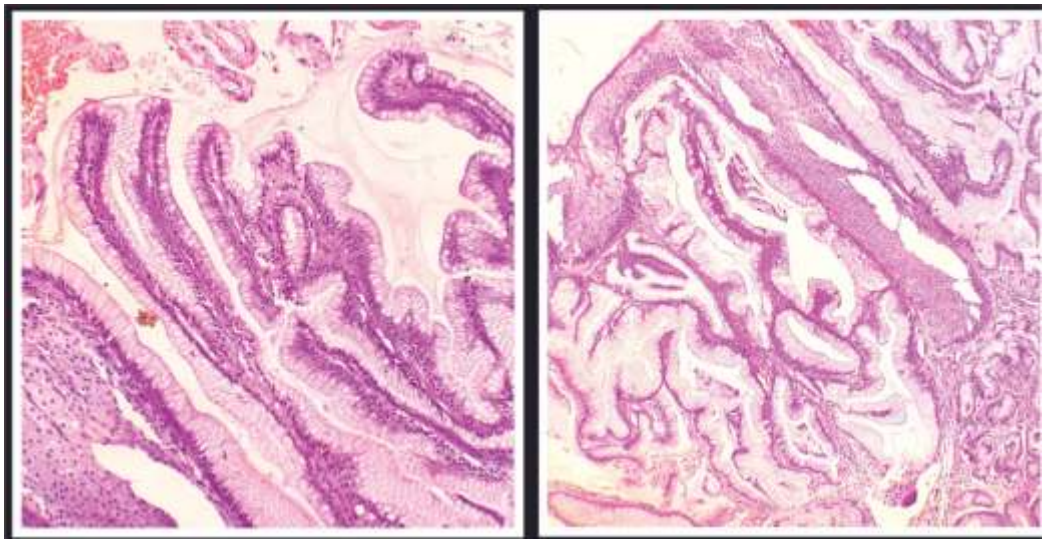

Fig. 2: Marked Foveolar Hyperplasia with Tortuous Glands with Corkscrew Appearance and Squamous Metaplasia, Oxyntic Glands are Atrophic (HE 20×)

The foveolae were seen extending to muscularis mucosae. The oxyntic glands were atrophic with reduced number of parietal cells. The lamina propria showed prominent vertical strands of smooth muscle bundles and diffuse infiltration by mononuclear cells. Even after extensive search, intranuclear inclusions of CMV or *H. pylori* bacilli were not seen. The child was treated with albumin infusion, high protein diet with nutrient supplements and esomeprasole (1 mg/kg/day). Child improved symptomatically over 6 months with mild resolution of gastroscopic findings.

Discussion:

Menetrier's Disease is a hypertrophied gastropathy named after a French physician Pierre Eugène Ménétrier [2]. In pediatric, Menetrier's Disease excessive production of Transforming Growth Factor Alpha (TGF-α) sends an elevated alert to the Epidermal Growth Factor Receptors (EGFR) which results in hypertrophied gastropathy [2]. Protein loss through these abnormally thick gastric mucosa leads to hypoalbuminemia and associated findings like oedema, ascites and pleural effusion. These patients may also complain of anaemia, vomiting, pain in abdomen, weight loss, diarrhoea and failure to thrive [3]. Children usually have a benign self-limited course with resolution of symptoms in 4-6 weeks. The endoscopic resolution may take longer than symptomatic resolution [4]. Aetiology of Menetrier's Disease is thought to be unknown but association with *H.pylori* or cytomegalovirus infection, auto-immune diseases like inflammatory bowel disease is also noted by some authors [5, 3].

The clinical features, endoscopic and histopathological findings are alike the metanalysis carried out by Krikilion *et al*. However, Menetrier's Disease in children in transient as studied by Krikilion *et al.*, unlike in our case which had long term disease evolution [3].

Diagnosis of Menetrier's Disease includes multidisciplinary approach with gastroscopic biopsy with histopathology being gold standard. Investigations for *H. pylori* and CMV infection are also mandatory. Other contributing investigations include 24 hour stomach pH monitoring which may reveal hypochlorhydria/ achlorhydria, gastric protein loss assessment by measuring protein content in the gastric juice and 99mTc-labeled human serum albumin abdominal scintigraphy [6].

Microscopy is diagnostic for Menetrier's Disease with characteristic findings like elongation and corkscrew like appearance of foveolar glands with focal cystic dilatation, lined by hyperplastic foveolar epithelium. Diffuse or patchy glandular atrophy and hypoplasia of parietal or chief cells is also seen. [5]

Differential diagnosis of Menetrier's Disease includes other hypertrophic gastropathies presenting with thickened mucosal folds like Zollinger-Ellison, showing foveolar and parietal cell hyperplasia with architectural distortion. Eosinophilic gastroenteritis commonly involves gastric antrum and small intestine with history of allergic disorders with tissue eosinophilia. Gastric lymphoma and carcinoma are rare in children and not related with edema or hypoproteinemia. Sarcoidosis of stomach generally presents with ulceration or diffuse involvement like lenities plastic which reveal non caseating granuloma on microscopy. Other conditions associated with hypertrophic gastric folds, like Crohn's disease and Peutz-Jeghers syndrome, have different signs and symptoms and the histology is diagnostic. Lesions like gastric varices and lymphangiectasis also mimic radiologically with Menetrier's disease. Endoscopy with histopathology should be performed in all suspected cases to come to final diagnosis.[7]

Squamous metaplasia is stomach is a rare finding and to our knowledge this is the first case of childhood Menetrier's disease with squamous metaplasia, although has been observed in squamous cell carcinoma of stomach adjacent to the tumour. A number of theories regarding the origin of squamous cell of the stomach have been proposed, including totipotent stem cells, squamous metaplasia, foci of heterotopic squamous

epithelium and the overgrowth of a squamous epithelium element in a primary adenocarcinoma [8]. As our patient had long standing disease course with multiple therapy options attempted by multiple treating doctors, squamous metaplasia would have been caused due to chronic irritation as reaction to the same as process of repair. However detailed study with the help of molecular analysis would help in understanding the pathogenesis of squamous metaplasia in this patient better. Menetrier's disease is known to be associated with adenocarcinoma but not with squamous metaplasia [8].

A monoclonal antibody against Epidermal Growth Factor Receptor [EGFR] named cetuximab is been used in treating Menetrier's disease. Other medications being tried in treating Menetrier's are anticholinergic agents, prostaglandins, proton pump inhibitors/ H2 receptor antagonists and prednisone. High protein diet is recommended to cope up with protein loss. In children many cases are self-limited responding very well to conservative management [9].

Conclusion:

Menetrier's disease is a rare hypertrophic gastropathy uncommon in children. It has short and self-limiting disease course in children but in our case it had a chronic disease evolution with squamous metaplasia. Squamous metaplasia is an unusual finding in Menetrier's disease could have been caused due to multi therapy attempts over long duration. Clinical suspicion with endoscopy and histopathology is essential for diagnosis of this rare disease.

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