

Atypical presentation of Coeliac disease in infancy, case report

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Introduction: Coeliac disease is rare in infancy. This is a case report of an unusual presentation of coeliac disease. The presentation combined eosinophilic gastritis and oesophagitis as well as cow's milk intolerance symptoms in a 4-month-old baby girl. Up to current publications, these conditions presented atypically at such a young age and were diagnosed following full investigations.

Case Report:

A 4-month-old baby girl presented with a history of poor weight gain. She was born at 40⁺⁶ weeks via a normal vaginal delivery at a weight of 3.57kg with unremarkable pre-natal scans. Apgar score 9, 9 at 5 and 10 minutes respectively. She passed meconium immediately after delivery. 1 month later, she was noted to have episodes of non-bilious and non-projectile vomiting. On physical examination, the patient was afebrile, mildly dehydrated with poor peripheral perfusion. Unremarkable abdominal examination; abdomen was soft and non-distended. After initial IV resuscitation, blood sampling and urine collection were done. Urine was negative for infection. Normal white cell count, eosinophil count and haemoglobin. Venous blood gas showed compensated metabolic alkalosis. Electrolytes: normal sodium, slightly low chloride and potassium. Ultrasound scan (USS) of the abdomen revealed no pyloric stenosis, no evidence of malrotation, non-dilated bowel loops and unremarkable urinary tract. Her urine output was always of good volume and no loose stools were ever reported.

The patient was admitted and Naso-gastric Tube (NGT) was inserted for proper monitoring. She was started on anti-reflux medications, milk thickener and hypoallergenic formula. Metabolic screen, auto-antibodies, liver function tests and ammonia were all found to be within normal range.

Brain imaging USS and Magnetic resonance Imaging were reported being normal. A Barium swallow and meal was done. The gastric contour was unremarkable, and the duodenal loop was reported as having normal configuration. The duodeno-jejunal flexure was normally sited with no evidence of malrotation and no gastroesophageal reflux was detected throughout the course of the study. Prompt gastric emptying and unremarkable proximal small bowel transit were recorded. An MRCP was then done which showed normal examination.

Speech language pathologist confirmed normal swallowing reflex and advised to feed her foods of syrup consistency. Direct laryngoscope excluded laryngeal cleft. A diagnostic Oesophago-Gastro-Duodenal scope (OGD) was performed (fig 1). Positive rapid urase test (CLO test) and duodenal and gastric biopsies reported inflammation with significant eosinophilia and high possibility of coeliac disease. Thus, a prospective anti-TTG screen and cystic fibrosis were suggested. Surprisingly results were negative for both. HLA DQ2/8 and sweat test were negative. Faecal elastase

165 levels were indicative of moderate to weak pancreatic insufficiency. Stools for H. Pylori and for ova, cysts and parasites were negative.

Due to positive CLO test, the patient was started on triple therapy including Amoxicillin, Clarithromycin and Omeprazole for 14 days. Ranitidine was also continued. The patient was put on a strict lactose and gluten free diet. Dietician input was sought who recommended introduction of a high calorific formula milk. Thus, the patient was noted to gain weight on hypo allergic, lactose free, high calorific formula milk. She was thus discharged home after gaining weight and tolerating feeds orally.

Case Discussion:

Coeliac disease is an autoimmune disorder triggered by gluten and prolamins found in wheat, barley and rye in genetically susceptible individuals¹. Haplotypes in the Human leukocyte antigen (HLA) class II region (DR3 or DR5/7 or HLA DR4) have been identified in genetically susceptible patients. Coeliac disease primarily affects the duodenum segment of small bowel causing flattening of the mucosa².

Coeliac disease classically presents in the proximal small intestine and crypt hyperplasia, villous atrophy, and increased intraepithelial lymphocytosis are seen on histology. The Marsh classification is used for the histological staging of the disease³.

Young children typically present with abdominal pain and distension, chronic diarrhoea, weight loss and anorexia and symptoms may appear as young as 9-24month old. Moreover, the variability of symptoms at this age of presentation depends on many factors. The amount of gluten in the diet, the duration of breast feeding and the introduction of gluten during breastfeeding leads to gastrointestinal symptoms presenting later in life. Older children tend to present with bloating, constipation, abdominal pain and intermittent diarrhoea⁴.

Another unusual finding picked up during the patient's OGD was the positive CLO test for which she was then treated with triple therapy. *Helicobacter pylori* (H.pylori) is a microaerophilic gram-negative bacillus which produces the enzyme urease. H.pylori *inhibits* the mucus adjacent to the gastric mucosa and neutralizes the gastric

¹Guandalini S, Setty M. Celiac disease. *Curr Opin Gastroenterol*. 2008 Nov. 24(6):707-12.

²Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. *J Pediatr Gastroenterol Nutr*. 2012 Jan. 54(1):136-60.

³Marsh MN, Hinde J. Inflammatory component of celiac sprue mucosa. I. Mast cells, basophils, and eosinophils. *Gastroenterology*. 1985 Jul. 89(1):92-101.

⁴Guandalini S, ed. Celiac Disease. In. *Textbook of Pediatric Gastroenterology and Nutrition*. London: Taylor & Francis; 2004: 435-50.

acid by converting urea to ammonium and bicarbonate thus causing gastritis and gastric/duodenal ulcers⁵.

Upper GI endoscopy allows direct visualisation of the mucosa; therefore, ulcers and areas of inflammation and bleeding may be biopsied, sent for histology and cytology. H.pylori may be identified by means of biopsies. In addition, a quick test based on the detection of urase activity is also performed during OGD. This is termed Campylobacter-like organism test (CLO) which allows for H.pylori diagnosis within 24hours⁶. Urase, being a highly specific marker for H.pylori, makes the CLO test sensitivity at 98.2%. Biopsy specimens taken from the prepyloric antrum during OGD have the highest yield of H.pylori infection⁷.

H.pylori eradication treatment is based on triple therapy consisting of Proton Pump Inhibitor (PPI) and two antibiotics for a duration of 14 days. To achieve a high eradication rate, therapy should be based on antibiotic resistance profiles which is not available in this case. If the strain is susceptible to clarithromycin and to metronidazole, triple therapy (PPI, amoxicillin and clarithromycin) for 14 days is the preferred choice⁸.

Eosinophilic oesophagitis and eosinophilic gastritis were diagnosed from the biopsies taken during OGD. Eosinophilic gastritis typically presents with postprandial vomiting, abdominal pain, early satiety and failure to thrive. It is commonly localised to the antrum, fundus of the stomach in children and may be associated with increased levels of eosinophils in other parts of the GI tract. Eosinophilic gastritis may be associated with atopic features in around half of the patients affected and in children it is highly responsive to dietary restriction therapies⁹. On the other hand, eosinophilic oesophagitis rarely occurs in infants and is more often found in older children. It is typically a chronic condition and is treated with anti-reflux medications. It may be a common finding with eosinophilic gastritis and presents with similar

⁵Stadelmann O, Elster K, Stolte M, Miederer SE, Deyhle P, Demling L, Siegenthaler W. The peptic gastric ulcer--histotopographic and functional investigations. *Scand J Gastroenterol.* 1971;6:613–623.

⁶Sultan, M. (2018, February 18). Pediatric Helicobacter Pylori Infection Workup. Retrieved from: <https://emedicine.medscape.com>.

⁷Vincenzo De F, Bellesia A, Ridola L, Manta R, Zullo A. First-line therapies for Helicobacter pylori eradication: a critical reappraisal of updated guidelines. *Ann. Gastroenterol.* 2017; 30(4): 373–379. Published online 2017 Jun 1. doi: 10.20524/aog.2017.0166.

⁸Hsu PI, Wu DC, Chen WC, et al. Randomized controlled trial comparing 7-day triple, 10-day sequential, and 7-day concomitant therapies for Helicobacter pylori infection. *Antimicrob Agents Chemother.* 2014 Oct. 58(10):5936-42.

⁹Ko HM, Morotti RA, Yershov O, Chehade M. Eosinophilic gastritis in children: clinicopathological correlation, disease course, and response to therapy. *Am J Gastroenterol.* 2014 Aug. 109 (8):1277-85.

symptoms of irritability, vomiting, food refusal and abdominal pain. Reflux symptoms which persist despite treatment, may be a sign of allergic oesophagitis¹⁰.

Another possible explanation for her repeated vomiting is food protein intolerance causing food protein-induced allergy. Food protein intolerance presents within the first six months of life and is commonly due to cow's milk protein and/or soy protein intolerance. It also presents with gastrointestinal symptoms of vomiting and/or diarrhoea and may lead to weight loss, malabsorption and failure to thrive if untreated. The diagnosis is made clinically by exclusion, yet small bowel biopsies show mild villous injury with inflammatory infiltration whereas colonic specimens reveal crypt abscesses with diffuse inflammatory infiltrates. A differential diagnosis based on the biopsies is coeliac disease which in this case was found to be negative when blood sample tested for. Most cases of food protein intolerance are observed in infants younger than 3 months of age and protracted vomiting, 1-3 hours following feeds and/or diarrhoea 5-8 hours after feeds are the most common features¹¹.

In infants without lactose intolerance, breastfeeding is the first choice. The mother should eliminate cow's milk and products from her diet. Up to 50% of children affected by cow's milk protein intolerance may develop soy protein intolerance if they are fed with soy-based formulas, thus soy-based formulas are not used as treatment for cow's milk protein intolerance. Complete milk protein hydrolysates are used in infants who cannot be breastfed and partially hydrolysed formulas are contraindicated in infants with cow's milk protein intolerance. Sometimes intolerance to hydrolysed formulas may also develop and in such situation amino acid-based formulas containing vitamins and minerals are used instead¹².

Conclusion:

We report atypical case of coeliac disease associated with milk-protein intolerance in terms of age of presentation as well symptoms. The diagnosis was reached through multi-disciplinary effort involving both Paediatricians and surgical expertise. The patient in fact improved on formula milk based on corn starch and on hypoallergenic protein source (extensively hydrolysed casein) and in view of having a positive CLO test, the patient was treated with triple therapy. Further research through specialised paediatric multi-centres is required on the presentation of these conditions at a young age as well as on the pathophysiology of the combination of different conditions.

¹⁰Straumann A, Aceves SS, Blanchard C, Collins MH, Furuta GT, Hirano I. Pediatric and adult eosinophilic esophagitis: similarities and differences. *Allergy*. 2012 Apr. 67(4):477-90.

¹¹Järvinen KM, Nowak-Węgrzyn A. Food protein-induced enterocolitis syndrome (FPIES): current management strategies and review of the literature. *J Allergy Clin Immunol Pract*. 2013 Jul-Aug. 1 (4):317-22.

¹²Nocerino, A. (2017, October 20). Protein Intolerance Workup. Retrieved from: <https://emedicine.medscape.com>.



Figure 1: Endoscopic view taken during the patient's OGD showing erythematous inflamed pyloric aspect of the stomach.

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Patient consent:

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Conflict of interest:

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