Ménétrier's disease in a Saudi child

Fahad A. Alfares, MD, Emad M. Raddaoui, MD, Mohammad I. El-Mouzan, MD, FAAP, Abdullah A. Alangari, MD, FAAAAI.

ABSTRACT

يعتبر مرض "مينتريه" من أمراض الجهاز الهضمي النادرة عادة ما يصيب البالغين ونسبة ظهوره في الأطفال قليلة جداً. يتم تشخيص المرض بربط العلامات الإكلينيكية للمريض التي تتلخص بظهور آلام البطن مع استفراغ وتورم في كافة الجسم نتيجة لفقد البروتين. يتم ربط هذه العلامات مع التشخيص النسيجي لجدار المعدة الذي يظهر طيات عملاقة في قاع وجسم المعدة مع ضمور غدي للمعدة. في هذه المقالة نصف لأول مرة ظهور هذا المرض لطفل سعودي مع وجود دليل مصلي للإصابة بفيروس المضخم للخلايا (سايتوميقالو فايرس) في دم الطفل.

Ménétrier's disease is a rare form of acquired gastropathy that presents mostly during adulthood, but is extremely rare in children. It is a clinicopathological diagnosis that typically presents with abdominal pain, vomiting, and edema secondary to hypoalbuminemia. Endoscopy usually shows giant gastric mucosal folds, and gastric biopsy shows foveolar hyperplasia and decreased oxyntic glands. Here, we describe a 5-year-old boy from Saudi Arabia with typical presentation of Ménétrier's disease and serological evidence of acute cytomegalovirus infection.

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From the Departments of Pediatrics (Alfares, El-Mouzan, Alangari), Pathology (Raddaoui), College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Abdullah A. Alangari, Department of Pediatrics, College of Medicine, King Saud University, PO Box 2925, Riyadh 11461, Kingdom of Saudi Arabia. Tel. +966 506287276. E-mail: aangari@ksu.edu.sa

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Ménétrier's disease, also known as giant hypertrophic gastritis or hypoproteinemic hypertrophic gastropathy was first described in 1888. It is a rare form of acquired gastropathy that usually presents with abdominal pain, vomiting, and edema. It is characterized by hypoalbuminemia with an upper gastrointestinal endoscopic picture of giant folds in the gastric body and fundus, but antral sparing. Histopathology of the gastric mucosa typically shows foveolar hyperplasia (expansion of the superficial gastric mucus cells) and decreased or absent oxyntic glands (acid-producing parietal cells and pepsinogen-producing chief cells).[1] In adults, Ménétrier's disease has usually an insidious onset and progressive clinical course with considerable morbidity and mortality, and an increased risk of malignant transformation. On the other hand, Ménétrier's disease is extremely rare in children. It usually presents acutely, follows a benign course and most of the time resolves spontaneously.[2] Children with this disease frequently have history of a viral prodrome in the form of non-specific abdominal pain, vomiting, and anorexia. Facial and limb swelling is a consistent finding due to protein loss through the abnormal gastric mucosa. Only about 60 cases of Ménétrier's disease have been reported in children.[3] Ménétrier's disease is idiopathic, but few possible triggers have been suggested, most commonly cytomegalovirus (CMV) infection.[3] Here, we report a Saudi child with classical presentation of Ménétrier's disease and positive serology for CMV.

Case Report. A 5-year-old previously healthy boy, presented with 10 days history of periorbital and lower limb swelling associated with vomiting immediately after meals, abdominal pain mainly localized to the epigastrium, and progressive abdominal distention, with lethargy, and fatigability. There was no history of fever or preceding upper respiratory tract infection. The systemic review, past medical history, and family history were unremarkable. Vaccinations were completed as per local schedule. Physical exam revealed a stable child with a pulse rate of 95 beats/minute, respiratory rate of 32 breaths/minute, temperature of 36.9°C, and

blood pressure of 109/58 mm Hg. His height is 113 cm (25th centile), and he weighs 18 kg (10th centile). He had periorbital swelling and pitting edema on his legs. Abdominal exam showed no evidence of organomegaly but positive shifting dullness. There was no sacral or scrotal edema. Other systemic examination was normal. Complete blood count showed a white blood cell count of 12.1x10^9/L with a normal differential cell count, hemoglobin - 142 g/L, and platelets - 197 x10^9/L. Urinalysis was negative for protein. Serum electrolytes, urea, and creatinine were normal, as well as liver functions test. Albumin level was 11 g/L (normal: 30-50 g/L). Twenty-four hours urine collection revealed a total urine protein of 0.1 g/L (normal: 0.01-0.15 g/L). Abdominal ultrasound showed mild ascites. Upper gastrointestinal endoscopy showed hypertrophic gastric folds with erythematous mucosa. Histopathologic examination of a biopsy from the body of the stomach (**Figure 1** & **Figure 2**) showed hyperplastic mucosal surface epithelium with no evidence of metaplasia or malignancy, while a biopsy from the gastric antrum showed only mild chronic nonspecific gastritis. No *Helicobacter pylori* (*H. pylori*) like organisms were detected. Immunohistochemistry staining for CMV was negative. However, serum anti CMV IgM titer was 1:20, which is elevated. Symptoms spontaneously improved over the next few days and albumin level gradually increased reaching 19 g/l within 10 days. Repeated levels after 3 week and after 6 months were both normal.

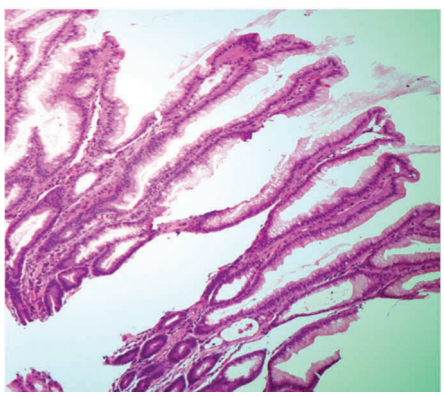

Figure 1 - Marked foveolar hyperplasia of the superficial gastric mucosa. Hematoxylin and Eosin staining. Original magnification x20.

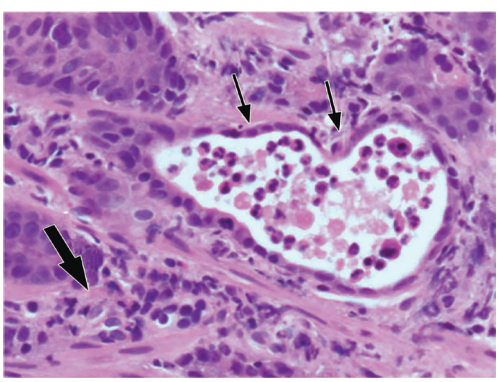

Figure 2 - Remarkable mixed inflammatory cellular infiltrate seen in both lamina propria (thick arrowhead) and within the stomach mucosal crypts (thin arrowheads). Hematoxylin and Eosin staining. Original magnification x400.

Discussion. Our reported patient had a classical presentation of Ménétrier's disease. He satisfied the main diagnostic features including hypoalbuminemia with evidence of giant gastric mucosal folds in the fundus and body with histologic features of foveolar hyperplasia.[4] Many modalities can be used to look for the thickened mucosal folds, including upper gastrointestinal contrast study, upper gastrointestinal endoscopy (like in our reported patient), or by CT scanning.[5]

Our patient had serological evidence of acute CMV infection. However, in the absence of immunohistochemical evidence of CMV in gastric biopsies, a cause and effect relationship to the child's presentation is hard to establish. The relationship between Ménétrier's disease and CMV infection has been described in children. In a review of 27 cases of childhood Ménétrier's disease, evidence of CMV infection was found in 19 children.[6] Other factors have been postulated to trigger Ménétrier's disease including *H. pylori*, protein milk allergy, or medications like prostaglandin E1.[7]

In most children, the disease resolves spontaneously and treatment is largely supportive, including adequate hydration and albumin transfusion. Some children, however, do not follow this course. In a case study, a child with atypical Ménétrier's disease was treated successfully with octreotide.[8] It has been demonstrated that there is overexpression of TGF-α by the gastric epithelium in patients with Ménétrier's disease. In addition, changes in the gastric mucosa similar to those in Menetrier's disease have been observed in TGF-α transgenic mice.[9] Treatment with cetuximab, a monoclonal antibody against epidermal growth factor receptor (EGFR), which is also a receptor for TGF-α, resulted in amelioration of symptoms, and almost normalization of gastric mucosa histological picture in 7 adults with the disease.[10]

In conclusion, Ménétrier's disease should be considered in children presenting with edema and hypoalbuminemia in whom renal and hepatic causes have been ruled out.

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