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Case Report

Ménétrier's Disease in A 5-Year-Old Girl without Cytomegalovirus Infection: Case Report

Nour A. Tashtush[1*]; Eyad M. Altamimi[1]; Abdelwahab J. Aleshawi[2]

[1]Department Pediatrics and Neonatology, Faculty of Medicine, Jordan University of Science & Technology, Irbid-22110, Jordan.

[2]Department of General Surgery and Urology, Faculty of Medicine, Jordan University of Science & Technology, Irbid-22110, Jordan.

Correspondence to: Nour A. Tashtush. Department of Pediatrics and Neonatology, Faculty of Medicine Jordan University of Science and Technology P. O. Box: 3030, Irbid-22110, Jordan; Tel: +962796562725; Fax: +962 2 7201064; Email: nour_abedtashtoush@yahoo.com

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ABSTRACT

A previously healthy 5-year-old girl presented with a 2-day history of abdominal distention and periorbital swelling. Physical exam showed periorbital edema, ascites and pitting lower limb edema. On investigations: her albumin was 15.6 g/l (38-54g/l), while her serum protein was 26.7g/l (60-80g/l). Abdominal CT scan showed moderately thickened rugal folds in both fundus and body of the stomach, ascites and bilateral pleural effusion. Upper endoscopy revealed giant gastric folds. Gastric biopsy demonstrated foveolar hyperplasia. The clinical presentation and work-up highly suggested a diagnosis of Ménétrier's disease. Ménétrier's disease is a rare form of idiopathic hypertrophic gastropathy. It is characterized by giant stomach rugae associated with hypoproteinemia and edema.

Keywords: *Cytomegalovirus; Gastroenteropathy; Protein-losing gastroenteropathy; TGFα.*

Abbreviations

CMV: Cytomegalovirus; EGFR: Epidermal Growth Factor Receptor; MD; Ménétrier's Disease; TGFα: Transforming Growth Factor-α.

INTRODUCTION

Ménétrier's Disease (MD), is a rare protein-losing hypertrophic gastroenteropathy. It is an acquired disorder characterized by giant gastric rugal folds in the body and fundus, decreased acid secretion, increased gastric mucus production, and hypoalbuminemia secondary to protein loss in the gastric mucosa. It affects men more frequently than women, and the typical age at diagnosis is between 30 to 60-years with a prolonged course of the disease.[1-3]

However, pediatric MD often presents as edema and hypoalbuminemia due to protein loss through the abnormal gastric mucosa and usually has a benign self-limited course with the acute symptoms resolve within 5-weeks.[4] Pediatric MD often linked to Cytomegalovirus (CMV) infection.[4] We present a case of a 5-year-old girl with a self-limited MD without evidence of acute (CMV) infection.

CASE PRESENTATION

A 5-year-old girl, not known to have any medical illness prior to her complaint, presented to our center complaining of abdominal distension for two days. One week prior to her presentation, she experienced facial puffiness that increased gradually over time with periorbital distribution, bilateral lower limb swelling, vomiting, and abdominal pain. Her mother documented a decrease in her activity and poor oral intake. No history of neonatal intensive care unit admission. No family history of liver or kidney diseases or any kind of malignancies. She had a normal physical development with regular growth curve.

On physical examination, a periorbital swelling without icteric sclera was disclosed. Also, soft abdominal distension that was dull on percussion with a positive transmitted thrill and shifting dullness was detected. Additionally, the examination revealed a pitting lower limb edema. She was pale with stable vitals.

Laboratory investigations were performed (summarized in Table 1). Complete blood count revealed a mild leukocytosis (11.1*10^3 /mm^3) with eosinophilia (7.5%) and monocytosis (6.30 %). While she had hypoalbuminemia (15.6 g/l) and hypoproteinemia (1.60 umol /l), liver panel, kidney function test, electrolytes, C-reactive protein, and erythrocyte sedimentation rate were within normal values. Coagulation profile was performed and showed prolonged prothrombin time (15.8 sec). Urine analysis yielded no proteinuria. Anti-tissue transglutaminase IgA was negative. In addition, IgM for CMV was not detectable.

Table 1. Laboratory investigations for the patient

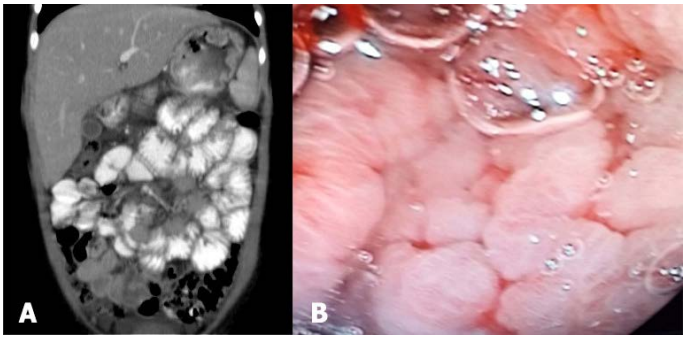
Complete Blood Count		Liver Function Test	
Wbc	11.10 10*3/mm*3, Abnormal (4.00-11.00)	Direct bilirubin	0.60 umol/l Normal Range: Neonates <10, infants/children<3.4, adults<=5
Hb	13.50 g/dl (11.20- 16.50)	Total Bilirubin	1.60 umol /l, abnormal (5.00-21.00)
Hct	41.00% (30.00-42.00)	Albumin	15.6 g/l, abnormal (38.0-54.0)
Rdw	15.00% (11.50 -17.00)	Total Protein	26.70 g/l, abnormal (60.00-80.00)
Rbc	5.26 10*6 /mm*3, abnormal (3.50-5.20)	Alanine Transaminase (ALT)	30.40 U/L, (0.0-33.0)
Platelets	477.0 10*6/mm*3, Abnormal (150.0-400.0)	Aspartate Aminotransferase (AST)	33.4 U/L, abnormal (0.0-32.00)
Mpv	8.10 um*3 (6.00-10.00)	Alkaline Phosphtase	75 U/L, abnormal (142-335)
Mcv	77.90 um*3, abnormal (78.00-100.00)	Gamma Gt	6.00 U/L (5.00-36.00)
Mch	25.70 pg, abnormal(27.00-35.00)	**Urine analysis**	
Mon%	6.30%, abnormal (2.00-6.00)	Amorphous Urate	Light
Neu%	44.50 %, abnormal (60.00-75.00)	Appearance	Clear
Bas %	0.30 % (0.00-1.00)	Color	Yellow
Eos %	7.50 %, abnormal (1.00-3.00)	EP.cells	Few
Lym%	41.40 % (20.00-45.00)	Mucus Threads	Moderate
Electrolytes		Protein in urine	Negative
Calcium	1.73 mmol /l, abnormal (2.20-2.70)	RBC	0-2
Sodium	137.00 mmol /l (135.00-153.00)	Reaction	7
Magnesium	0.81 mmol/l (0.70-0.95)	Urine Glucose	Negative
Phosphorus	1.63 mmol/l (1.05-1.80)	S.Gravity	1.0110
Potassium	4.20 mmol/l (3.10-5.10)	WBC	0-2
Serology test			
IGG1	1600.000 mg/l	**Coagulation profile**	
IGG2	153.000 mg/l	PT-INR	1.28
IGG3	109.000 mg/l	PT-SEC	15.80 second, abnormal (12.00-14.50)
IGG4	10.300 mg/l	Partial Thromboplastin Time	27.00 seconds, abnormal (29.00-35.00)
IgA	531.000 mg/l, abnormal (700.000-4000.000)	**Kidney function test**	
IgD	18.800 mg/l (1.300-152.700)	Creatinine	37.00 umol/l
IgG	1830.000 mg/l, abnormal (7000.000-16000.000)	Urea	2.80 mmol/l (1.79-6.43)
IgM	557.000 mg/l (400.000-2300.000)		
IgE	86 IU/ml Normal Ranges : Neonates : up to 1.5 Infants in 1st year of life : up to 15 Children aged 1-5 years : up to 60 Children aged 6-9 years : up to 90 Children aged from 10-15 years : up to 200 Adults : up to 100		
Anti-tissue Transglutaminase IgA	Negative: negative <10 Positive >=10	**Acute phase Reactant**	
		CRP	0.12 mg /l (0.00-5.00)
		ESR	2m/I hr (0-20)
CMV panel		**Additional tests**	
IgM CMV	Negative	Ceruloplasmin	1.20 mmol /l (1.20-3.38)

		Copper in serum	11.40 umol /l , (10.20-26.00) <4 mth : 1.4-7.2 umol/l 4-6 mth : 4-17 umol/l 6mth -13 yr : 8-19 umol/l Female 14-19 yr : 11-25 umol/l Male 14-19 yr : 10-18 umol/l Female adult : 12-24 umol/l Male adult : 11-22 umol/l
		Zinc level	7.00 umol/l <4 mth : 10-21 umol/l 4-12 mth : 10-20umol/l 1-5 yrs : 10-18 umol/l 6-9 yrs : 12-19 umol/l 10-13 years (male) : 12-15 umol/l 10-13 years (female) : 12-18 umol/l 14-19 years (male) : 10-18 umol/l 14-19 years (female) : 9-15 umol/l Adults : 7-23 umol/l
		Sudan 3	Negative

Abdomen–pelvic ultrasound yielded a significant amount of free fluid seen in Morrison pouch, sub-hepatic space & pelvis. Also, the homogenous surface of the liver with normal dimension was seen. The portal vein was patent with normal Doppler flow. Enhanced abdominopelvic CT was performed and revealed moderately thickening rugal folds of the stomach noted at the fundus and body. Also, moderate ascites was noted with thickening of valvulae conniventes and slightly thickened gallbladder wall with pericholecystic fluid Figure 1(A)

The decision was to go to for esophagogastroduodenoscopy (EGD) which revealed giant gastric folds and exaggerated rugation of the stomach on markedly edematous mucosal background Fig 1-B. Biopsy from stomach and duodenum was taken; the former revealed foveolar hyperplasia at the surface with some fragments showing some glandular atrophy accompanied by chronic active gastritis, while the latter showed variable villous abnormalities (intraepithelial lymphocytes). No Helicobacter Pylori colonization. The diagnosis of MD was established in Figure 1(B).

Figure I. A: Abdominal CT scan showed moderately thickened rugal folds in both fundus and body of the stomach, ascites and bilateral pleural effusion.
B: Upper endoscopy revealed giant gastric folds



The patient was admitted for 1 week of conservative management. She was commenced on IV vitamin K and albumin then discharged home proton pump inhibitor. Two months later, the patient was in a good condition with no ascites. EGD was performed which showed normal gastric folds. Previously noted giant folds at body and fundus resolved completely.

DISCUSSION

MD is a type of protein-losing gastroenteropathy characterized by gastric hypertrophy and hypoalbuminemia with resultant peripheral edema and, in severe cases, pleural or pericardial effusions. [2] MD was the first disease entity in which protein-losing gastroenteropathy was documented and quantitated.[5] In protein-losing gastroenteropathies there is an increase in intestinal leakage of plasma proteins into the GI tract due to a variety of causes including nearly all gastrointestinal diseases (Crohn's disease, celiac, Whipple's, intestinal infections, and so on) and a large number of non-gut conditions (cardiac and liver diseases, lupus, sarcoidosis, and so on).[6] Children with MD have a severe gastrointestinal protein loss with marked hypoalbuminemia. The disease is usually self-limited, and resolution of the clinical features is common within 6 weeks.[7] In contrast, adults MD is a chronic and more severe condition in most cases, often associated with gastrointestinal bleeding.[8]

Pathophysiologically, the strongest causative agent in pediatric cases of MD is acute CMV infection.[9-11] Overexpression of transforming growth factor-α (TGFα) in affected gastric mucosal cells has a crucial role in MD pathogenesis.[12] The overexpressed TGFα stimulates foveolar mucus cell proliferation with enhanced mucin secretion through enhancing signals to the epidermal growth factor receptor (EGFR).[12,13] In this process, CMV is considered to induce the overexpression of TGFα and sequentially activate EGFR signaling.[9,12,13] However, Son et al reported a case of MD without evidence of CMV infection.[14]

Clinically, patients can present with a history of a viral infection and a variety of clinical features including abdominal pain, weight loss, anorexia, nausea, vomiting, abdominal distention, GI bleeding, diarrhea, and dependent peripheral edema including periorbital swelling, lower limb edema, scrotal swelling in boys or even anasarca.[15] Radiologic findings in patients with pediatric MD are thickening of the gastric

rugae (folds) predominantly involving the fundus and often sparing the antrum.[8,16] However, in pediatrics, endoscopy with full-thickness biopsy remains the gold standard for this diagnosis.[16] In the presenting case, the patient presented with abdominal distention in association with periorbital swelling, lower limb edema, vomiting, and abdominal pain.

MD and eosinophilic gastrointestinal disorder (EGID) is the most common GI causes of protein-losing gastroenteropathy.[17] The differential diagnosis for MD includes lymphoma, gastric varices, Zollinger-Ellison syndrome, gastric involvement of Crohn's disease, multiple polyps, and eosinophilic gastritis.[16] In this case, while the endoscopic findings included giant rugal folds, we favored the diagnosis of MD based on the histological findings. Moreover, the disease course was relatively short and spontaneously remitted with only supportive care, compared to other severe aforementioned conditions.

Therapy in children is supportive and includes adequate hydration, histamine type-2 receptor antagonists or proton pump inhibitors, and albumin replacement.[3,4] Treatment of CMV, when detected, is usually associated with remission.[17] Also, Di Nardo et al reported pediatric MD case successfully treated with octreotide.[18]

We report yet a case of pediatric MD, in hope of expanding the knowledge of a rare occurrence and increasing the demand for further research about the etiology, clinical course and prognosis such disease. This case also highlights the importance of considering the diagnosis of MD in patients with a history of hypoproteinemia, edema, and abdominal symptoms.

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None.

ETHICS AND PATIENT CONSENT

Written informed consent was obtained from the patient for publication.

DISCLOSURE STATEMENT

This article has not been published or presented elsewhere in part or in entirely and is not under consideration by another journal. All authors have approved the manuscript and agreed with submission to your esteemed journal. There are no conflicts of interest to declare.

CONFLICTS OF INTEREST

We have no conflict of interests with no body and have nothing to declare.

REFERENCES

1. Ménétrier P. Des polyadenomes gastriques et de leurs rapport avec le cancer de l'estomac. *Arch Physiol Norm Pathol*. 1888; 1: 236-62.

2. Huh WJ, Coffey RJ, Washington MK. Ménétrier's Disease: Its Mimickers and Pathogenesis. *J Pathol Transl Med*. 2016; 50(1): 10-16. doi: 10.4132/jptm.2015.09.15

3. Scharschmidt BF. The natural history of hypertrophic gastrophy (Ménétrier's disease): Report of a case with 16 year follow-up and review of 120 cases from the literature. *Am J Med*. 1997; 63(4): 644-652. doi: 10.1016/0002-9343(77)90210-8

4. Blackstone MM, Mittal MK. The edematous toddler: A case of pediatric Ménétrier disease. *Pediatr Emerg Care*. 2008; 24(10): 682-684. doi: 10.1097/PEC.0b013e3181887e895

5. Citrin Y, Sterling K, Halsted JA. The mechanism of hypoproteinemia associated with giant hypertrophy of the gastric mucosa. *N Engl J Med*. 1957; 257(19): 906–912. doi: 10.1056/NEJM195711072571902

6. Greenwald DA. Protein-losing gastroenteropathy. In: Feldman M, Friedman LS, Brandt LJ, editors. Sleisenger and Fordtran's Gastrointestinal and Liver Disease. Vol 1. 10th ed. Philadelphia, PA: Saunders 2016; 464–447.

7. Chouraqui JP, Roy CC, Brochu P, Gregoire H, Morin CL, Weber AM. Menetriers's disease in children: Report of a patient and review of sixteen other cases. *Gastroenterology*. 1981; 80(5):1042-1047.

8. Baker A, Volberg F, Sumner T, Moran R. Childhood Menetrier's disease: four new cases and discussion of the literature. *Gastrointest Radiol.* 1986; 11(2) :131-134.

9. Hong J, Lee S, Shon Y. Ménétrier's disease as a gastrointestinal Manifestation of active cytomegalovirus infection in a 22-month-old boy: A case report with a review of the literature of Korean pediatric cases. *Clin Endosc*. 2018; 51(1): 89-94. doi: 10.5946/ce.2017.038

10. Yoo Y, Lee Y, Lee YM, Choe YH. Co-infection with cytomegalovirus and helicobacter pylori in a child with Menetrier's disease. *Pediatr Gastroenterol Hepatol Nutr*. 2013; 16(2): 123-126. doi: 10.5223/pghn.2013.16.2.123

11. Eisenstat DD, Griffiths AM, Cutz E, Petric M, Drumm B. Acute cytomegalovirus infection in a child with Ménétrier's disease. *Gastroenterology*. 1995; 109(2):592-595.

12. Dempsey PJ, Goldenring JR, Soroka CJ, et al. Possible role of transforming growth factor alpha in the pathogenesis of Menetrier's disease: supportive evidence form humans and transgenic mice. Gastroenterology. 1992; 103(6) :1950-1963.

13. Sferra TJ, Pawel BR, Qualman SJ, Li BU. Menetrier disease of childhood: Role of cytomegalovirus and transforming growth factor alpha. *J Pediatr*. 1996; 128(2): 213-219.

14. Son KH, Kwak JJ, Park JO. A case of cytomegalovirus-negative Menetrier's disease with eosinophilia in a child. *Korean J Pediatr*. 2012; 55(8): 293-296. doi: 10.3345/kjp.2012.55.8.293

15. Williamson K, Park HK, Schacht R, Kaistha A. A Case of Menetrier Disease in a Child. *Pediatr Emerg Care*. 2012; 28(3): 277-279. doi: 10.1097/PEC.0b013e31824957b8

16. Trout AT, Dillman JR, Neef HC, Rabah R, Gadepalli S, Geiger JD.

Case 189: Pediatric Menetrier disease. *Radiology*. 2013; 266(1): 357-361. doi: 10.1148/radiol.12111841

17. Umar SB, DiBaise JK. Protein-losing enteropathy: Case illustrations and clinical review. *Am J Gastroenterol*. 2010; 105(1): 43-49; quiz 50. doi: 10.1038/ajg.2009.561

18. Di Nardo G, Oliva S, Aloi M, et al. A pediatric non-protein losing Menetrier's disease successfully treated with octreotide long acting release. *World J Gastroenterol*. 2012; 18(21): 2727-2729. doi: 10.3748/wjg.v18.i21.2727