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CASE REPORT

Hyperplastic gastropathy as a presenting manifestation of systemic lupus erythematosus

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A patient is described who had severe hyperplastic gastropathy as the presenting manifestation of systemic lupus erythematosus (SLE). Aggressive immunosuppressive therapy with systemic corticosteroids and immunoglobulins resulted in complete remission of lupus, and a prompt clinical and radiological regression of hyperplastic gastropathy. Hyperplastic gastropathy is an uncommon gastric illness, which is usually idiopathic but rarely is associated with *Helicobacter pylori* infection, cytomegalovirus infection or lymphocytic gastritis. Three previous case reports have noted a response of idiopathic hyperplastic gastropathy to systemic corticosteroid treatment, yet none of the presented patients had a systemic inflammatory disease. The presented case is the first in the medical literature in which hyperplastic gastropathy is directly linked to the development of clinical and laboratory manifestations of SLE. We suggest that hyperplastic gastropathy be added to the list of rare gastrointestinal manifestations of SLE, and that autoimmune disease be considered a possible cause of hyperplastic gastropathy. As such, any patient with symptomatic idiopathic hyperplastic gastropathy accompanied by other evidence of systemic inflammation should be considered for SLE evaluation and immunosuppressive treatment. *Lupus* (2004) 13, 60–63.

Key words: antiphospholipid syndrome; hyperplastic gastropathy; Menetrier; systemic lupus erythematosus

Case report

A 25-year old Caucasian female was admitted for an evaluation of two weeks of nausea, low-grade fever and diffuse epigastric pain described as intense (9 on a 1 to 10 visual scale), nonradiating, and unaffected by eating or changing of posture. The patient noted no urinary symptoms, jaundice, vaginal discharge or shortness of breath. Empiric treatment with antacids and oral ranitidine was ineffective.

Past medical history was significant for the antiphospholipid syndrome, diagnosed a year earlier. It first manifested as a second trimester abortion, high titre of antiphospholipid antibodies and mild thrombocytopenia. Five months later she experienced pre-eclampsia and the HELLP syndrome during the 21st week of her second pregnancy, which necessitated its urgent

interruption. At that time she showed no evidence of any of the currently recognized hypercoagulable disorders other than the high titres of antiphospholipid antibodies and did not fulfill any of the clinical or laboratory criteria for systemic lupus erythematosus (SLE) or any other autoimmune disorders. She was started on treatment with enoxaparin, with no additional symptoms noted until her current admission. She did not use any other prescribed, over the counter or natural medications, or abuse illicit drugs or alcohol.

On admission the patient appeared ill, with normal blood pressure, temperature and arterial oxygen saturation, but with a tachycardia of 100 beats per minute. Physical examination was notable for pallor, a mildly distended abdomen, marked tenderness at the epigastric region and a palpable spleen; the rest of the examination was unremarkable.

The patient's laboratory results at admission are summarized in Table 1. Of note is the pancytopenia with negative haemagglutinin test and morphologically normal blood smears, the prolonged partial prothrombin time, which normalized after the addition of excess phospholipid, and the severe hypoalbuminemia. Chest

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Table 1 Laboratory results

Variable	Day of admission	Two months after discharge
ESR (mm/hr)	80	30
White cells (mm ³)	2900	7600
Differential count (%)		
Neutrophils	60	73
Lymphocytes	32	17
Monocytes	6	7
Eosinophils	1	0
Hgb (gram%)	9	9.4
Platelets (mm ³)	60000	288000
INR	1.4	2.9 (warfarin)
PTT	199	70
Urea (mmol/L)	1.8	3.6
Creatinine (mmol/L)	86	71
Protein (g/L)	64	72
Albumin	23	40
Globulin	41	32

ESR, erythrocyte sedimentation rate;

INR, international normalized ratio;

PTT, partial prothrombin time.

X-ray, electrocardiography and echocardiography were unremarkable. Microscopic examination of the urinary sediment was normal, and there was no proteinuria.

Blood, urine, sputum and faecal cultures for bacteria, mycobacterium, fungi and parasites were repeatedly sterile. Faecal ELISA assays for *Clostridium difficile* toxin were negative. Serology was negative for infection with Epstein-Bar virus, cytomegalo virus, syphilis, brucella, rickettsia, the human immunodeficiency virus and hepatitis A, B and C viruses.

Serum ferritin, iron, B₁₂ and folic acid were normal. Bone marrow biopsy showed a normal trilineal lineage, with no evidence of chromosomal translocations or monoclonal immunoglobulin gene rearrangement. Transvaginal ultrasonography was unremarkable.

Abdominal ultrasonography was normal. Abdominal CT angiography demonstrated a normal-looking, non-distended small and large bowel and patent mesenteric vessels with no evidence of abdominal lymphadenopathy, but revealed a mildly enlarged spleen and markedly thickened gastric folds, particularly along the lesser curvature and antrum of the stomach (Figure 1).

Autoimmune serology was positive for anti-nuclear antibodies (4/4), antiphospholipid antibodies, anti-β₂-microglobulin and anti-dsDNA antibodies (1:84). Cytoplasmatic and perinuclear anti-neutrophilic cytoplasmatic antibodies, cryoglobulins and rheumatoid factor were negative. No paraprotein was found in the patient's serum or urine.

Upper gastrointestinal barium swallow and passage series demonstrated severely hypertrophic gastric folds at the antrum and distal portion of the body of the stomach, highly suggestive of hyperplastic gastropathy (Figure 2). The gastric fundus was intact.

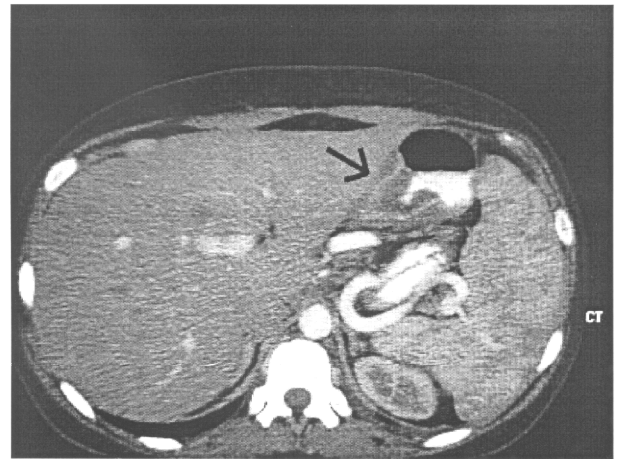


Figure 1 Computed tomography of the upper abdomen, with IV contrast injection, demonstrating markedly thickened antral wall (arrow). Note also enlargement of the spleen.

Endoscopy revealed a diffuse infiltrative mucosal process, extending throughout the gastric body and antrum, accompanied by markedly thickened and distorted, but not inflamed, gastric rugae. No evidence of gastritis or gastric ulcer was noted. Five gastric biopsies, including a snare biopsy, revealed extensive gastric pit hyperplasia and cystic dilatation, with foveolar cell hyperplasia, highly compatible with hyperplastic gastropathy (Figure 3). Very few *Helicobacter pylori* bacteria were noted, and there was no pathological evidence of gastritis, vasculitis or mucosal ischaemia. Duodenal biopsy was normal.

During the patient's hospitalization she suffered agonizing epigastric pain, necessitating the administration of escalating doses of narcotics (up to 150 μg transdermal fentanyl daily plus occasional extra

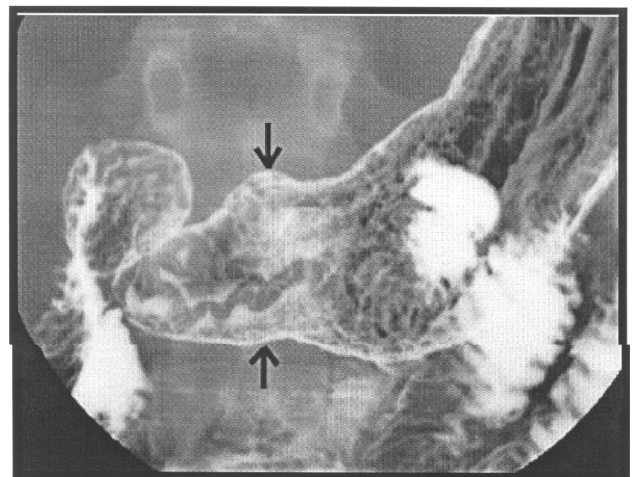


Figure 2 A barium meal showing coarse and thickened gastric folds along the antrum and lesser curvature (arrows).

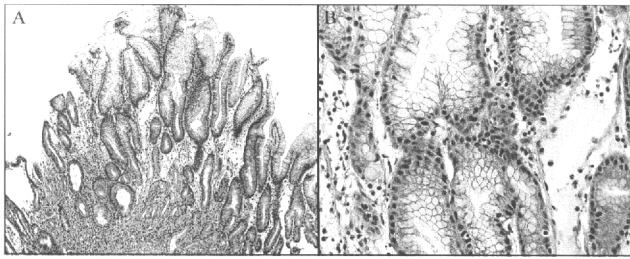


Figure 3 (A) Gastric biopsy showing gastric pit hyperplasia with cystic dilatation (H&E, $\times 100$); (B) Mucus-distended foveolar cells lining the hyperplastic pits (H&E, $\times 400$).

intravenous doses of fentanyl). Triple therapy for *H. pylori* with clarithromycin, metronidazole and omeprazole resulted in no improvement.

On the second week of hospitalization the patient developed a bilateral malar rash, an intense right-sided pleuritic chest pain, accompanied with a small amount of right pleural effusion. Electrocardiography, echocardiography, chest radiography and spiral CT scan showed no evidence of a pulmonary infiltrate, pulmonary thromboembolism or pericarditis. A repeated 24-hour urine collection and sediment examination showed proteinuria of 500mg per day and numerous red and white cell casts.

At that point it was clear that the patient had new onset SLE consisting of pleuritis, nephritis, pancytopenia and positive serology and hyperplastic gastropathy, possibly related to her lupus exacerbation.

Treatment with intravenous hydrocortisone (600mg daily) and immunoglobulins (30g daily for five days) was begun. The nausea and epigastric pain subsided within two days. Within a week she reached deffervescence and noted a complete resolution of her chest pain. She was rapidly weaned off the high-



Figure 4 A repeated barium meal after immunosuppressive therapy demonstrating a normal stomach.

dose narcotic treatment and oral corticosteroids were started (prednisone, 60mg daily). Her urinary sediment and blood counts normalized within a few more days, while her albumin levels normalized after two months (Table 1).

Upon discharge the patient was treated with oral azathioprine (50mg daily), and began to slowly wean off steroids. After six months of follow-up she was totally asymptomatic, with completely normalized blood counts, sedimentation rate, albumin levels and urinary examination. A repeated barium swallow revealed a normal stomach with complete resolution of gastric fold hypertrophy (Figure 4).

Discussion

Menetrier's original description of epigastric pain, weight loss, anorexia and protein-losing enteropathy, associated with thickened gastric folds due to foveolar hyperplasia and glandular atrophy, is currently named hyperplastic gastropathy. This condition is at times linked to several other entities, including *H. pylori* gastritis,¹ cytomegalovirus infection in children² and lymphocytic gastritis.³

Treatment, with antacids, anti-cholinergic drugs, H₂ blockers and proton-pump inhibitors is disappointing, shown to be effective in only a minority of patients.⁴ Experimental treatment with octreotide⁵ and anti epidermal growth factor receptor antibodies⁶ has been recently suggested to be of some therapeutic value, while intractable symptoms may even require total gastrectomy.

Three previous reports of patients suffering of idiopathic hyperplastic gastropathy have noted a therapeutic response to empiric systemic corticosteroid treatment.⁷⁻⁹ In one of the described cases⁹ it was suggested that a nonspecific autoimmune response was associated with the development of hyperplastic gastropathy. These reports, along with the presumed involvement of transforming growth factor α in the pathogenesis of hyperplastic gastropathy¹⁰ may suggest that, at least in some patients, an inflammatory component may exist as part of its pathogenesis. As seen in our patient, hyperplastic gastropathy may indeed be at times part of a systemic multi-organ inflammatory disorder, and as such may promptly respond to anti-inflammatory treatment.

Although a few rare *H. pylori* bacteria were noted in our patient's gastric biopsy specimens, there was no evidence of acute or chronic gastritis, which is uniformly present in all previously reported cases of *Helicobacter*-related hyperplastic gastropathy. Furthermore, the patient's agonizing abdominal pain, protein-losing enteropathy and marked gastric fold thickening

did not improve after *H. pylori* eradication, while dramatically improving days after the institution of high-dose steroid therapy directed at SLE.

In conclusion, we suggest that hyperplastic gastropathy be added to the list of rare gastrointestinal manifestations of SLE, and that autoimmune disease be considered as a possible cause of hyperplastic gastropathy. As such, any patient with symptomatic idiopathic hyperplastic gastropathy accompanied by other evidence of systemic inflammation should be considered for SLE evaluation. Treatment of hyperplastic gastropathy in such a patient, as in other systemic manifestations of lupus, may include corticosteroids or intravenous immunoglobulin.

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