Primary gastric lymphoma and Helicobacter pylori infection with gastric amyloidosis

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Primary gastric lymphoma, an uncommon gastric tumor caused by infection with Helicobacter pylori, is rarely associated with gastric amyloidosis. Chronic bacterial infection is known to cause amyloidosis. We report a 53-year-old man who had an antral and duodenal mass with narrowing and ulceration on endoscopy and CT scan; endoscopic biopsy revealed gastric amyloidosis. Rapid urease test and serology for H. pylori were positive. Histology of resected specimen of distal stomach revealed primary gastric lymphoma, amyloid deposits and spiral organisms suggestive of H. pylori. Rectal biopsy was negative for amyloid. He remained well on follow-up after surgery and eradication of H. pylori. [Indian J Gastroenterol 2005;24:220-221]

Primary gastric lymphoma (PGL) accounts for 1%-5% of malignant tumors of the stomach.1 Most PGL arise from the B cells of the mucosa-associated lymphoid tissue (MALT), commonly in association with chronic Helicobacter pylori infection.1 Amyloidosis is characterized by deposition of extracellular, dense, acellular, congophilic material secondary to chronic infection, inflammation or malignancy.2,3 Non-Hodgkin lymphomas, including extranodal MALToma, have been rarely reported to present with amyloidosis.4,5,6

A 53-year old man presented with dyspepsia since one year, increasing since 3 months. He complained of anorexia and had lost 5 Kg weight during the last 3 months. He reported having occasional vomiting and melena for one week before presentation. He had received multiple courses of proton-pump inhibitors during the last year.
without significant relief. He had no history of hematemesis, jaundice, fever or dysphagia. Physical examination revealed mild pallor, and succussion splash over the epigastrium; rest of the clinical examination was unremarkable.

Upper GI endoscopy revealed a large, irregular, nodular ulcer with few satellite ulcers in the incisura, with surrounding nodularity. The endoscope could not be negotiated into the duodenum. Contrast-enhanced CT scan revealed ill-defined nodular thickening of the gastric antrum and proximal duodenum causing circumferential narrowing with proximal gastric dilatation. No lymphadenopathy, hepatic metastasis or involvement of adjacent organs could be detected. Hemoglobin was 9.1 g/dL and ESR was 54 mm in first hour; renal and liver function tests were within normal limits. Serum was positive for anti-\textit{H. pylori} IgG and anti-CagA IgG antibodies. Histology of gastric biopsies revealed focal ulceration of the gastric mucosa with dense infiltration of the lamina propria by mixed inflammatory cell infiltrate and focal perivascular deposits of acellular congophilic material that showed apple-green birefringence on polarizing microscopy.

With a diagnosis of gastric amyloidosis, distal radical gastrectomy with Billroth I reconstruction was performed. At surgery, a growth measuring 5 cm in diameter was detected in the region of the incisura extending into the posterior wall, with a satellite lesion about 7 cm proximal to the first growth. There were enlarged perigastric lymph nodes around the right gastro-epiploic and left gastric arteries. Serum electrophoresis revealed a normal pattern and urine was negative for Bence-Jones protein; 24-h urinary protein excretion was normal. Skeletal survey and bone marrow biopsy were normal. Rectal biopsy was negative for amyloid. Electrocardiogram and echocardiogram were normal.

Examination of the resected stomach revealed normal serosa. Cut section showed ulceration, hyperemia and nodular thickening of the antrum. The ulcer bed was lined by necrotic debris with dense infiltration of the underlying lamina and submucosa by sheets of plasma cells, plasmacytoid lymphocytes, and small to medium-sized lymphoid cells with round to irregular nuclei and scant cytoplasm, with formation of lymphoid follicles in places (Fig). The infiltrating cells formed lymphoepithelial lesions. The muscular coat and serosa were spared. Admixed with this infiltrate was deposit of acellular amorphous congophilic material (KMnO$_4$ resistant), displaying apple-green birefringence on polarizing microscopy. The mucosal and submucosal blood vessels showed myxoid degeneration and similar congophilic deposits in the wall; immunohistochemistry revealed \textit{kappa} light chain. The adjacent mucosa showed presence of few spiral organisms consistent with \textit{H. pylori}. Sections from the lymph nodes showed no lymphomatous infiltrate.

A diagnosis of gastric low-grade marginal-zone B-cell lymphoma of MALT type (stage EI disease, Musshof modification of Ann Arbor classification), with amyloidosis and \textit{H. pylori} infection was made. The patient received 4 drugs (tetracycline, amoxycillin, clarithromycin and lansoprazole) for two weeks to eradicate \textit{H. pylori}. Endoscopy after 3 months documented eradication of \textit{H. pylori} (negative rapid urease test and histology).

Two and half years after surgery, the patient is asymptomatic and has gained 6 Kg weight. Repeat endoscopic biopsies from the remnant stomach at 6-monthly intervals after surgery showed no evidence of malignancy. A follow-up contrast-enhanced CT scan done 18 mo after surgery showed no thickening of the remnant stomach or lymphadenopathy.

Association of extranodal MALToma with amyloidosis has been reported uncommonly.\textsuperscript{4,5,6} The site of origin of MALToma has ranged from stomach and large intestine to lungs and thymus. Goteri \textit{et al}\textsuperscript{4} reported 3 patients with gastric MALToma-associated localized amyloidosis. Our patient had PGL with gastric amyloidosis of AL type. Presence of amyloid deposits in close proximity to a MALToma has been reported in literature and their origin has been attributed to lymphoma.\textsuperscript{4,5,6}

With the initial identification of amyloid deposits in the endoscopic biopsy in our patient, the PGL might have been missed. Since gastric lymphomas arise from the submucosa they might not be picked up on superficial endoscopic biopsies. Thus, the presence of amyloidosis in biopsies from an ulcer should prompt a search for an underlying lymphoma. The presence of \textit{kappa} light chain on immunohistochemistry of gastric tissue in our patient suggests that the amyloid deposit was primary. Since evaluation and follow-up did not reveal plasma cell dyscrasia, the AL amyloid in gastric tissue may be attributed to PGL than to chronic infection with \textit{H. pylori}. 

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\textsuperscript{4}Indian Journal of Gastroenterology 2005 Vol 24 September - October 221
A striking feature of gastric and extragastric MALToma-associated amyloidosis has been the presence of marked plasma-cell differentiation of the malignant cells.\textsuperscript{4,5,6} Moreover, in the reported cases of NHL-associated localized or systemic amyloidosis the underlying lymphoma has always been the lymphoplasmacytic variant.\textsuperscript{7} Plasma-cell differentiation is a feature of 30% of gastric MALTomas.\textsuperscript{1} Our patient also showed a prominent plasma-cell differentiation of the tumor. Since it is known that plasma cells seen in MALTomas could be monoclonal tumor cells or polyclonal reactive cells,\textsuperscript{1} it is tempting to speculate that amyloidosis occurs in only those tumors where the monoclonal malignant plasma cell secretes an amyloidogenic light chain. Cohen \textit{et al}\textsuperscript{7} had reported the presence of amyloidogenic germline Ig $V_L$ gene rearrangement in 6 cases of NHL-associated systemic amyloidosis.

In summary, the association of \textit{H. pylori}-associated PGL with amyloidosis is rare. Superficial endoscopic biopsies can miss underlying lymphoma; the presence of amyloidosis should prompt a search for underlying PGL. PGL is a known complication of chronic \textit{H. pylori} infection and has been implicated in localized gastric amyloidosis.\textsuperscript{3,4}

\textbf{References}


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\textbf{Acknowledgement:} This work was supported by a grant from the Indian Council of Medical Research to UCG (No. 5/4/3-5/03/99-NCD-II)

\textbf{Received February 9, 2005. Accepted March 26, 2005}