Tumor-associated gastroparesis, though reported in association with various malignancies, is rare in patients with cholangiocarcinoma. We report a 55-year-old woman who presented with dysphagia and recurrent vomiting. Esophagogastrroduodenoscopy revealed dilated stomach and excess residue without organic obstruction. $^{99m}$Tc sulfur colloid solid gastric emptying study, radio-opaque marker gut transit study, and esophageal manometry showed features suggestive of gastroparesis and achalasia cardia; electrogastrography revealed bradygastria. Cholangiocarcinoma was detected on CT scan performed after the patient developed jaundice two months later. The lesion was deemed surgically unresectable. She died four months later. [Indian J Gastroenterol 2005;24:167-168]

Visceral and somatic neuropathy and myopathy are known paraneoplastic manifestations of various malignancies. Gastroparesis, which results from neuromyopathy of stomach, is rarely reported in pancreatobiliary malignancies.\(^1\)^\(^2\)^\(^3\) Gall bladder carcinoma and cholangiocarcinoma have been described to be associated with gastroparesis.\(^3\)^\(^4\) We report the second patient in literature with cholangiocarcinoma presenting with symptomatic gastroparesis and pseudoachalasia.

**Case Report**

A 55-year-old woman presented with epigastric fullness and discomfort, prolonged satiety, nausea, recurrent vomiting (sometimes bilious), mild diffuse non-colicky abdominal pain, and constipation for 5 months. She complained of non-progressive dysphagia both to solids and liquids for three months. She lost 7 Kg weight in the last 5 months. She underwent cholecystectomy for symptomatic gallstones and hysterectomy for uterine fibroids 14 and 9 years ago, respectively. She was non-diabetic and was not on any drugs that can delay gastric emptying. Physical examination was unremarkable except for mild pallor. Abdominal ultrasonography done elsewhere showed no abnormality except dilated stomach.

**Investigations:** hemoglobin 10.8 g/dL (normal >13), normocytic-normochromic red blood cells; normal leucocyte and platelet counts; ESR 41 mm in first hour (normal 0-20); prothrombin time 13.6 seconds (control 11.8); normal serum creatinine, sodium, potassium, calcium, phosphorus, magnesium, T4, TSH, blood sugar, total serum proteins and albumin, bilirubin, AST and ALT; serum alkaline phosphatase was 741 IU/L (normal 35-150). Antinuclear antibody was negative. Urine examination and chest x-ray were normal. Esophagogastrroduodenoscopy showed dilated stomach with excess food residue but no organic obstruction; duodenal biopsy histology was normal. Electrocardiography based autonomic function tests (Valsalva, expiration-inspiration ratio, cold pressor tests) were normal.

$^{99m}$Tc sulfur colloid solid gastric emptying study (using chatapi), which has been validated previously in our center,\(^7\) revealed a flat time-activity curve; the calculated T$_c$ was grossly prolonged (160.5 min, normal 59 to 109 min). Colonic transit study using radio-opaque markers (Sgmark; Indus Medical Innovations, Kolkata) was performed utilizing a modified protocol suitable for Indian subjects\(^6\) (20 markers each given at time 0 h, 12 h, 24 h, and abdominal radiographs taken at 36 h and 60 h). Most of the markers were retained in the stomach even at 60 h. Abdominal radiograph 3 weeks later showed most of the markers still lying in the stomach. On barium meal follow-through study, the stomach was dilated, retained most of the barium even 24 hours after ingestion, and small bowel was opacified on day 5 after ingestion. Antroduodenal manometry could not be performed as the catheter could not be negotiated into the duodenum. Esophagel manometry using a water perfusion system (Redtech, Calabasas, CA, USA) showed aperistalsis of esophageal body; lower esophageal sphincter pressure was raised (43 mmHg). These findings were suggestive of achalasia cardia. Cutaneous electrogastrography (EGG) recording (Redtech, Calabasas, CA, USA) over 90 min (fasting record 59 min and post-prandial 31 min) showed 40% bradygastria and 3% tachygastria (mean frequency 2.5 cpm; Fig), suggesting an abnormal EGG.\(^7\) She was prescribed low-roughage diet and prokinetic drugs for gastroparesis.

Two months later she developed deep jaundice, lost more weight, and anorexia and vomiting increased; she was admitted with dehydration and pre-renal failure. Examination revealed dehydration, pallor, jaundice, ascites and succussion splash. Liver function tests showed serum bilirubin 18.5 mg/dL, AST 79 IU/L, ALT 80 IU/L and alkaline phosphatase 1444 IU/L. Ultrasonography showed focal intrahepatic biliary radical dilatation in the left lobe of liver with isolation of segments 3 and 4, focal dilatation of right posterior segmental duct, thrombosis of left branch of portal vein, and free fluid. Contrast-enhanced CT scan confirmed these findings and also showed an ill-defined mass lesion in the left main hepatic duct suggestive of cholangiocarcinoma.

Ascitic fluid analysis showed a high serum-to-ascitic fluid albumin gradient (3.7 and 2.1 g/dL, respectively), total cell count...
of 150/mm³ with lymphocytic predominance, adenosine deaminase 22 U/L, and cytology for malignant cells negative thrice. The lesion was deemed surgically unresectable. Nasojejunal feeding resulted in symptoms and signs of intestinal obstruction and multiple air-fluid levels on abdominal radiograph. Hence, she was managed with parenteral nutrition. Her relatives refused further invasive tests to confirm the diagnosis of malignancy. She died within four months.

Though tumor-associated gastroparesis has been described in association with several malignancies,1-4,8 only one case associated with cholangiocarcinoma has been reported in the literature till date.4 These authors described a patient who presented with progressive dysphagia and symptomatic gastroparesis, and was found to have cholangiocarcinoma (on CT scan) which had extended to the gastroesophageal junction and lesser curvature of stomach. Esophageal manometry and barium swallow were suggestive of achalasia cardia. They postulated that the constricting tumor at the gastroesophageal junction with probable invasion of vagus nerves might have led to features of achalasia and gastroparesis. Autoimmune impairment and destruction of the enteric nervous plexus have recently been shown to play a role in the pathogenesis of paraneoplastic gastrointestinal motility disorders.9,10 Since our patient did not have infiltration of the gastroesophageal junction by the tumor, paraneoplastic autonomic neuropathy is a likely pathogenesis. More diffuse gut involvement including of the small intestine, supports our contention. Absence of severe symptoms of intestinal dysmotility, except constipation at presentation, might be explained by buffering effect of delayed emptying of foods and liquids from the stomach to the intestine before starting nasojejunal feeds.

The present case highlights that gastroparesis without an obvious cause, particularly in the elderly, may be a paraneoplastic manifestation of internal malignancy. Cholangiocarcinoma should be included in the list of occult neoplasms that can present with gastroparesis and secondary achalasia, as in our patient.

References


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