Gastric adenocarcinoma occurring in a young patient with common variable immunodeficiency syndrome

Yap Y L, So J B Y

ABSTRACT

Patients with common variable immunodeficiency syndrome (CVID) have an increased risk of gastric adenocarcinoma. We describe a case of gastric adenocarcinoma in a 29-year-old man with CVID. He complained of dyspepsia and weight loss. Endoscopy showed an antral lesion. He underwent subtotal gastrectomy with postoperative adjuvant chemoradiation, and remained disease-free for three years. CVID is a predisposing factor for gastric adenocarcinoma. Gastric complaints are common among these patients and should be viewed seriously. Endoscopy is performed to detect any pathology. Premalignant conditions like chronic atrophic gastritis, intestinal metaplasia and dysplasia require regular endoscopic surveillance in these high-risk patients.

Keywords: B-cell deficiency, common variable immunodeficiency syndrome, gastric adenocarcinoma, hypogammaglobinaemia

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INTRODUCTION

Patients with common variable immunodeficiency syndrome (CVID) have an increased risk of malignancy, including gastric adenocarcinoma. Gastric complaints are very common among these patients and should be viewed seriously. We describe a case of gastric adenocarcinoma in a young CVID patient, who presented with dyspepsia. Endoscopy was performed to investigate his complaint. In these high-risk patients, premalignant conditions like chronic atrophic gastritis, intestinal metaplasia and dysplasia require regular endoscopic surveillance.

CASE REPORT

Our patient was a 29-year-old Chinese man with CVID on follow-up with a rheumatologist. He required a monthly infusion of intravenous immunoglobulins. On one of his visits, he complained of symptoms of dyspepsia, early satiety as well as a loss of weight of about 4 kg over a two-month period. He was given omeprazole but the symptoms did not improve. A gastroscopy (Fig.1) was done to investigate these complaints. An antral pyloric mass causing pyloric stenosis was seen on endoscopy, and biopsies of the mass were taken. Histology showed poorly-differentiated adenocarcinoma with signet ring cells in a background of chronic gastritis with intestinal metaplasia (Fig. 2). No *Helicobacter* (*H.*) *pylori* was present. Staging computed tomography (CT) (Fig. 3) showed circumferential thickening of the pylorus with no serosal involvement or distant spread.

The patient underwent a D2 subtotal gastrectomy. Intraoperatively, there was a bulky pyloric mass adherent to the pancreatic head, with an enlarged peripancreatic lymph node. No liver metastasis or peritoneal disease was present. Following subtotal gastrectomy, a Roux-en-Y retrocolic gastrojejunostomy with a functional end-to-end jejunojejunostomy was performed. His postoperative course was uneventful, and he was discharged well on the eighth postoperative day. Histology was that of the diffuse invasive type of adenocarcinoma. According to the Lauren classification, the pathological staging was T3N2M0 with nine out of 33 nodes involved. The resection margin of the specimen (Fig. 4) was not involved. The peritonaeal lavage fluid did not reveal any malignant cells. He had adjuvant chemoradiation and has remained disease-free for three years to date.

DISCUSSION

CVID is an immunodeficiency disease characterised by B-cell deficiency, leading to hypogammaglobinaemia, mainly IgG and IgA. It is the most common form of hypogammaglobinaemia. The mean age of diagnosis is 29 years for males and 33 years for females.[1] Patients tend to present with frequent, recurrent bacterial infections by encapsulated pathogens like *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Haemophilus influenzae*. It is unknown what triggers off the condition. Possible causes include infection, drugs and a genetic predisposition. Autoantibodies then develop against normal blood, leading to lymphoid neoplastic crowding, and subsequently abnormal B cells, defective

Department of Surgery, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074

Yap YL, MBBS, MMed, MRCSE
Registrar

So JBY, FRCSE, FRCS, FAMS
Senior Consultant

Correspondence to:
Dr Yap Yan Lin
Tel: (65) 6772 4240
Fax: (65) 6777 8427
Email: yapyanlin@yahoo.com.sg

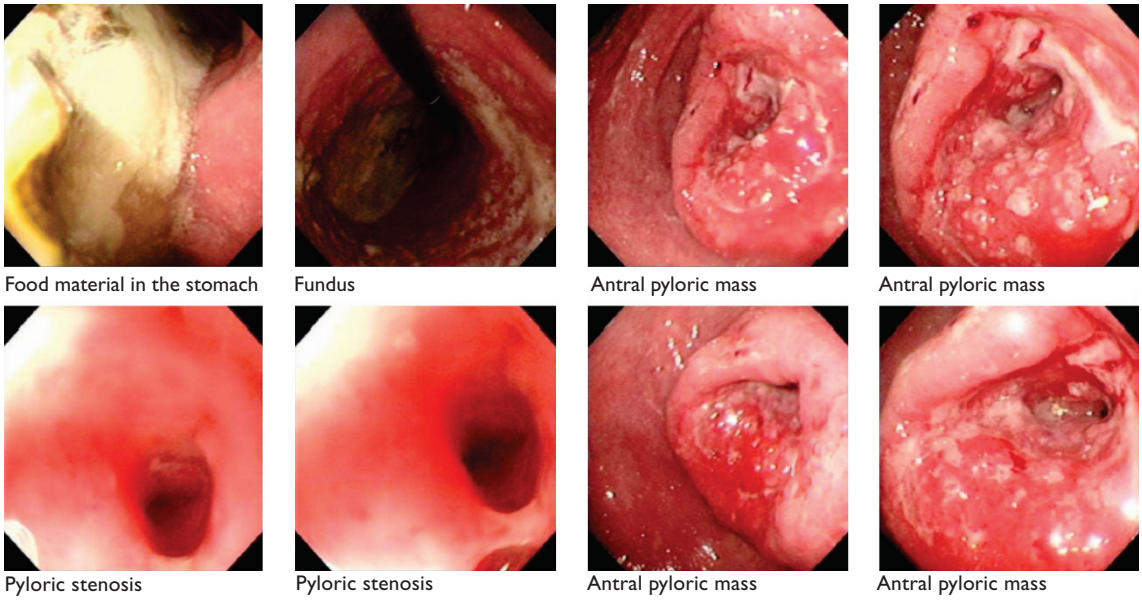

Fig. 1 Endoscopic photographs show pyloric stenosis with antral ulcer.

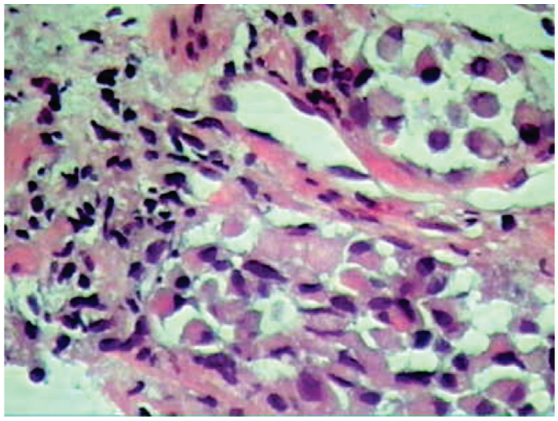

Fig. 2 Photomicrograph shows poorly differentiated adenocarcinoma with signet ring cells (Haematoxylin & eosin, × 400).

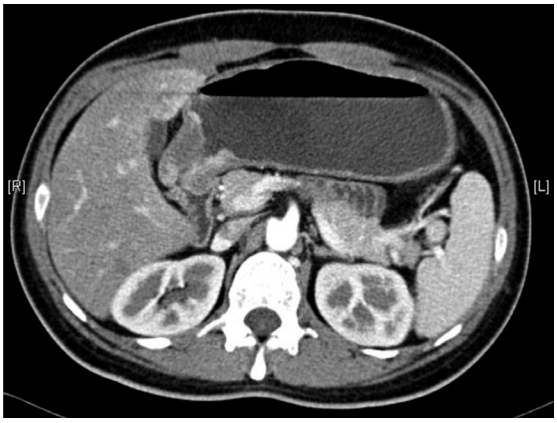

Fig. 3 Staging axial CT image shows antral thickening.

immmunoglobulin production and the impairment of T-cell function. Patients require monthly administration of intravenous immunoglobulins. The 20-year survival rate after diagnosis of this condition is 64% for males and 67% for females.

Patients with CVID are at an increased risk of malignancy, especially lymphoma and gastric cancers. In a combined Danish and Swedish study of the cancer risk in 176 patients with common variable immunodeficiency, it was found that the incidence of cancer at all sites combined was increased. This was due mainly to significant excesses of malignant lymphoma and stomach cancers. However, there was no increase in the level of risk among the 626 relatives of the patients.[2] The absence of an increased risk in the family suggests that the increased cancer incidence in patients was related to immunodeficiency, rather than the genetic traits shared with relatives. Adenocarcinoma of the stomach in CVID has been reported as early as 1978.[3]

A case of multifocal adenocarcinoma in an 11-year-old child with CVID was reported in 1988.[4] Clinicians should recognise that the average age of onset of gastric carcinoma in patients with CVID may be earlier than in those without immunodeficiency (50 years vs. 67 years). In a prospective study of cancer in patients with hypogammaglobinaemia by Kinlen et al, there was a five-fold increase in cancer in 220 patients with CVID. This was due mainly to large excesses of stomach cancer (47-fold) and lymphomas (30-fold).[5]

Gastric cancer is a result of an interaction between environmental factors and genetic predisposition. The role of *H. pylori* as an environmental factor in gastric cancer is of current interest. Zullo et al published a study that focused on the gastric pathology of patients with CVID

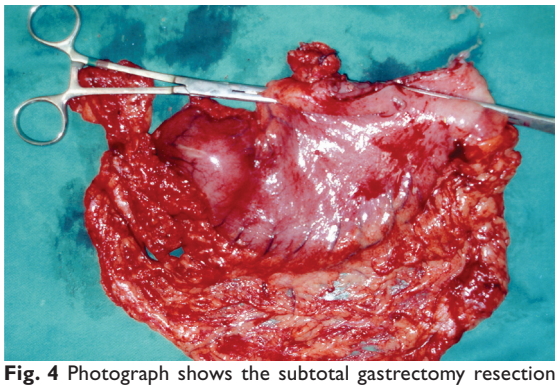

Fig. 4 Photograph shows the subtotal gastrectomy resection specimen.

and its correlation with *H. pylori* infection. *H. pylori* infection was detected in 41% of the patients. Chronic active gastritis involving both the antrum and the body was also observed more frequently in *H. pylori*-positive (79%) than in *H. pylori*-negative patients (20%).[6] Histological features of multifocal atrophic gastritis were found in the infected patients. It is hypothesised that *H. pylori* plays a role in the gastric carcinogenesis of patients with CVID. Chronic atrophic gastritis with or without pernicious anaemia is a common finding that predisposes patients to gastric adenocarcinoma.[7] It is also linked to mucosal-associated lymphoid tissue lymphoma. Gastric hormones like gastrin, somatostatin and gastrin-releasing peptide were studied in 47 patients with antibody deficiency. Baseline gastrin levels were normal or increased, compared to controls with an absence of a normal response of gastrin to a hyperproteic diet. Serum somatostatin and gastrin-releasing peptide (GRP) levels were higher than normal. However, there is no correlation between this finding and the clinical manifestation.[8]

Gastric symptoms are common in CVID patients who receive steroids for treatment. These symptoms usually improve with medical therapy. The lack of improvement and persistence of these symptoms should alert the clinician to a more sinister cause like malignancy. We recommend early investigation with gastroscopy in CVID patients, including in young patients, in view of the high incidence of gastric adenocarcinoma and lymphoma in these patients. Premalignant lesions observed on gastroscopy, like chronic atrophic gastritis, intestinal metaplasia and dysplasia, require regular follow-up as they can develop into carcinoma later.

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