Second case report of a metachronous double primary gastric cancer

Introduction

The development of metachronous histologically different neoplasms in a single organ is very rare. Synchronous multiple gastric tumours have been reported infrequently (Kaffes et al, 2002; Tang et al, 2002) and there have been a few case reports of patients developing early gastric cancer up to 5 years after remission of gastric lymphoma of mucosa-associated lymphatic tissue (MALT)-type (Morgner et al, 2001). However, the association of a gastric non-Hodgkin's lymphoma and subsequent gastric adenocarcinoma has only been reported once in the literature (Garcia et al, 1990).

This article presents the second case report of a patient who developed a metachronous primary gastric adenocarcinoma 2 years following successful treatment of a gastric non-Hodgkin's lymphoma by chemotherapy.

Discussion

The stomach is the most common site of extranodal non-Hodgkin's lymphoma (Wainess et al, 2003). However, compared to the incidence of gastric adenocarcinoma, gastric non-Hodgkin's lymphoma is rare, representing only 2–8% of all gastric malignancies. The occurrence of synchronous gastric lymphomas and gastric adenocarcinomas has been reported infrequently. In contrast, the finding of a metachronous gastric lymphoma and a gastric adenocarcinoma is a very rare finding.

This case report is only the second reported case of a metachronous second primary gastric adenocarcinoma following successful treatment of a gastric non-Hodgkin's lymphoma. The first report of such an association came from a Spanish group in 1990 (Garcia et al, 1990). Their patient initially underwent a subtotal gastrectomy on diagnosis of a gastric non-Hodgkin's lymphoma, followed by a course of radiotherapy. The patient subsequently developed a metachronous primary adenocarcinoma at the gastro-jejunal anastomosis. Morgner et al reported three cases of early gastric adenocarcinoma developing 4 and 5 years after complete remission of B cell lymphoma of MALT type (Morgner et al, 2001).

Helicobacter pylori infection is associated with chronic atrophic gastritis, and patients with a history of prolonged gastritis have a six-fold increase in their risk of developing gastric cancer. Gastric non-Hodgkin's lymphomas arise submucosally, originating from the lymphoid tissue in the lamina propria. Most cases develop in patients with gastric damage such as chronic gastritis and pseudolymphomatous lesions (Guindi, 1999). This patient was initially found to be *H. pylori* positive but this was successfully eradicated. It may

Case Report

A 72-year-old man was referred to the authors' hospital in December 1999 with a 2–3-month history of dyspepsia, abdominal bloating and loss of appetite. Upper gastrointestinal endoscopy with biopsy revealed a moderate active atrophic gastritis with widespread intestinal metaplasia. Gastric biopsies also showed the presence of *Helicobacter pylori* which was subsequently treated with standard triple therapy. His symptoms improved with *H. pylori* eradication treatment and a subsequent 6-month follow-up endoscopy with biopsy showed no evidence of residual gastritis or *H. pylori* infection.

He re-presented with similar symptoms 18 months later and a repeat upper gastrointestinal endoscopy showed a diffuse lesion in the gastric fundus. Histological biopsy showed features consistent with a high-grade diffuse non-Hodgkin's lymphoma of the stomach (*Figure 1*). There was no evidence of further *H. pylori* infection.

A subsequent staging whole body computed tomography scan and laparoscopy revealed no other lymphoid tissue involvement. Omental biopsies undertaken at laparoscopy showed focal infiltration by malignant non-Hodgkin's lymphoma. Immunohistochemistry showed the cells to be CD20 (a B-cell lymphoid marker) positive and CD3 (a T-cell lymphoid marker) negative, confirming the tumour to be a non-Hodgkin's lymphoma of B-cell type. Immunohistochemistry of bone marrow aspirates showed no evidence of infiltration.

He was treated with 6 cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy in November 2001. A carbon-13-urea breath test in December 2001 was negative. Repeat gastroscopy 4 months after starting chemotherapy showed only erosive gastritis at the gastro-oesophageal junction with no histological evidence of residual lymphoma. Subsequently, the patient's body weight started to increase and his initial symptoms resolved.

A surveillance gastroscopy in October 2002 showed a new ulcerative lesion at the incisura of the stomach. Initially, this was thought to be a recurrence of the non-Hodgkin's lymphoma. However, subsequent histology of this lesion showed features of a gastric mucinous adenocarcinoma with signet ring features (*Figure 2*). He then underwent a subtotal gastrectomy and histological examination of the resected stomach confirmed the presence of a gastric adenocarcinoma with no residual non-Hodgkin's lymphoma. He made a good postoperative recovery and was further treated with chemoradiotherapy. Unfortunately the patient developed a recurrence of the adenocarcinoma in the gastric remnant 3 years later. He is currently alive and has declined any further treatment.

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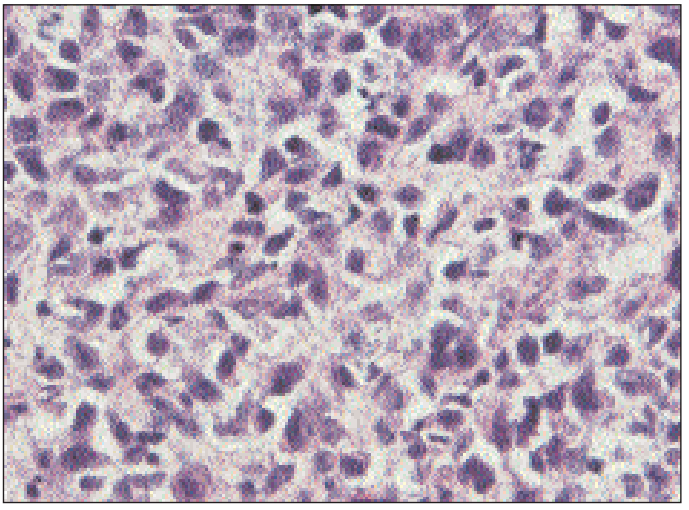

Figure 1. Gastric non-Hodgkin's lymphoma. Histological staining was negative for an epithelial wall marker and positive for a lymphoid marker, indicating the cells to be of lymphoid in origin.

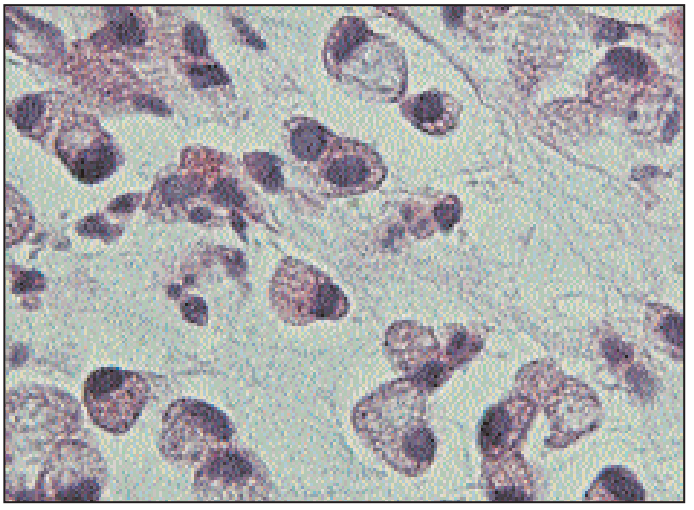

Figure 2. Gastric adenocarcinoma. Cells demonstrate typical appearances of a gastric mucinous adenocarcinoma with signet ring features.

be presumed that the initial antigenic *H. pylori* infection that led to chronic inflammation and immunostimulation was the trigger for the development of multiple gastric cancers in this patient. However, little is known about the genetic alterations of patients who are *H. pylori* positive and who present with multiple primary cancers. Some researchers have hypothesized that microsatellite instability is one of the underlying genetic factors in the development of double primary cancers in colorectal cancer patients (Planck et al, 2002).

This patient was initially treated with chemotherapy and this could have been a risk factor for the development of the second primary. Adjuvant therapy for gastric cancer has not yet been shown to significantly increase the risk for second primaries, but previous surgery is implicated as a risk factor (Kinoshita et al, 2000). The rationale is that surgery alters the normal pH of the stomach.

Therefore multiple factors have probably contributed to the development of this patient's double gastric cancers. It remains a rare occurrence and this patient represents only the second reported case of a metachronous gastric non-Hodgkin's lymphoma and a gastric adenocarcinoma in the literature. **BJHM**

Garcia GC, Feliu J, Ordonez A, Zamora P, Blanco S, Sanchez MJ, Gonzalez BM (1990) Gastric adenocarcinoma following the treatment of a gastric Non-Hodgkin's lymphoma. *Med Clin (Barc)* **95:** 698–701

Guindi M (1999) Role of *Helicobacter pylori* in the pathogenesis of gastric carcinoma and progression of lymphoid nodules to lymphoma. *Can J Gastroenterol* **13**(3): 224–7

Kaffes A, Hughes L, Hollinshead J, Katelaris P (2002) Synchronous primary adenocarcinoma, mucosa-associated lymphoid tissue lymphoma and a stromal tumour in a *Helicobacter pylori*-infected stomach. *J Gastroenterol Hepatol* **17**(9): 1033–6

Kinoshita Y, Tsukuma H, Ajiki W, Kinoshita N, Oshima A, Hiratsuka M, Furukawa H (2000) The risk for second primaries in gastric cancer patients: adjuvant therapy and habitual smoking and drinking. *J Epidemiol* **10**(5): 300–4

Morgner A, Miehlke S, Stolte M et al (2001) Development of early gastric cancer 4 and 5 years after complete remission of *Helicobacter pylori* associated gastric low grade marginal zone B cell lymphoma of MALT type. *World J Gastroenterol* **7**(2): 248–53

Planck M, Rambech E, Moslein G, Muller W, Olsson H, Nilbert M (2002) High frequency of microsatellite instability and loss of mismatch-repair protein expression in patients with double primary tumours of the endometrium and colorectum. *Cancer* **94**(9): 2502–10

Tang CC, Shih LY, Chen PC, Chen TC (2002) Simultaneous occurrence of gastric adenocarcinoma and low-grade gastric lymphoma of mucosa-associated lymphoid tissue. *Chang Gung Med J* **25**(2): 115–21

Wainess RM, Dimick JB, Upchurch GR, Cowan JA, Mulholland MW (2003) Epidemiology of surgically treated gastric cancer in the United States, 1988–2000. *J Gastrointest Surg* **7**(7): 879–83