An indolent diffuse infiltrating gastric carcinoma

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ABSTRACT

Gastric cancer is a common gastrointestinal cancer and is an important cause of cancer mortality. Unfortunately, it is often diagnosed late due to delayed presentation. We report the case of a 48-year-old man who was diagnosed with diffuse infiltrating gastric adenocarcinoma and who had initially declined surgery. The patient presented again the following year, and the repeat evaluations showed similar findings. Despite this, the patient continued to decline interventions. Six years later, as his symptoms increased, the patient finally underwent surgery. Histology revealed a diffuse infiltrating stage T3 tumour, with significant desmoplastic reaction and negative lymphadenopathies. Seven years after the surgery, the patient remained well and recurrence-free. This case highlights that some cancers have an indolent course, and even with significant delay, curative interventions can still be performed.

Keywords: gastric cancer, mucinous adenocarcinoma, signet ring cell carcinoma, survival

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INTRODUCTION

Gastric cancer is the second most common gastrointestinal cancer and is an important cause of cancer mortality, with an estimated 600,000 deaths annually worldwide.[1] Unfortunately, gastric cancers are often diagnosed late due to delayed presentation. Gastric cancer is broadly divided into two histological types: the intestinal type and diffuse infiltrating type.[2] Diffuse infiltrating gastric carcinoma is typically aggressive and associated with a very poor prognosis.[2] We report a case of diffuse infiltrating gastric adenocarcinoma that was in the histologically early stage, even though it was more than six years after the initial diagnosis.

CASE REPORT

A 48-year-old Malay man presented with a one-year history of dyspepsia and two days of melaena. There was no significant past medical or family history of malignancy. Upper gastrointestinal endoscopy showed a superficial flat/excavated gastric ulcer (1.5 cm, type IIb + III) with nodular edges located at the incisura. Biopsies revealed atrophic gastritis that was negative for malignancy. The patient tested positive for *Helicobacter (H.) pylori*, and eradication of the bacteria with triple therapy (omeprazole 20 mg bid, tinidazole 500 mg bid and clarithromycin 500 mg bid) was started. Unfortunately, the patient defaulted follow-up for assessment of ulcer healing and eradication of *H. pylori*.

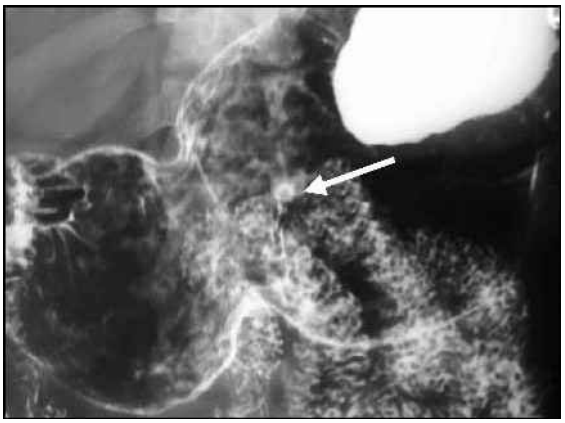

Fig. 1 Barium meal shows a small ulcer, indicated by the pooling of contrast (arrow).

The patient presented again the following year with dyspepsia, and the barium meal showed a small gastric ulcer located in the body area (Fig. 1). Upper gastrointestinal endoscopy again showed a gastric ulcer corresponding to the ulcer in the gastric body on barium study. Biopsies performed this time revealed a diffuse infiltrating type of gastric adenocarcinoma with scattered signet cells. Histology was negative for *H. pylori*. Staging computed tomography (CT) imaging was negative for any spread. Despite thorough and repeated explanations, the patient declined surgery as he was feeling well apart from mild dyspepsia. Again, the patient defaulted clinic follow-up.

Five years later, the patient again presented with melaena. Over the five-year period, he had gradually lost 10 kg of weight. Upper gastrointestinal endoscopy

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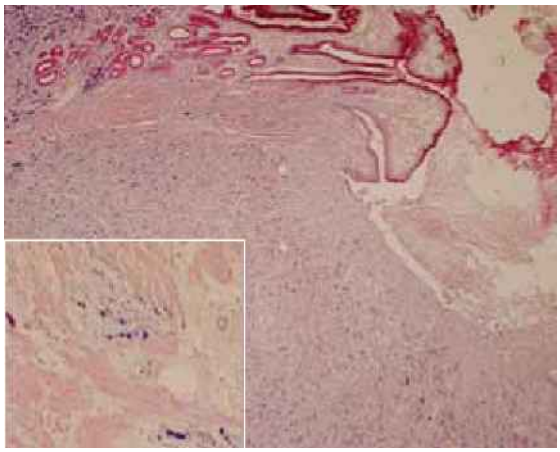

Fig. 2 Photomicrograph of the ulcer margin shows individual tumour cells that are stained purple, scattered among a dense desmoplastic area (alcian blue/periodic acid-Schiff [AB/PAS] stain, × 40). Insert shows tumour cells in the perineural space (AB/PAS stain, × 100).

performed this time showed that the tumour had increased to approximately 3.5 cm in diameter. CT imaging showed localised disease without any obvious evidence of spread. On this occasion, the patient consented to surgery. Intraoperatively, there was no evidence of spread, so we proceeded to perform a partial gastrectomy (Billroth II). Macroscopically, the tumour measured 4.0 cm × 3.5 cm, and histology revealed a diffuse infiltrating tumour restricted to the serosa layer with significant desmoplastic reaction, indicating only a T3 gastric tumour (Fig. 2). Signet ring cells were also seen. The resection margins and lymph nodes were clear. The patient remained well seven years after the surgery and has since gained back the weight he had lost. Regular follow-up showed no evidence of recurrence. His last endoscopy was two years ago, and this did not show any evidence of disease recurrence.

DISCUSSION

In the majority of cases (up to 80%), gastric cancer is located distally, and the distribution has been reported to correlate with the underlying histology. The intestinal type of tumours are usually located distally and are strongly associated with *H. pylori* infection, whereas the diffuse type are often poorly differentiated and usually located in the proximal part of the stomach. The diffuse infiltrating type of tumours are characterised by the production of discohesive agents and secrete mucus, giving a signet ring cell appearance. This tumour type is particularly aggressive and is often diagnosed at the advanced stages of the disease.[2] In the early stages, the changes usually occur beneath the mucosal layer and can therefore be missed during endoscopy. Unlike the intestinal type, there is no strong association between diffuse infiltrating gastric cancer and *H. pylori* infection, but it is often more associated with abnormal host genetic factors. Abnormal expression of E-cadherin is reported to be responsible for the rapid progression of such tumours.[3,4]

Despite the histological type of gastric cancer in our patient, it is interesting to note that the progression had been very slow. Depending on whether the malignancy was already present at the initial presentation, the estimated doubling time would have been approximately less than 1.5 times, ranging from 48 to 56 months. This is longer than the reported doubling time in the literature, which is estimated to be 24–36 months, with a range of 9.2 days to ten years.[5,6] The doubling time has been reported to progressively decrease as the degree of differentiation of the tumour decreases.

Interestingly, our patient's tumour was only at stage T3, even though the initial diagnosis was made more than six years ago. The exact reasons for the indolent nature of some gastric carcinomas despite the aggressive histology type are not known. The significant desmoplastic reaction noted around the tumour in our patient indicated that the underlying immune system might have played an important part in the disease progression. Despite the absence of a strong association between *H. pylori* infection and the diffuse infiltrating gastric carcinoma,[7] it is possible that the eradication of the *H. pylori* infection might have affected the disease progression in our patient. Eradication of *H. pylori* has been reported to induce complete regression of early stage mucosa-associated lymphoid-related tissue lymphomas.[8] The successful eradication of *H. pylori* has also been shown to cause regression of associated gastric mucosal changes, but this is only if the damages have not reached the atrophic stages or beyond.[9] However, the impact of *H. pylori* eradication on the progression of diffuse infiltrating tumour type is not fully known. Our patient had denied having undergone any other treatment or chemotherapy during the course of the five years. Overall, both genetic and environmental factors are likely to be important.[4,10,11]

Patients who decline interventions are not uncommon, especially in certain cultures. In fact, the refusal of investigations and interventions is not uncommon in our setting. Fear, cultural beliefs and educational levels are important factors that may influence a patient's acceptance of interventions. However, it is important for clinicians to be aware of these rare cases of indolent malignancies, as curative therapies can still be achieved despite significant delays.

In conclusion, our case highlighted that in some cases of gastric diffuse infiltrating cancer, the progression may be indolent, and patients should still be evaluated for curative treatment, even if there has been a significant delay.

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