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## ENDOSCOPIC TREATMENT FOR EARLY GASTRIC CANCER IN A PATIENT WITH PERNICIOUS ANAEMIA

Dear Sir,

The surgical treatment for gastric cancer has progressed rapidly for the past thirty years. Gastric cancers are diagnosed at an earlier stage with better endoscopic and imaging modalities. Minimally invasive surgery, such as laparoscopic gastrectomy, is now done at major centres around the world, to treat early disease. Endoscopic treatment is another new and exciting option in the treatment of early gastric cancers. Endoscopic submucosal dissection (ESD) is now being performed for these cancers, with good results and less morbidity. We share an interesting case of a patient who had pernicious anaemia and who underwent ESD for treatment of early gastric cancer.

Our patient is a 55-year-old Chinese man who presented with symptomatic anaemia and weight loss. On examination, there was pallor with no other significant physical finding. Laboratory investigations showed megaloblastic anaemia secondary to Vitamin B12 deficiency, with positive anti-intrinsic factor and parietal cell antibodies. A gastroscopy was performed, which showed atrophic gastritis with elevated mucosa near the antrum. Biopsies taken from the elevated mucosa showed a moderately-differentiated adenocarcinoma. Staging was done using endoscopic ultrasonography (US) and computed tomography (CT) of the abdomen and pelvis. The tumour was seen as a 15-mm diameter expansion of

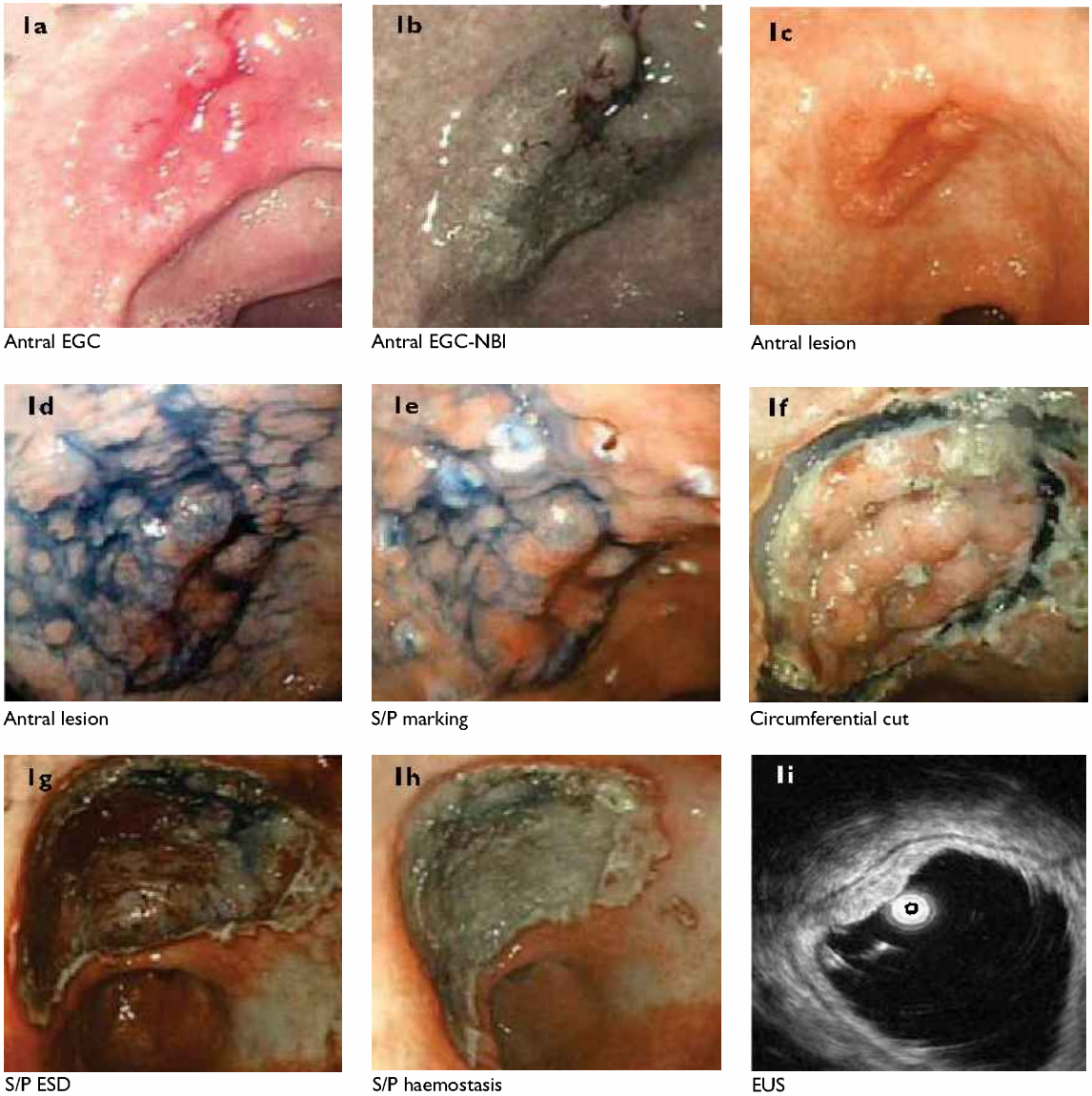


**Fig. 1** Endoscopic photographs show (a) early gastric cancer located at the antrum, (b) the same lesion seen with narrow band imaging, (c) the lesion at the start of the endoscopic submucosal dissection, (d & e) the lesion marked with blue dye, prior to the dissection, (f) the dissection around the lesion, done with an insulated tip knife, and (g) the base of the lesion. (i) Endoscopic US image of the antral mucosa shows that the lesion was confined to the mucosa.

the mucosa at the antrum, with no submucosal involvement or any perigastric lymphadenopathy on the endoscopic US. CT showed no distant metastases. It was staged as T1N0M0 and deemed suitable for ESD.

We decided to repeat the gastroscopy with further biopsies from the non-lesional areas of the stomach to detect any multifocal disease. The histology of these biopsies showed chronic gastritis with intestinal metaplasia and no evidence of malignancy. This patient had a focus of early gastric cancer located at the antrum. The treatment options were either ESD, laparoscopic gastrectomy or open gastrectomy. The risks and benefits of each option were discussed with the patient, who decided on ESD (Fig. 1). The outcome was successful and the patient remained disease-free for three years.

Pernicious anaemia is a known risk factor for gastric cancer. It is associated with a two- to three-fold increase in the incidence of gastric carcinoma.[1] The prevalence of gastric adenocarcinoma in patients with pernicious anaemia is 1%–3%, and only 2% of gastric adenocarcinoma cases are associated with pernicious anaemia. Patients with pernicious anaemia have achlorhydria secondary to destruction of the parietal cells by the autoantibodies, leading to atrophic gastritis. This chronic inflammatory process results in metaplasia and dysplasia, and eventually leads to a malignant transformation, as described by Correa.[2] With the understanding of this disease process, the possibility of a field change with multifocal disease needs to be kept in mind when planning for surgery.

The first case of ESD in early gastric cancer was performed in 1983. Early gastric cancer is defined as cancer confined to the mucosa and submucosa (T1), regardless of the lymph node status. It has been reported in pernicious anaemia patients with early gastric cancer.[3] The original indications were as follows: (1) Well- to moderately-differentiated mucosal adenocarcinoma, dyplastic lesion or premalignant lesion. (2) Elevated-type mucosal cancer < 20 mm in the largest diameter. (3) Flat or depressed-type lesion (without ulceration) < 10 mm in size. An extended indication for early gastric cancer has been proposed by the Japan Gastroenterological Endoscopy Society, i.e. (1) Well-differentiated lesions up to 30 mm, without an ulcer or ulcer scar. (2) Mucosal cancers < 20 mm, with an ulcer or ulcer scar. (3) Submucosal lesions < 20 mm, without an ulcer or ulcer scar. (4) Poorly-differentiated lesions < 10 mm.[4]

If all three of the original criteria are met, and if no lymphatic involvement is noted on histological evaluation, the incidence of lymph node involvement is less than 0.4%. The incidence of lymph node metastasis has been reported to be 1%–3% for mucosal cancers and 11%–20% for submucosal cancers.[5] Hence, ESD may be an appropriate curative procedure for early gastric cancer. ESD is minimally invasive, safe and associated with a shorter hospital stay. It also avoids operative wound infection. The specimen has preserved histological architecture compared to earlier methods of electrocautery and laser ablation. The problems include bleeding, perforation, infection, incomplete resection and recurrence.

The complete resection rates (defined as tumour-free horizontal and vertical margins, no submucosal invasion and no lymphatic invasion) have been reported to be 74%–97% with the use of ESD. 41% of the patients with incompletely-resected tumour went on to undergo surgery, while the rest underwent a repeat procedure or were observed.[6] ESD, unlike endoscopic mucosal resection, offers the possibility of re-treatment. It can be done in areas of submucosal fibrosis. Repeat ESD is however more difficult to perform because of submucosal fibrosis induced by the initial procedure. There is no difference in survival rates between ESD and surgery.[7] However, patients with ESD appear to have a better post-procedure quality of life, compared to patients who underwent surgical gastrectomy.

Endoscopic submucosal dissection is a minimally-invasive treatment for early gastric cancer. When offered to patients with a background of pernicious anaemia, a careful gastric mapping pre-procedure is required to exclude field change and multifocal disease. Surgery should be considered in patients with multifocal or residual disease. Post-resection, a surveillance endoscopy to detect the development of new or recurrent cancer is required in such patients due to a high risk of malignant field change.

Yours sincerely,

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## REFERENCES

1. Ye W, Nyrén O. Risk of cancers of the oesophagus and stomach by histology or subsite in patients hospitalised for pernicious anaemia. Gut 2003; 52:938-41.
2. Correa P. Human gastric carcinogenesis: a multistep and multifactorial process--First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention. Cancer Res 1992; 52:6735-40.
3. Ahn MJ, Han D, Park YJ, et al. A case of type IIa early gastric cancer developed in pernicious anemia. J Korean Med Sci 1998; 13:81-4.
4. Gotoda T. Endoscopic resection for premalignant and malignant lesions of the gastrointestinal tract from the esophagus to the colon. Gastrointest Endosc Clin N Am 2008; 18:435-50, viii.
5. Yamao T, Shirao K, Ono H, et al. Risk factors for lymph node metastasis from intramucosal gastric carcinoma. Cancer 1996; 77:602-6.
6. Ono H, Kondo H, Gotoda T, et al. Endoscopic mucosal resection for treatment of early gastric cancer. Gut 2001; 48:225-9.
7. Tada M, Tanaka Y, Matsuo N, Shimamura T, Yamaguchi K. Mucosectomy for gastric cancer: current status in Japan. J Gastroenterol Hepatol 2000; 15 Suppl:D98-102.