Endoscopic mucosal resection (EMR) for the management of poorly differentiated adenocarcinoma of the stomach: a patient who had recurrence and died 4 years after EMR

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Abstract

Recent studies have explored the possibility of using endoscopic mucosal resection (EMR) to treat lesions with a relative indication for endoscopic therapy. We used EMR to manage poorly differentiated adenocarcinoma, a relative indication for endoscopic treatment, in a patient who requested such treatment and refused surgical intervention. We describe our experience with this patient, who died of tumor recurrence 4 years after the EMR. This case describes the problems of using EMR for the treatment of poorly differentiated adenocarcinoma.

Key words Early gastric cancer · Endoscopic mucosal resection · Poorly differentiated adenocarcinoma

Introduction

Endoscopic mucosal resection (EMR) is now widely used to treat early gastric cancer, and good results have been obtained [1]. Recent studies have explored the possibility of using EMR to treat lesions with a relative indication for endoscopic therapy, such as those in patients who are elderly or those who have serious concurrent disease [2]. We used EMR to manage a poorly differentiated adenocarcinoma, a relative indication for endoscopic treatment, in a patient who requested such treatment and refused surgical intervention. We describe our experience with this patient, who died of tumor recurrence 4 years after the EMR.

Case report

The patient was a 61-year-old woman. In 1978, distal gastrectomy was performed to treat a IIc + III type

advanced gastric cancer located in the lesser curvature of the angulus. On operation, the tumor stage was T2. There was no evidence of lymph node metastasis, hepatic metastasis, peritoneal seeding, or distant metastasis. On histological examination of the resected specimen, the depth of invasion was subserosal. The tumor showed infiltrative growth and was not clearly demarcated from the surrounding tissue (INF γ). Mild lymphatic invasion and mild venous invasion were present. There was no lymph node metastasis (n0) or tumor invasion of the distal or proximal resection margins. Histologically, the tumor contained components of both poorly differentiated adenocarcinoma and signet-ring cell carcinoma. The patient was followed up on an outpatient basis.

In December 1990, a IIc lesion was noted in the greater curvature of the upper third of the remnant stomach (Fig. 1). The depth of invasion was diagnosed as mucosal. Because the histologic type was poorly differentiated adenocarcinoma and the general condition of the patient was good, surgical treatment was recommended, but the patient refused. EMR was therefore performed to treat the lesion locally. The procedure used was strip biopsy, as described by Tada et al. [3]. The tumor measured 6 $\times$ 3 mm. Histologically, the depth of invasion was mucosal. There was no lymphatic or venous invasion. The histologic type was poorly differentiated. The distal margin of specimen was tumor-positive (Fig. 2). Examination of the resected specimen revealed a poorly differentiated carcinoma. Because the resection margin was tumor-positive, we again recommended radical surgery, but the patient did not consent. We therefore performed EMR a second time; 7 days after the first EMR, this region underwent EMR. On examination of the resected specimen, small amounts of tumor were found only at the proximal margin. After 23 days, the ulcer remaining after EMR with a margin of about 4 cm included received follow-up treatment by

laser irradiation. Subsequently, the patient periodically underwent endoscopic examination with biopsy. There was no evidence of recurrence (Fig. 3). Ultrasonographic examinations were done at regular intervals. There was no evidence of lymph node metastasis or peritoneal dissemination of tumor cells, and no elevation of tumor markers such as carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9.

In April 1995, about 4 years after the EMR, the scar remaining after the EMR was found to be tumor-positive. The tumor was primarily poorly differentiated adenocarcinoma, with some components of signet-ring cell carcinoma (Fig. 4). Because the depth of invasion was diagnosed as mucosal on endoscopic ultrasonography (Fig. 5), and there was no evidence of lymph node metastasis or peritoneal dissemination, laser irradiation

Fig. 1. A IIc lesion arising in the greater curvature of the upper third of the remnant stomach

Fig. 3. Only a scar is evident about 2½ years after treatment. Also, a biopsy specimen was tumor-negative

Fig. 2. The specimen obtained by the first endoscopic mucosal resection (EMR) showed mucosal cancer. There was no lymphatic or venous invasion. The histologic type was poorly differentiated. The distal resection margin was tumor-positive

therapy was done, in May. In August, an advanced type 4 cancer was diagnosed (Fig. 6). In September, the tumor had spread to the esophagus, anastomosis, transverse colon, and left ureter. There was also peritoneal seeding of tumor cells. In February, the patient's general condition deteriorated and she died.

Fig. 4. The lesion protrudes slightly. A biopsy specimen taken from the central portion was tumor-positive

Fig. 5. On endoscopic ultrasonography, the fourth layer was thickened because of fibrosis, but the third layer was maintained. The diagnosis was, therefore, a mucosal carcinoma

Discussion

EMR has recently become an important treatment option for early gastric cancer. EMR is now also used to treat patients in whom the procedure is relatively indicated, i.e., those with early gastric cancer who are elderly, those who have serious concurrent disease, or those who refuse surgery.

Our hospital has developed guidelines defining early gastric cancers with an "absolute indication" for EMR, i.e., tumors likely to be completely resected by endoscopic procedures. These guidelines are based on surgical pathological studies, physical restrictions on the size of completely resectable lesions, and factors such as whether the tumor has a clearly demarcated border. Absolute indications for EMR include differentiated adenocarcinomas, i.e., protruding lesions that have a mucosal depth of invasion and a diameter of 20mm or less; and depressed lesions that have no ulcer, a mucosal depth of invasion, and a diameter of 10mm or less [4]. Lesions not satisfying these conditions are considered to have "relative indications" for EMR.

Besides lesions with an absolute indication for EMR (see above), other types of lesions can be radically treated by this procedure. Such lesions include larger tumors, submucosal cancer, undifferentiated cancer, and lesions with an ulcer. Studies are now in progress to establish the validity of extending indications for EMR to include these types of lesions.

Our patient had poorly differentiated adenocarcinoma, a relative indication for EMR. Ishihara et al. [5] found that all mucosal carcinomas with metastasis were

Fig. 6. Four months after the recurrence, a type 4 advanced carcinoma was diagnosed

undifferentiated depressed-type carcinomas. However, Ida et al. [6] reported that intramucosal undifferentiated carcinomas up to 10mm in diameter with definable tumor spread could be managed by EMR. Hamada et al. [7] similarly proposed that minute gastric cancer measuring 5mm or less should be included in the indication range for EMR. Pathological studies done by Nakamura et al. [8] and Takekoshi et al. [9] recommended that lesions indicated for EMR should be limited to those arising near the pyloric glands. Nakamura et al. [8] additionally proposed that lesions could measure up to 10mm in diameter, whereas Takekoshi et al. [9] recommended that lesions should be 5mm or less in diameter and not have an ulcer. Takekoshi et al. [9] pointed out that EMR was associated with high rates of recurrence and residual tumor. Ashida et al. [10] performed EMR for a lesion diagnosed as IIc moderately differentiated adenocarcinoma that measured 3mm in diameter and was located in the antrum. Because poorly differentiated adenocarcinoma was found around the IIc region on histopathological examination of the resected specimen, and the resection margin was tumor-positive, distal gastrectomy was performed. A residual poorly differentiated adenocarcinoma measuring 27 × 25mm was found. Their patient had no evidence of residual tumor on endoscopic examination after EMR or on gross examination of the surgically resected stomach. Targeted biopsy of the site suspected to be residual tumor after EMR also failed to demonstrate cancer. Ashida et al. [10] therefore concluded that poorly differentiated adenocarcinoma should not be considered an absolute indication for EMR, owing to the difficulty in accurately assessing the extent of tumor invasion before EMR.

The tumor in our patient did not satisfy the conditions for EMR in terms of lesion size (5mm or less) as proposed by Hamada et al. [7]. Also, it was not located near the pyloric glands, contrary to the indications proposed by Nakamura et al. [8] and Takekoshi et al. [9], but it showed no lymph node metastasis on imaging studies. Follow-up EMR and laser therapy were done to treat the residual tumor, but the detection of local residual tumor and recurrence suggested that small amounts of the tumor had remained. During the 4 years until the detection of residual tumor and recurrence, the patient was closely observed and underwent endo-

scopic examinations at least once every half year. Macroscopically, only a scar was found, and biopsy revealed no evidence of tumor. On the diagnosis of residual tumor and recurrence, the lesion was evaluated as being intramucosal, and follow-up laser treatment was done. After 3 months, however, advanced cancer was diagnosed.

We believe that EMR is useful in the treatment of relative indications, because studies have shown long-term survival, with most patients dying of diseases other than cancer. Although our experience is limited, the patient we described died of cancer after EMR. At present, therefore, the results of surgical pathological studies, the presence of lesions with an unclear extent of invasion, and the rapid progression of disease associated with residual tumor and recurrence suggest that it is premature to extend the indication range of EMR to undifferentiated carcinoma.

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