Rare case of early mucosal gastric cancer presenting with metastasis to the bulbar conjunctiva

JO TOKUYAMA¹, TETSURO KUBOTA¹, YOSHIHIDE OTANI¹, TOMOHISA EGAWA¹, NORIHITO WADA,¹ KOICHIRO KUMAI², YOSHINORI SUGINO³, YUKIHIRO MASHIMA⁴, YU NAKAMURA⁴, MAKIO MUKAI⁶, HIROMASA ISHII⁵, and MASAKI KITAJIMA^{1,2}

¹Department of Surgery, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan

²Center for Diagnostic and Therapeutic Endoscopy, School of Medicine, Keio University, Tokyo, Japan

³Department of Diagnostic Radiology, School of Medicine, Keio University, Tokyo, Japan

⁴Department of Ophthalmology, School of Medicine, Keio University, Tokyo, Japan

⁵Department of Internal Medicine, School of Medicine, Keio University, Tokyo, Japan

⁶Division of Surgical Pathology, School of Medicine, Keio University, Tokyo, Japan

Abstract

Early gastric cancer has an excellent outcome following surgical treatment. In particular, mucosal gastric cancer (m-cancer) very rarely results in metastatic dissemination and may be successfully treated by local surgical resection. We report a 64-year-old Japanese woman who presented with a recurrent cystic lesion on the left bulbar conjunctiva, with a biopsy specimen revealing metastatic signet-ring cell carcinoma. Gastrointestinal investigations revealed an early gastric cancer in the lesser curvature of the stomach. Biopsy specimen of the gastric lesion indicated poorly differentiated adenocarcinoma, which was identical to findings in the lesion in the bulbar conjunctiva. She underwent a distal gastrectomy and made an uneventful recovery. Histopathological analysis indicated a gastric signet-ring cell carcinoma that was limited to the mucosal layer, without evidence of lymphatic spread. Although the exact mechanism of metastatic dissemination to the bulbar conjunctiva is unclear, this case is very unusual, because ocular metastases almost invariably occur in the context of documented and established malignant disease. This is, to our knowledge, the first reported case of a patient with gastric mucosal cancer who presented with a conjunctival metastatic deposit and who subsequently received curative surgical treatment for both conditions.

Key words Distant metastasis · Mucosal gastric cancer

Introduction

Early gastric cancer has an excellent outcome following surgery. In particular, mucosal gastric cancer (m-cancer) very rarely results in distant metastasis, and warrants treatment with local resection, including endoscopic mucosal resection and laparoscopic wedge resection. The incidence of lymph node metastasis of

m-cancer is very low. Indeed, analysis of 1000 cases of m-cancer at our institute revealed an overall incidence of lymph node metastasis of 2%, and the incidence was actually 0% when the size of the m-cancer was less than 2 cm. In the present report, we describe a rare case of gastric m-cancer that was diagnosed following investigation of a distant metastasis to the left bulbar conjunctiva.

Case report

A 64-year-old Japanese woman noticed a small cystic nodule on her left bulbar conjunctiva and visited her local hospital. She was referred to the Department of Ophthalmology at our hospital because the cystic lesion persistently recurred following aspiration. A biopsy of the lesion was performed on February 4, 2000, and the pathological findings indicated a signet-ring cell carcinoma, suggesting a metastasis from a primary visceral tumor (Fig. 1a,1b). No other ocular lesions were evident.

Although she had no gastrointestinal symptoms, she underwent radiological investigation of the upper gastrointestinal tract, together with upper gastrointestinal endoscopy (Fig. 2). This revealed an early 4.5-cm diameter gastric cancer, a clinical type 0IIc lesion, in the lesser curvature of the middle stomach that exhibited mild deformity secondary to scar formation. A biopsy specimen of the gastric lesion revealed a poorly differentiated adenocarcinoma, identical to the findings in the lesion of the bulbar conjunctiva. Abdominal computed tomography (CT) scanning and ultrasonography revealed no evidence of metastatic dissemination. There was no family history of malignancy, except for her father, who had bladder and esophageal carcinoma. Results of physical examination and routine laboratory examinations were unremarkable, including carcinoembryonic antigen (CEA) and carbohydrate antigen

Fig. 1. **a** Biopsy specimen of cystic lesion on left bulbar conjunctiva. **b** High-power view of **a**. **a** H&E, $\times 50$; **b** H&E, $\times 200$

(CA)19-9, which were within normal limits, at 1.0 ng/ml and 11 U/ml, respectively.

She was admitted on June 13, 2000, for surgical treatment, which consisted of distal gastrectomy with D1 + α lymph node dissection, together with a cholecystectomy, performed in view of her gallbladder calculi. She made an uneventful recovery and was discharged on July 12, 2000, and was free of disease until March 2002. Pathological findings included a gastric signet-ring cell carcinoma, which was limited to the mucosal layer, with no evidence of lymphatic metastasis (Fig. 3). The ulcer scar was observed within the submucosal layer, a small distance from the cancer nest.

Pathological findings

Hematoxylin and eosin staining revealed aggregations of signet-ring cells in the dilated cyst of the conjunctiva, and periodic acid Schiff staining revealed abundant mucus in the signet-ring cells. Immunohistochemical staining for CEA, cytokeratin, and epithelial membrane antigen in the conjunctival cyst and the resected gastric specimen showed positivity for both specimens (Fig. 4). These findings strongly suggested the possible metastasis from a primary cancer originating in a visceral organ, most likely, the stomach. Hematoxylin and eosin staining of the resected gastric specimen showed signet-ring

cells and poorly differentiated adenocarcinoma cells within the mucosal layer.

Discussion

Almost 10% of eyelid tumors arise as a consequence of distant metastasis from primary tumors, such as carcinoma of the breast (42%) on lung (11%), melanoma (5%), or carcinoma of gastrointestinal organs (4%) [2].

Fig. 2. Photograph of gastrointestinal endoscopy

A Medline analysis revealed only a few cases of metastatic dissemination from gastric cancer to the eyelid over the past 10 years. The initial complaint of the patient presented in this report was a recurrent cystic lesion on the left bulbar conjunctiva, with histological analysis of a biopsy specimen indicating signet-ring cell carcinoma, suggestive of a metastatic deposit of visceral origin. Further investigations revealed an early mucosal gastric cancer, and subsequent surgery of the stomach was performed without complications. Histological examination of the resected specimen revealed limited invasion of the gastric cancer within the mucosal layer. Furthermore, the histological characteristics of the tumor cells were compatible with those of the metastatic lesion on the bulbar conjunctiva, with both lesions being poorly differentiated adenocarcinoma with signet-ring cell carcinoma.

We have analyzed the clinical features of 1000 patients with early gastric cancer treated at our institute in order to evaluate the metastatic potential of mucosal gastric cancer [1]. We found that only 10, or approximately 2%, of 483 patients with m-cancer had lymph node metastasis, with no distant metastases being observed, and 14% of 517 patients with submucosal cancer had lymph node metastasis, with no distant metastasis. Because lymphatic or vascular vessels are absent in the mucosal layer, it is unlikely that mucosal cancer will result in lymphatic or distant metastasis. Careful analysis of the specimens from the 10 patients with mucosal gastric cancer with metastasis to lymph nodes at our institute revealed that the lesions were large, and suggested that a degree of submucosal invasion may have been present which was not recognized initially in the

Fig. 3. Microscopic view of the gastric tumor. H&E, $\times 100$

Fig. 4. Immunohistochemical staining of the conjunctival specimen for carcinoembryonic antigen (CEA). $\times 100$

histological specimens. However, in the present patient, no submucosal invasion was observed, even when the entire lesion was cut for stringent histological examination. The ulcer scar within the submucosal lesion, which was observed on endoscopy and by the histological findings, may have accounted for the distant metastasis in the present patient, through a malignant cycle, although the scar formation was located a small distance from the cancer nest.

Although signet-ring cell carcinoma may also arise from breast cancer [2], our patient had no evidence of breast neoplasia on clinical examination, mammography, and ultrasonography. Although an occult primary breast carcinoma cannot be completely excluded in our patient, the comparable histological findings in the gastric and bulbar lesions strongly suggest that the patient had a rare metastasis to the bulbar conjunctiva from the 4.5-cm-diameter mucosal gastric cancer.

There are few reports describing conjunctival metastasis of distant origin [3–5]. Hayyam et al. [6] described the clinical aspects of ten patients with metastatic tumors of the conjunctiva. In their study, the primary malignancy was carcinoma of the breast (four patients), lung cancer (two patients), laryngeal carcinoma (one patient), cutaneous melanoma (two patients), and unknown in one patient. The conjunctival metastases appeared at a mean period of 44 months (range, 8–130 months) after the clinical appearance of the primary tumor. The ocular metastases were solitary in eight patients, and were located in the bulbar conjunctiva in six patients, the palpebral conjunctiva in two, and in the limbus and forniceal conjunctiva in one patient each. Eight patients had metastases to other ocular

structures. Seven patients received external beam radiotherapy to the affected eye, two were managed by excisional biopsy, and one patient received chemotherapy. However, the mean survival after the diagnosis of conjunctival metastasis was limited to 9 months (range, 2–26 months). In view of the fact that the metastatic conjunctival tumors appeared at an advanced stage of the disease, they proposed that the presence of a conjunctival mass in a patient with a history of malignancy was strongly suggestive of a conjunctival metastasis.

Our patient, who represents a rare case of conjunctival metastasis from gastric mucosal cancer, underwent curative surgical treatment of both the gastric and the conjunctival lesions. However, the exact mechanism underlying the metastasis from the gastric lesion to this bulbar site is currently unclear. It may be the case that dissociated gastric cancer cells may have lodged in a benign cystic lesion on the bulbar conjunctiva. In summary, we have reported a rare case of mucosal gastric cancer that was diagnosed following investigations of a solitary distant metastasis to the bulbar conjunctiva.

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