A Case of Primary Gastric Small-Cell Carcinoma in an Elderly Patient

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1. Introduction

Primary small-cell carcinoma (SmCC) of the stomach is a rare neoplasm, accounting for 0.1% of all gastric cancers. This tumor is extremely aggressive, with a poor prognosis after diagnosis. The mean survival of patient with primary gastric SmCC is reported to be 7 months, but the therapeutic value of surgery or systemic chemotherapy has not been conclusively proven. In this report, we describe a patient with advanced primary SmCC of the stomach, diagnosed preoperatively, and analyze the clinicopathological characteristics of this tumor in light of recently published literature.

2. Case report

A 78-year-old male had been undergoing treatment for congestive heart failure (New York Heart Association functional class II), chronic ischemic heart disease, and atrial fibrillation for several years. He was admitted to our hospital on December 15, 2009 due to a 1-week history of intermittent tarry stools. He also had epigastric pain, acid reflux, and a 3-kg weight loss over 1 month.

The initial physical examination was unremarkable except for epigastric pain on pressure and pale conjunctiva. His hemoglobin was 61 g/L (normal: 115–150 g/d), hematocrit 0.19 (normal: 0.35–0.47), and albumin 31 g/L (normal: 35–50 g/L). Hypotension (133 mmol/L; normal: 135–147 mmol/L) and hypouricemia (208 μmol/L; normal: 262–452 μmol/L) were also noted. The tumor markers carbohydrate antigen 19-9 and alpha fetoprotein were both within the normal range, but carcinoembryonic antigen level was 249.40 μg/L (normal <3.4 μg/L).

Initial treatment included blood transfusion, electrolyte support, and high-dose intravenous proton pump inhibitors. Upper gastrointestinal endoscopy revealed a large stage A2 ulcer on the greater curvature of the gastric body. Pathological findings from biopsy specimens revealed small-cell carcinoma. The tumor cells were composed of hyperchromatic nuclei with scant cytoplasm, and stained positive for cytokeratin, synaptophysin, and chromogranin A. The patient was diagnosed with primary small-cell carcinoma of the stomach. He declined further evaluation and received palliative management. This is a rare carcinoma of the stomach, with aggressive manifestations and a poor prognosis. The mean survival of patients with primary gastric small-cell carcinoma is reported to be 7 months. The choice of treatment for this disease is still controversial. This rare gastric tumor should be listed in the differential diagnosis of gastric carcinoma in the elderly.

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3. Discussion

The vast majority of SmCC develop from the lung, with only 2.5% presenting at extrapulmonary sites, including the esophagus, stomach, colon, pancreas, pharynx, bladder, and uterine cervix7,8. Primary gastric SmCC was first reported in 1976 and accounts for only 11% of all gastrointestinal SmCC9. The incidence of gastric carcinoma is higher in Asia than in Western countries, but primary gastric SmCC is still rare. One recent study presented the clinico-pathological characteristics of gastric SmCC in 213 patients10. Of these cases, 78.9% developed in males and 21.1% in females. The age of patients ranged from 28 to 89 years, with a mean of 65.1 years. Fifteen cases of the tumor were limited to the mucosa or submucosa, whereas 112 cases presented in an advanced stage. Median survival time was only 9 months (range 0–96 months).

The histological features of gastric SmCC are similar to those of pulmonary SmCC, with solid, organoid, trabecular, and pseudoglandular patterns. The tumor cells demonstrate a high nuclear grade, with minimal cytoplasm, indistinct nucleoli and nuclear molding11. Microscopically, gastric SmCC are of two types: (1) pure type, accounting for 60% of the total2,4, and (2) composite type, with glandular or squamous differentiation3.

Since primary SmCC of the stomach is as aggressive as SmCC of the lung, the prognosis is extremely poor. Local nodal involvement and distant metastasis are frequent presentations, even at an early clinical stage. Primary gastric SmCC has nonspecific clinical manifestations, and the laboratory findings are similar to those of other gastric carcinoma. Therefore, it is difficult to diagnose preoperatively, and a definitive diagnosis requires both histological features and immunohistochemical presentation. In one study of 15 reported cases, only six (40%) were diagnosed correctly before surgery7. Gastric SmCC has a similar immunohistochemical presentation to that of lung SmCC, but is distinct for its positive reaction to chromogranin-A, synaptophysin, neuron-specific enolase, CD56, and S-100 protein5,9. In our patient, the immunohistochemical examination showed positive expression of keratin and two neuroendocrine markers — chromogranin-A and synaptophysin — confirming the diagnosis of SmCC.

The standard therapy for primary SmCC of stomach has not yet been established. Operation and operation with adjuvant chemotherapy are the most used therapies reported. In one study using chemotherapy alone in patients with primary gastric SmCC, carboplatin and etoposide were used in the salvage regimens usually applied to patients with small-cell lung cancer, and a longer median survival time (over 12 months) was observed10,12–14. Therefore, this
chemotherapy regimen may provide a survival benefit for patients with primary gastric SmCC and distant metastases. Surgery may benefit patients who do not have distant metastases\(^\text{10}\).

Tegafur/gimeracil/oteracil potassium, or S-1-based chemotherapy, is the most effective regiment for adjuvant chemotherapy for primary gastric SmCC\(^\text{12}\). Thus, S-1 may improve the prognosis for patients with primary gastric SmCC\(^\text{15}\). Larger studies are needed to confirm this finding.

In conclusion, gastric SmCC is a rare tumor appearing mostly in older adults, especially males. It has nonspecific clinical manifestations, and the parameters, including tumor markers and imaging studies, cannot be used alone to reliably establish a preoperative diagnosis. Histological features and immunohistochemical examination together are required for a definitive diagnosis. The standard treatment has not been established, and larger trials are needed to determine the best treatment for gastric SmCC. This rare gastric tumor should be listed in the differential diagnosis of gastric carcinoma in older adults.

References