Minute gastric carcinoid tumor with regional lymph node metastasis: A case report and review of literature

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Abstract

We have encountered an unusual case of gastric carcinoid tumor. Gastroscopic examination of this 32-year-old male patient showed a smooth protrusion at the greater curvature of the gastric body with a central depression, identified by subsequent biopsy as carcinoma. The patient had a normal serum gastrin level and was negative for anti-parietal cell antibody. Histological examination of the resected gastric tissues showed that the tumor was a carcinoid, 0.3 cm × 0.3 cm in size with only one regional lymph node metastasis. We reviewed the pathogenesis, clinical presentation, diagnosis and treatment of gastric carcinoids and raise the possibility of being a lymph vessel-related metastasis even for a minute carcinoid tumor. Sentinel lymph node biopsy is recommended for surgery of minute carcinoid tumors.

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INTRODUCTION

Carcinoid tumors represent an unusual and complex disease spectrum with protean clinical manifestations. Gastric carcinoids account for 3 of every 1,000 gastric neoplasms. Gastric carcinoids types I and II generally follow a benign course, with 9% to 30% developing metastases, usually multiple and small characterized by infiltration restricted to the mucosa and submucosa. The third type of gastric carcinoids (type III, sporadic tumors) occurs without hypergastrinemia but often progresses in an aggressive course, 54% to 66% of which may develop metastases. Approximately 50% of these often large, single tumors have atypical histology, and some patients may develop carcinoid syndrome; but except for rare cases, carcinoid tumor of the stomach less than 1 cm in size generally does not give rise to regional metastasis.

CASE REPORT

The patient in question was male, aged 32 years old, admitted for upper gastric discomfort after dinner for six mo, which worsened in the past two mo prior to admission. The patient complained of epigastric distention, but this did not affect his normal diet. He had no vomiting, abdominal pain, melena or regurgitation. The symptoms waxed and waned, but clearly worsened in the last two mo. Physical examination revealed no obvious anemia, the lung and heart sounds were normal, the abdomen was soft and flat, and no hepatomegaly or splenomegaly was noted, nor was an abdominal mass palpated; rectal examination found no abnormalities, and no enlargement of the superficial lymph nodes was present. The patient was free of symptoms of hypergastrinemia or carcinoid. Gastroscopy identified a nodule on the greater curvature of the stomach, 0.6 cm by 0.6 cm in size, with erosive lesion above the nodule. Biopsy was done and the results indicated carcinoid. The patient received subsequently laparotomy in which a node was found near the pylorus, yellowish in color and 0.5 cm by 0.5 cm in size. The node was extensively resected along with the marginal area 2 cm in width. One enlarged lymph node below the pylorus was also resected. Post-operative histology revealed a 0.3 cm node, gray-white or gray-red, beneath the mucosa. Under microscope, tumor cells were seen in the submucosa and mucosa propria, uniform in shape and arranged in cribriform nests. A radical distal subtotal gastrectomy was subsequently performed, and the post-operative histology reported no residual cancer or additional metastasis in the 23 lymph nodes. The patient was then discharged and followed up for one year without findings indicative of recurrence or distant metastasis.

DISCUSSION

Carcinoid is also known as chromaffin cell carcinoma and belongs to an unusual type of tumor with relatively low malignant potential. The most frequent sites for carcinoid tumors in human are the gastrointestinal (GI) tract (74%) and the bronchopulmonary system (25%). Within the GI tract, most carcinoid tumors occur in the small bowel (29%), appendix (19%), and rectum (13%) [1]. However, the frequency of gastric carcinoid tumors has increased markedly due to endoscopic screening, performed in patients with chronic atrophic gastritis. In Japan, mass endoscopic screening for gastric lesions is common, which results in an identified frequency of gastric carcinoid tumor as high as 41% of all carcinoid tumors [2]. Zhen et al. reviewed 26 reports of carcinoid in China and reported 126 cases of carcinoid in the stomach from a total of 1,080 cases of GI tract carcinoid. Most gastric carcinoids occur in 40- to 60-year-old patients, irrespective of genders. Recently, a classification system was proposed to distinguish gastric carcinoid tumors into three types, namely, tumors associated with chronic atrophic gastritis (type I), tumors associated with Zollinger-Ellison syndrome (ZES, type II), and biologically more aggressive, sporadic lesions (type III) [3-4]. Currently little is known about the factors that may induce or promote the malignant growth of carcinoids [5]. For some gastric carcinoids, studies show that gastrin is an important growth factor [6], and an increased incidence of gastric carcinoids can be expected in disease states (pernicious anemia, atrophic gastritis, Zollinger-Ellison syndrome) that result in hypergastrinemia. In pernicious anemia and atrophic gastritis, 4% to 11% of the patients develop gastric carcinoids [7,8]. Patients with Zollinger-Ellison syndrome...
also develop gastric carcinoids, although they are much more frequent in the subgroup with MEN 1 \(^{19}\). Studies suggest that other important growth factors in some carcinoid tumors include transforming growth factor alpha (TGF-alpha) and TGF-beta \(^{10,11}\), insulin-like growth factor-1 (IGF-1) \(^{7,11}\), trefoil peptides (TFF1, TFF2, TFF3) \(^{7}\), platelet-derived growth factor \(^{10}\), vascular endothelial growth factor \(^{12}\), acidic and basic fibroblast growth factor, and epidermal growth factor \(^{10,11}\). Mutations in common oncogenes, such as K-ras, are uncommon in GI carcinoids. Over amplification of HER2/neu, c-erbB-2, and c-jun have been described in some cell lines derived from GI endocrine tumors and some carcinoids \(^{13}\). Alterations in the common tumor suppressor gene p53 are also uncommon in carcinoids. MEN 1 has been shown to be due to defects in the 10-exon gene on chromosome 11q13 that encodes a 610-amino acid nuclear protein \(^{14,15}\). Loss of heterozygosity at this locus has been reported to occur in 26% to 78% of cases of carcinoids, and mutations in the MEN 1 gene in 18% \(^{16,17}\). Microsatellite instability is rare in carcinoids \(^{18}\), however, by comparative genomic hybridization, both frequent gains (of chromosome 5, 14, 17q; 7) and losses (especially of chromosome 9p) are reported \(^{19}\).

Gastric carcinoids originate from paranchromaffin cells of the gastric mucosa. Tumor cells can occur virtually anywhere in the stomach, but mostly occur in the antrum. Gastric carcinoid is often difficult to diagnose due to the absence of specific symptoms or signs, especially in the early stage. When the tumor protrudes into the gastric cavity, the patient usually feels epigastric pain, suffers bloody vomiting, melena, epigastric burning, nausea or other digestive disorders. Carcinoid syndrome is seen in only a few gastric carcinoid cases where extensive dissemination or liver metastasis can be present. Gastric carcinoid in its early stage frequently escapes detection, and is usually found by gastroscopy. When the tumor grows to more than 2 cm, barium meal will help the diagnosis. The patient in this report was a young man who had only non-specific symptoms like epigastric distension without carcinoid syndrome and the tumor was near the antrum only 0.5 cm in size. The pathology was typical carcinoid. This patient did not have chronic gastritis or Zollinger-Ellison syndrome and the lesion was single, which belonged therefore to type III.

Surgical resection is the major strategy for treatment of gastric carcinoid, and chemotherapy and radiotherapy have not proved to produce obvious effects. For gastric carcinoids, the treatment is generally decided on the basis of the presence of hypergastrinemia \(^{20,21}\). Most researchers recommend that in patients with type I or II, in which hypergastrinemia is present with small lesions of less than 1 cm, the carcinoid should be removed endoscopically \(^{22,24,25}\), while when the tumor exceeds 2 cm or local invasion is present, disputes over total gastrectomy \(^{26}\) or only resection with antrectomy arise for type I (pernicious anemia) lesions \(^{21}\). For type I or II lesions of 1 to 2 cm, no agreement has been reached on the treatment. Some recommend that these lesions should be treated surgically \(^{21}\) whereas others urge endoscopic treatment \(^{25}\). In type III gastric carcinoids not associated with hypergastrinemia, which tend to be larger and more aggressive, excision and regional lymph node clearance is recommended when the tumor grows to larger than 2 cm \(^{21,23,25}\). Some researchers prefer a similar approach for any carcinoid larger than 1 cm, whereas others consider such a resection be reserved for tumors in this size range showing histologic invasion. Most tumors smaller than 1 cm can be treated endoscopically. Tumors less than 1 cm in size are called minute carcinoids, which seldom give rise to regional lymph node metastasis, especially tumors less than 0.5 cm in size. But very rarely, minute carcinoids do have lymph node metastasis, as reported by a Japanese researcher Naitoh \(^{27}\). Such a case has not previously been reported in China. The case reported in this paper is similar to the case reported in Japan. The post-operative pathology showed only a single lesion 0.3 cm in size invading the submucosa. There was just one lymph node metastasis, which is also uncommon. Local resection of the stomach was done in the first operation, and one enlarged lymph node was resected that was identified as metastasis by histology, so subtotal gastrectomy and lymph node dissection were done in the second operation. The other lymph nodes were normal, however, we regarded this approach was appropriate.

Sentinel lymph node biopsy has been used widely for surgery of melanoma \(^{28,29}\) and is currently receiving intensive study on its application for other malignant tumors such as breast, rectal and gastric cancer \(^{30,31}\). The sentinel node is the most likely lymph node that harbors metastasis. A negative sentinel lymph node (SLN) would suggest that metastatic disease has not occurred, whereas a positive SLN would indicate possible involvement of other nodes in the same basin. Therefore sentinel lymph node biopsy may be attempted in operations for minute carcinoid. If the sentinel lymph node is positive, excision and regional lymph node clearance is needed, otherwise, local resection of the stomach is sufficient.

The prognosis of gastric carcinoid is favorable and patients may expect long postoperative survival. In patients with localized disease, 5-year survival rate may reach 64%, and it was 40% for regional involvement. Postoperative chemotherapy or radiotherapy was not performed in this particular case and the one-year follow-up found no recurrence or distant metastasis.

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