Multiple Gastric Carcinoids and Pituitary Adenoma in Type A Gastritis

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A 48-year-old male with type A atrophic gastritis developed multiple gastric carcinoids and a pituitary adenoma. Laboratory tests revealed high levels of serum gastrin and growth hormone (GH). He underwent subtotal gastrectomy, resulting in a return of the previously elevated gastrin level to normal. Serum GH concentration remained high. Three months after the surgery, the pituitary tumor, composed greatly of GH-immunoreactive cells, was partially removed. Since hypergastrinemia plays a pivotal role in gastric carcinoid formation and induces GH-releasing factor (GHRH) release resulting in GH-producing pituitary tumor formation, GH-producing pituitary adenoma might be a clinical manifestation in type A gastritis.

(Key words: atrophic gastritis, gastrin, growth hormone (GH), hypergastrinemia)

Introduction

The development of argyrophil endocrine cell hyperplasia and carcinoid tumors in the gastric fundus has been sporadically described in patients with type A atrophic gastritis (1, 2). Recent studies have revealed that hypergastrinemia associated with atrophic gastritis is responsible for gastric carcinoid formation (3–5). Gastrin also regulates hypothalamic growth hormone (GH)-releasing factor (GHRH) secretion (6–8), resulting in eventual GH-producing pituitary adenoma formation (9–11). The following is the first case report of a patient with type A gastritis who had gastric argyrophil carcinoids and a GH-producing pituitary adenoma.

Case Report

A 48-year-old male was admitted to our hospital on July 31, 1992, with diagnoses of gastric polyposis and acromegaly. He had been aware of the gradual increase in the size of the nose, lips, nasolabial skin fold and forehead as well as increased extremities over a period of 10 years. Five years before admission he was found to have a gastric polyp in a barium examination of the upper gastrointestinal tract. His family history was noncontributory.

On physical examination, typical acromegaly associated with soft tissue and bone enlargement was noted. Visual fields and acuities were normal. Laboratory examinations were normal except for the marked elevation of a serum gastrin level to 2,910 pg/ml (normal range: 42–200 pg/ml) and a serum GH level to 77 ng/ml (normal range: under 0.42 ng/ml). Serum levels of other anterior pituitary hormones, antidiuretic hormone (ADH), parathyroid hormone (PTH) and calcitonin were within normal limits. Serum serotonin and urinary 5-hydroxyindoleacetic acid levels were also within normal range. Autoantibodies against the gastric parietal cells and thyroid peroxidase were positive.

Barium contrast studies of his stomach showed multiple filling defects, and endoscopy demonstrated 5 small polypoid lesions with characteristics of submucosal tumors in the gastric body-fundus (Fig. 1). Thin gray gastric mucosa with prominent vascular networks extended from the fundus to the body of the stomach, with relative sparing of the antrum. After insufflation, the submucosal vessels were still prominent and only a few folds were seen around the greater curve and the posterior wall. Biopsy of the polypoid lesions resulted in histological diagnosis of carcinoid.

Despite a considerable serum level of gastrin, both ultrasonogram and computerized tomographic (CT) scans of the abdomen failed to detect any tumor suggesting gastrinoma or other endocrine neoplasms. Magnetic resonance (MR) images of the head showed a large mass in the pituitary region, with 27 mm of suprasellar extension (Fig. 2). A barium enema revealed...
no colorectal tumors. Ultrasonogram and CT scans of the neck revealed no abnormal findings. He underwent subtotal gastrectomy on September 22, 1992, and several perigastric lymph nodes were removed. Two weeks after the operation, the serum gastrin level returned to normal. On the contrary, serum GH concentration remained high (58 ng/ml). Three months after the initial surgery, the pituitary tumor was partially removed with a transsphenoidal approach. Serum GH level was decreased to under 10 ng/ml and thereafter he has not developed any clinical manifestations due to the recurrence of the disease at the time of this report.

Pathological findings

Macroscopically, there were 9 small polypoid lesions (maximally 9 mm in diameter) in the gastric body-fundus. Among them, 7 lesions were carcinoids and the others hyperplastic polyp histologically. The carcinoids were composed of small monomorphic cells with rounded nuclei and eosinophilic cytoplasm, growing with alveolar and ribbon-like structures, and infiltrated into the submucosa (Fig. 3). The carcinoid cells were argentaffin by Grimelius staining but non-argentaffin by Masson-Fontana staining. Immunohistochemistry was positive for chromogranin A, but negative for gastrin, serotonin, somatostatin and neuron-specific enolase. The gastric mucosa of the body-fundus showed severe atrophy with frequent areas of intestinal and pseudopyloric gland metaplasia. Diffuse...
intraglandular argyrophil cell proliferation was also noted in the pseudopyloric glands. The atrophic change of the pyloric mucosa was slight in comparison with that of the fundic regions. Immunohistochemical studies revealed diffuse intraglandular proliferation of gastrin-positive cells at the pyloric glands. There was no evidence of vascular or lymphatic invasion or lymph node metastasis.

The pituitary tumor composed of cells with an eosinophilic cytoplasm was proven to be adenoma (Fig. 4). Immunohistochemistry demonstrated a positive reaction with anti-GH.

Discussion

The occurrence of gastric carcinoid tumors in patients with type A gastritis is now well recognized (12). In response to the achlorhydria associated with type A gastritis, the antral gastrin-producing G cells generate hypergastrinemia and secondary fundic mucosal enterochromaffin-like (ECL) cell hyperplasia and neoplasia (12). Antral gastrin-producing G cell hyperplasia, hypergastrinemia, and fundic endocrine cell proliferation varying from simple argyrophil ECL cell hyperplasia to carcinoid tumors in this case all support this gastrin hypothesis. The argyrophil carcinoid cells were also positive for chromogranin A, which is the most sensitive marker for gastric ECL cell carcinoids (13).

The association of pituitary adenoma with type A gastritis and carcinoids might be coincidental. However, serum gastrin levels are often elevated in patients with pituitary adenoma, and the hypergastrinemia is mostly attributed to antral G-cell hypersecretion secondary to long lasting achlorhydria associated with atrophic gastritis (14, 15). A hypothesis of a cause-and-effect relationship between type A gastritis and pituitary adenoma is supported by several arguments: (1) gastrin stimulates GH secretion through a hypothalamic GHRH-dependent mechanism (6–8), (2) excessive and long-term stimulation of the somatotrophs by a GHRH provides the basis for GH hypersecretion and eventual pituitary tumor formation (9–11). Since the development of gastric carcinoids depends on the duration of hypergastrinemia (16–18), it seems to be possible that long-term hypergastrinemia also may promote the development of GH-producing pituitary adenoma, which is no longer affected by GHRH.

We could not investigate the possible GHRH production of gastric carcinoids. Hypergastrinemia-associated gastric carcinoids, however, commonly display a benign biological behavior and have not been reported to secrete such hormonal substances despite recent considerable attention (19).

There is even room for the causal relationship between hypergastrinemia and pituitary adenoma. Patients with hypergastrinemia, however, should be scrutinized for not only gastric carcinoid but also pituitary adenoma.

References