A Case of Zollinger-Ellison Syndrome in Multiple Endocrine Neoplasia Type 1 with Urolithiasis as the Initial Presentation

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Zollinger-Ellison syndrome (ZES) is characterized by gastrinoma and resultant hypergastrinemia, which leads to recurrent peptic ulcers. Because gastrinoma is the most common pancreatic endocrine tumor seen in multiple endocrine neoplasia type 1 (MEN 1), the possibility of gastrinoma should be investigated carefully when patients exhibit symptoms associated with hormonal changes. Ureteral stones associated with hyperparathyroidism in the early course of MEN 1 are known to be its most common clinical manifestation; appropriate evaluation and close follow-up of patients with hypercalcemic urolithiasis can lead to an early diagnosis of gastrinoma. We report a patient with ZES associated with MEN 1, and urolithiasis as the presenting entity. A 51-year-old man visited the emergency department with recurrent epigastric pain. He had a history of calcium urinary stone 3 years ago, and 2 years later he had 2 operations for multiple jejunal ulcer perforations; these surgeries were 9 months apart. He was taking intermittent courses of antulcer medication. Multiple peripancreatic nodular masses, a hepatic metastasis, parathyroid hyperplasia, and a pituitary microadenoma were confirmed by multimodal imaging studies. We diagnosed ZES with MEN 1 and performed sequential surgical excision of the gastrinomas and the parathyroid adenoma. The patient received octreotide injection therapy and close follow-up.

Key Words: Zollinger-Ellison syndrome; Multiple endocrine neoplasia type 1; Gastrinoma; Urolithiasis

INTRODUCTION

Zollinger-Ellison syndrome (ZES) is characterized by 1 or more gastrinomas, mainly located in the pancreas or duodenum. The resultant hypergastrinemia leads to recurrent peptic ulcers. ZES is rare, occurring in one person per 100,000.1 Gastrinoma, however, is the most common pancreatic endocrine tumor in patients with multiple endocrine neoplasm type I (MEN 1), which involves the pituitary, parathyroid, and adrenal glands.2,3 The possibility of a gastrinoma should therefore be investigated carefully when patients exhibit symptoms of the hormonal changes associated with MEN 1.

Ureteral stones are the most common clinical manifestation of the hyperparathyroidism associated with MEN 1 in its early stages.3 If a family history of urinary stones is confirmed at the time of the patient’s diagnosis, a review of hereditary diseases such as MEN should be performed.
Appropriate evaluation and close follow-up of patients with hypercalcemic urolithiasis can yield an early diagnosis of gastrinoma. Localized gastrinomas have a good prognosis when detected early. Otherwise they can metastasize rapidly to the regional lymph nodes and the liver. Patients with ZES often experience delayed diagnosis and unnecessary surgery. Those with advanced ZES at the time of initial treatment have a poor prognosis. The delayed diagnosis of gastrinoma should be avoided through proper investigation in patients with recurrent peptic ulcers or MEN 1-associated symptoms. We report a patient with ZES who had MEN 1-related urolithiasis as the initial manifestation.

CASE REPORT

A 51-year-old male presented to the emergency department of Presbyterian Medical Center complaining of recurrent epigastric pain. Three years prior, he had undergone 4 sessions of extracorporeal shockwave lithotripsy and surgical ureterocystostomy for removal of bilateral urinary stones (Fig. 1). He was subsequently treated with potassium citrate for recurrent calcium stones. Although his calcium level was 11.2 mg/dL, his urologist did not carry out any further evaluation.

For the next 18 months, he visited the emergency department repeatedly with recurrent abdominal pain. He underwent 2 surgeries, at an interval of 9 months, for multiple jejunal ulcer perforations. Despite this surgical treatment, he suffered from recurrent episodes of epigastric pain; he took antiulcer medication intermittently. Gastroscopy revealed a recurrent jejunal ulcer at the anastomosis site from a prior surgery.

At the time of his emergency department presentation, his vital signs were stable. On physical examination, he had mild direct tenderness in the epigastric and left upper quadrant abdominal areas, but no abdominal distension or unusual bowel sounds were noted. Peripheral blood testing revealed white blood cell count of 6,000/mm³, hemoglobin level of 14.8 mg/dL, hematocrit of 42.9%, and platelet count of 136,000/mm³. Biochemical testing demonstrated AST level of 19 IU/L, ALT level of 22 IU/L, ALP level of 449 IU/L, BUN level of 9 mg/dL, and creatinine level of 1.0 mg/dL. He had hypercalcemia, with calcium level of 11.5 mg/dL, and his phosphorus level of 2.5 mg/dL was at the lower limit of normal.

Given his history, ZES was suspected and hormonal testing carried out after discontinuing proton pump inhibitor (PPI) for 1 week. He exhibited hypergastrinemia with gastrin level of 711.7 pg/dL. Possible MEN 1-associated hormonal changes were then evaluated, revealing hyperparathyroidism with parathyroid hormone level of 66.5 pg/mL. Thyroid function indicators were in the normal range, and pituitary testing was normal, with a prolactin level of 5.67 ng/mL, growth hormone level of 0.51 ng/mL, and adrenocorticotropic hormone level of 33.2 pg/mL.

Multiple imaging studies were performed to evaluate ZES with MEN 1. Abdominal CT revealed multiple peripancreatic nodular masses, and MRI showed a dense, contrast-enhancing nodule in the superior segment of the left lobe of the liver (Fig. 2A, B). Compared to an abdominal CT performed 1 year prior, the peripancreatic nodules had increased slightly in size but the size of the hepatic lesion was unchanged. EUS

![Fig. 1. Clinical manifestation findings. (A) X-ray examination of the kidneys, ureter, and bladder showed calcified stones (arrows) in both ureters. (B, C) Abdominal nonenhanced CT showed calcified stones (arrows) in both ureters.](image-url)