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Peptic Ulcer Perforation as the First Manifestation of Previously Unknown Primary Hyperparathyroidism

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Key Words
Peptic ulcer · Primary hyperparathyroidism · Parathyroidectomy

Abstract
A patient admitted for acute abdomen was incidentally found with elevated serum calcium level. In surgery, under conservative treatment of the hypercalcemia, a perforated duodenal ulcer was found and simple closure was performed. Postoperatively, calcium level continued to rise, parathyroid hormone was elevated and ultrasonographic examination showed a lesion in the right anterior neck, while serum gastrin level was normal, thus documenting the diagnosis of primary hyperparathyroidism. Conservative treatment had no effect on calcium level and the patient was subjected to emergency neck exploration, where a large parathyroid adenoma was removed. After surgery, calcium and PTH levels were normalized and the patient was discharged on the 5th postoperative day. Peptic ulcer and its complications are usual manifestations of primary hyperparathyroidism, with or without increased gastrin level. On the other hand, cases of a perforation of peptic ulcer as the first clinical manifestation of primary hyperparathyroidism are extremely rare.

Introduction

In various studies, the association of hypercalcemia and peptic ulcer is well established [1–4], while in others this matter is still under debate [5–10]. The fact is that 12% of patients with primary hyperparathyroidism have peptic ulcer-related symptoms [11, 12],

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and these symptoms can be relieved after surgical removal of the abnormal parathyroid gland(s) because of the reported reduction of elevated basal acid output (BAO) [1–4]. Here, we present a rare case of perforated duodenal ulcer as the initial clinical manifestation of unknown primary hyperparathyroidism. After diagnosis of the disease and unsuccessful conservative treatment of the hypercalcemia, the patient was treated by performing an emergency parathyroidectomy due to very elevated serum calcium levels.

Case Report

A 48-year-old male patient was admitted to the First Surgical Department of the University General Hospital of Alexandroupolis with acute mid-epigastric abdominal pain, with sudden onset, accompanied by nausea, without vomiting. The patient had no personal history of any disease, but he reported vague symptoms of dyspepsia and nausea for 15 days. Clinical examination showed rebound tenderness, guarding and absence of bowel sounds. An upright chest radiograph showed pneumoperitoneum, which confirmed the clinical suspicion of a perforation in the stomach or the small intestine, while ultrasonography showed intra-abdominal fluid. On routine preoperative investigation, serum calcium level was found to be elevated (12.9 mg/dl, normal range 8.4–10.2 mg/dl), with low phosphorus level (2.1 mg/dl, normal range 2.7–4.5 mg/dl). After loop diuretics (furosemide) administration for reducing calcium level, a laparotomy was decided, where a perforation of a duodenal ulcer was found and simple closure was performed.

Postoperatively, calcium level continued to rise, reaching a maximum of 14.9 mg/dl despite the administration of diuretic treatment and calcitonin. In further examinations, plasma parathyroid hormone level was found to be elevated (340.3 pg/ml, normal range 15–65 pg/ml), while serum gastrin level was normal (99 pg/ml, normal range 5–200 pg/ml). Primary hyperparathyroidism was diagnosed and an ultrasonographic examination of the neck was performed in order to localize a possible adenoma of a parathyroid gland, the most common cause of primary hyperparathyroidism, which showed a lesion of 2.6 × 1.7 cm in the right anterior neck. Because of the very elevated calcium level, an emergency neck exploration was performed on the 6th postoperative day (after laparotomy). In surgery, the right inferior parathyroid gland was found to be hyperplastic and was removed (**fig. 1**, **fig. 2**), while 3 more hypoplastic parathyroid glands were identified. Histology of the lesion revealed a large typical parathyroid adenoma (3.2 × 2.0 × 1.5 cm, 6 g).

After surgery, PTH level was normalized and calcium level decreased rapidly (**fig. 3**), while monitoring of gastric pH was also performed on the 8th postoperative day after the parathyroidectomy, finding the gastric acidity at a normal level. The patient's postoperative course was uncomplicated and he was discharged on the 11th postoperative day after laparotomy with a PTH level of 42.1 pg/ml and a calcium level of 8.8 mg/dl. The follow-up endoscopy one month after discharge showed complete healing of the duodenal ulcer and the rapid urease test proved negative for *Helicobacter pylori*, while PTH and calcium levels were 62.3 pg/ml and 9.0 mg/dl, respectively. Additionally, gastrin level was within normal range (83 pg/ml).

Discussion

Primary hyperparathyroidism formerly presented with the 'classic' pentad of symptoms (kidney stones, painful bones, abdominal groans, psychic moans and fatigue overtones). In the last two decades, the evolution of technology led to routine measurements of serum calcium and parathyroid hormone levels, and most patients in our time are minimally symptomatic or asymptomatic. Nowadays, most symptomatic patients present with symptoms of muscle weakness (70%), myalgia-arthralgia (54%), constipation (32%), nephrolithiasis (30%), polyuria (28%), peptic ulcer disease (12%) etc. [11, 13]. In this report, the patient had no prior symptoms of primary

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hyperparathyroidism, and the first manifestation of the disease probably was the perforation of the peptic ulcer. This is an unusual case of asymptomatic hyperparathyroidism, considering the very elevated calcium level (12.9 mg/dl), the size of the adenoma (3.2 × 2.0 × 1.5 cm) and the very elevated parathyroid hormone level (340.3 pg/ml).

Primary hyperparathyroidism is associated with peptic ulcer disease, although the complete pathophysiological mechanism is not established yet. In cases where primary hyperparathyroidism is included in multiple endocrine neoplasia I (MEN I) and Zollinger-Ellison syndrome, peptic ulcer is generated by elevated gastrin level, which results in various clinical symptoms from the gastrointestinal system. On the other hand, in cases where primary hyperparathyroidism does not coexist with elevated gastrin level, the pathophysiological mechanism is still unknown. In various studies, an increased calcium level is reported to result in an increase of gastric acid secretion and gastrin level [14, 15]. On the other hand, several studies report that the association between hyperparathyroidism and an increased risk of peptic ulcer is controversial [5–10] and that chronic hypercalcemia does not affect gastric acid and gastrin secretion [5, 8, 16, 17]. Recently, many authors support the view that the activation of stomach calcium sensing receptor (SCAR) on the basolateral membrane of gastric parietal cells by Ca^{2+} leads to increased gastric acid secretion [18], but these results are based on acute elevation of calcium level, and further studies to support this model are necessary.

In our patient, the proposed hypothesis, since rapid urease test was negative and serum gastrin level was normal, is that for unknown reasons the serum calcium level of the patient increased rapidly, a fact that led to increased gastric acid secretion through activation of SCAR, and all this resulted in the acute formation of duodenal ulcer and perforation. Furthermore, one month after surgery, the endoscopic image of the stomach and duodenum is normal and the parathyroid hormone and calcium levels are normalized, which supports the hypothesis that the peptic ulcer was caused by hyperparathyroidism.

Conclusions

Peptic ulcer and its complications are usual manifestations of primary hyperparathyroidism, with or without increased gastrin level. On the other hand, cases of a perforation of peptic ulcer as the first clinical manifestation of primary hyperparathyroidism are extremely rare, and where possible, must be treated by a surgical team specialized in endocrine surgery, conservatively at first and surgically where needed.

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Fig. 1. A large adenoma of the right inferior parathyroid gland (black arrow).

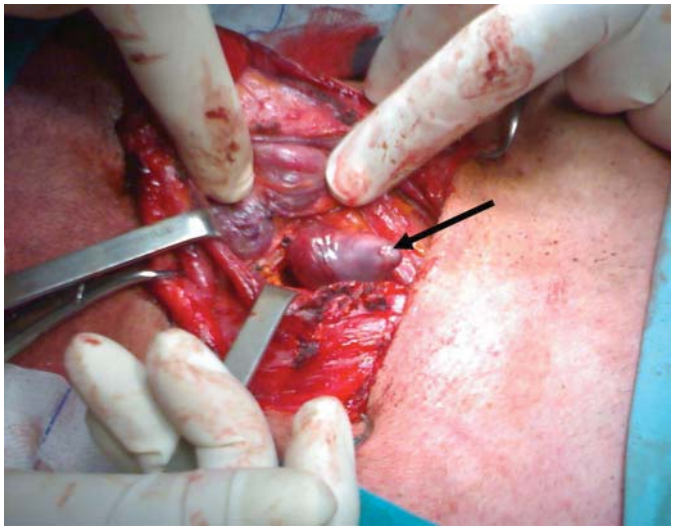

Fig. 2. The removed parathyroid adenoma, measuring 3.2 × 2.0 × 1.5 cm.

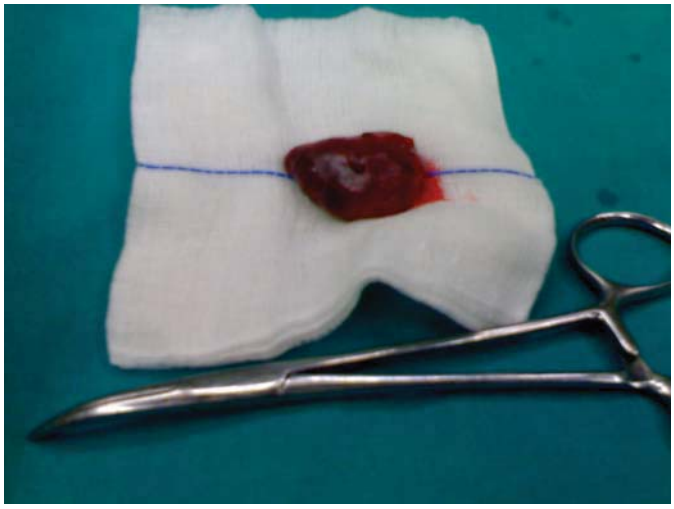

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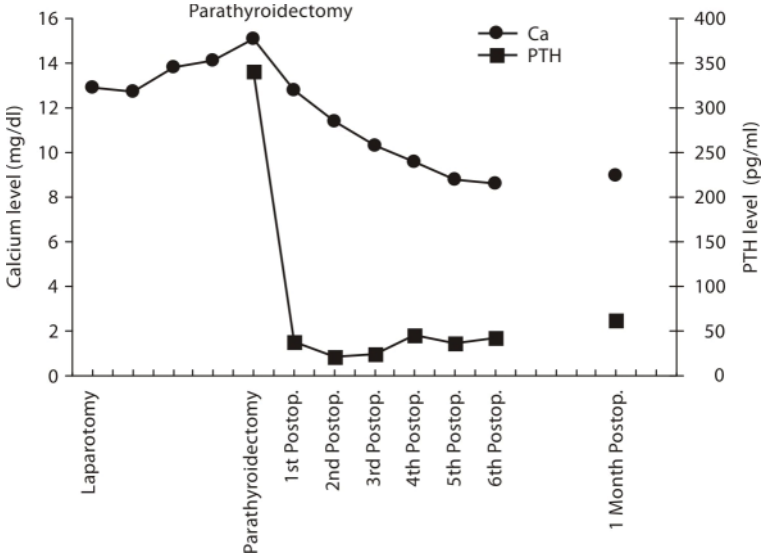
Fig. 3. Serum levels of calcium and parathyroid hormone before and after parathyroidectomy.



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