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ПЕРВИЧНЫЙ ГИПЕРПАРАТИРЕОЗ ВСЛЕДСТВИЕ АДЕНОМЫ ПАРАЩИТОВИДНОЙ ЖЕЛЕЗЫ: КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ

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Primary Hyperparathyroidism Due to Parathyroid Adenoma: Clinical Case

Резюме

Первичный гиперпаратиреоз — эндокринное заболевание, характеризующееся избыточной секрецией паратиреоидного гормона при верхне-нормальном или повышенном уровне кальция крови вследствие первичной патологии околощитовидных желез. Первичный гиперпаратироз в зависимости от клинических проявлений может протекать в нормокальциемической, мягкой и манифестной формах. В данной статье представлен клинический случай развития манифестной формы по типу висцеральных нарушений, которые проявились в виде патологии желудочно-кишечного тракта. Данная форма заболевания является показанием к оперативному лечению и дальнейшей коррекции кальций-фосфорного обмена.

Ключевые слова: *первичный гиперпаратиреоз, хронический панкреатит, аденома паращитовидных желез*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

Primary hyperparathyroidism (PGPT) is an endocrine disease characterized by excessive secretion of parathyroid hormone (PTH) in upper — normal or elevated blood calcium levels due to primary parathyroid gland pathology (osch). Primary hyperparathyrosis, depending on the clinical manifestations, can occur in the normocalcemic, mild and manifest form. This article presents a clinical case of the development of the manifest form by the type

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of visceral disorders. Which appeared in the form of pathology of the gastrointestinal tract. This form of the disease is an indication for surgical treatment and further correction of calcium-phosphorus metabolism.

Key words: *Primary hyperparathyroidism, chronic pancreatitis, adenoma of the parathyroid glands*

Conflict of interests

The authors declare that this study, its theme, subject and content do not affect competing interests

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BMI — body mass index, CL — cholelithiasis, FGD — fibrogastroduodenoscopy, GIT — gastrointestinal tract, NSAIDs — non-steroidal anti-inflammatory drugs, PHPT — primary hyperparathyroidism, PTG — parathyroid glands, PTH — parathyroid hormone, US — ultrasound

Introduction

Primary hyperparathyroidism (PHPT) is an endocrine disease characterized by excessive secretion of parathyroid hormone (PTH) in patients with abnormal or elevated blood calcium levels due to primary pathology of parathyroid glands. PHPT is manifested by a multisymptomatic clinical presentation involving various organs and systems in the pathological process, which leads to a significant decrease in the quality of life, disability of patients, and increased risk of premature death [2].

Depending on the severity of clinical symptoms, there are normocalcemic, mild and manifesting types of PHPT [1]. Depending on the variety of lesions in various systems and organs, the manifesting type is characterized by an intense clinical picture of bone lesions and/or visceral disorders and the risk of hypercalcemic crisis.

Damage to the gastrointestinal tract (GIT) is found in half of patients with PHPT. Patients have complaints of anorexia, constipation, nausea, flatulence, and weight loss. Gastric and/or duodenal peptic ulcers develop in 10–15% of cases, pancreatitis — in 7–12%; pancreatolithiasis and pancreatic calcinosis are less frequent [2]. The development of a gastric ulcer in cases of hypercalcemia is associated with increased secretion of gastrin and hydrochloric acid, which returns to normal after removal of parathyroid adenoma. The course of the gastric ulcer in cases of PHPT is characterized by a more intense clinical picture (frequent exacerbations with severe pain, perforations are possible) than in cases of a gastric ulcer caused by other factors. In this clinical case, we will observe the manifestation of the visceral type of disease, which is characterized by gastrointestinal lesions.

Case report

Patient K., 49 y.o., female, was admitted to the Gastroenterology Department on October 16, 2019 with complaints of severe general weakness, nausea during daytime, and vomiting bile up to four times a day (with relief), bitter taste in the mouth. There were no abdominal pains at the time of admission. Stool is formed, "pellet-like", sometimes with blood streaks, regular, up to three times a day (sometimes every other day), without mucus. No appetite. No skin itching. Low-grade body temperature occasionally in the evening. Fast satiation. Chewing within normal. Swallowing and food passage through the esophagus within normal.

The patient considers herself ill since 2015 when she was incidentally diagnosed with cholelithiasis (CL) during an ultrasound examination (US) of abdominal organs; no treatment was carried out. She started experiencing occasional aching pains in the epigastrium at night; she received outpatient treatment (proton pump inhibitor (omeprazole) with a positive effect). In 2015, there were three exacerbations; the patient was treated on an outpatient basis (omeprazole) with improvement. There were no GIT complaints until 2019. Worsening since February 2019, in the form of constant aching pain in the right upper quadrant, worsening at night. The patient took a non-steroidal anti-inflammatory drug (NSAID) up to several tablets per day. After two weeks, she visited a local therapist, was treated on an outpatient basis with a positive effect (proton pump inhibitor (omeprazole). In May 2019 — relapse of abdominal pain, again stopped by conservative treatment. At the beginning of August 2019 — relapse of pain; on August 16, 2019 a laparoscopic cholecystectomy was performed. Two days after discharge, the patient experienced repeated vomiting and epigastric pain; she was hospitalized with a diagnosis of "postcholecystectomy syndrome", was discharged with improvement. On October 4, 2019, she was again hospitalized for repeated vomiting bile and epigastric pain. The patient received treatment (infusion therapy, antiemetics, antibacterial therapy, proteolysis inhibitors, enzymes, proton pump inhibitors) with a slight improvement (less frequent vomiting, pain syndrome subsided). Considering persistent complaints, cancer alertness, weight loss of 20 kg over the past two months, the patient was transferred to the Gastroenterological Department

of the First Republican Clinical Hospital (Izhevsk) for examination and treatment.

Objectively on admission: general condition is satisfactory. Clear consciousness. Active position. Asthenic body type, hypotrophy (BMI 21.0 kg/m^2). Skin is pale, dry, of normal temperature, decreased turgor. Nails and hair are dull and brittle. Atrophic limb muscles. No peripheral edema. Respiratory rate 16 per minute. Vesicular breathing in the lungs, no rales. Regular heart rhythm with HR 84 per minute. Heart tones are clear. Rhythmic pulse of satisfactory filling. BP 100/70 mm Hg on both arms. Tongue is moist, with dense yellow fur. Abdomen of normal shape. On palpation, soft, painful in epigastrium and Shofar zone. Liver does not protrude from the edge of costal arch. Size according to Kurlov 11 × 8 × 7 cm. Gallbladder removed. Spleen not palpable. Kidneys not palpable. No CVA tenderness on percussion.

Laboratory and diagnostic test results

On admission on October 16, 2019: WBC — 7.47 × 10^9/l, RBC — 2.80 × 10^{12}/l, hemoglobin — 85 g/l, platelets — 232 × 10^9/l, ESR — 26 mm/h. Total protein — 56.7 g/l, albumin — 31.71 g/l, alpha$_1$ globulins — 2.72 g/l (1.4–3.0); alpha$_2$ globulins — 5.43 g/l (5.6–9.1); beta$_1$ globulins — 4.43 g/l (5.4–9.1); beta$_2$ globulins — 2.96 g/l (3.2–6.5); gamma globulins — 9.45 g/l (8.1–17.0); urea — 3.41 mmol/l, creatinine — 68.53 μmol/l, alkaline phosphatase (ALP) — 697.18 U/l, gamma-glutamyltranspeptidase (GGT) — 20.94 U/ml (7.0–32.0), aspartate aminotransferase (AST) — 9.3 U/l, alanine aminotransferase (ALT) — 5.30 U/l, sodium — 138.00 mmol/l, potassium — 3.00 mmol/l, glucose — 5.68 mmol/l, lipase — 16.78 U/l (0.0–60.0), alpha-amylase — 37.86 U/l (25.0–94.0), total bilirubin — 6.84 μmol/l, direct bilirubin — 2.20 μmol/l. Prothrombin index (PTI) — 95.0%; prothrombin time — 13.9 seconds; fibrinogen — 2.64 g/l; activated partial thromboplastin time (APTT) — 26.4 seconds.

Considering anemia, blood tests for serum iron, vitamin B$_{12}$ and folic acid were performed. Folic acid deficiency component of anemia was diagnosed (folic acid — 4.94 nmol/l (6.0–39.0)).

Urinalysis: specific gravity — 1004; pH — 6.5; protein — 0.1 g/l; glucose — 2.8 mmol/l; WBC — 0; RBC — 0; bacteria — 0. Urine amylase — 86.4 U/l (10.0–500.0).

Fecalysis: macroscopic examination — formed, brown, occult blood (++++); digestible muscle fibers +; indigestible fiber ++; neutral fat +. Stool culture for opportunistic flora: no growth of typhoid-paratyphoid-dysenteric bacteria was found.

Fibrogastroduodenoscopy (FGD) was performed: indirect signs of pancreatic pathology. Significant reflux — gastroduodenitis. Biliary duodenogastric reflux grade 3. Rough cicatricial-ulcerative deformation of duodenal bulb. Achalasia cardiae. Chronic reflux-esophagitis. Erythematous papillitis, moderate.

According to the biopsy — chronic atrophic gastritis of mild activity. Focal colonic metaplasia.

Colonoscopy: endoscopic signs of ischemic colitis in erosive stage, with damage to the blind, ascending, transverse, descending, sigmoid colon. Ileocecal valve dysfunction. Histological study revealed a picture of chronic nonspecific colitis with areas of stromal edema, reactive proliferation of glandular crypt epithelium, presence of neutrophil accumulations in the lumen of separate crypts, activity grade 1–2.

According to abdominal ultrasound, there were signs of diffuse changes in pancreatic parenchyma, with increase in size due to body and tail; calculus of left kidney.

Angiography of abdominal aorta and its branches to exclude ischemic origin of total erosive colitis: no data for stenotic-occlusive pathology of abdominal vessels were obtained.

On day 12 of therapy, negative clinical changes were observed (vomiting increased to 4–5 times a day) along with increase in alkaline phosphatase level to 837.0 mmol/l. In order to stop vomiting, a selective 5HT3 receptor antagonist was prescribed (ondansetron 8 mg/day).

Schwartz test revealed decompensated pyloric stenosis and slow passage of the contrast agent through the small intestine. Consultation with surgeon: at the time of examination, data for decompensated pyloric-bulbar stenosis are doubtful; no absolute indications for surgical treatment.

Considering persistent multiple vomiting, the daily dose of ondansetron was increased to 16 mg per day, potassium chloride was added to correct electrolyte disorders.

On day 18 of treatment, vomiting increased to 10 times a day, irrespective of food intake. To exclude the central origin of vomiting, magnetic resonance imaging (MRI) of the brain was performed: atrophic process of brain substance was revealed. Consultation with neurologist: no data for focal neurological pathology at the time of examination.

A multidisciplinary team meeting was held in connection with the negative changes; it was decided to adjust infusion therapy, monitor daily urine, review the pituitary gland on brain MRI, review adrenal glands on abdominal CT, perform ultrasound of the thyroid gland, blood test for calcium, thyroid hormones (thyroid stimulating hormone (TSH), free triiodothyronine ($T_{3)}$, free thyroxine (fT_4)), parathyroid hormone.-

Test results: TSH — 0.745 μIU/ml (0.4–5.5), free T_4 — 14.5 pmol/l (9.0–23.0), PTH — 2048 pg/ml (9.5–75.0 pg/ml), calcium — 2.53 mmol/l (2.10–2.55), phosphorus — 2.03 mmol/l (0.87–1.45). Ultrasound of thyroid and parathyroid glands revealed signs of parathyroid adenoma located on the back border of the lower pole on the right; the structure of the thyroid gland echographically

with slight changes. Consultation with endocrinologist: the patient was diagnosed with «primary hyperparathyroidism, adenoma of parathyroid glands», surgical treatment is recommended.

The following treatment was performed in the Gastroenterology Department: infusion therapy, antispasmodics, enzymes, H_2 blockers, antimicrobials (metronidazole, rifamixin), glucocorticoids, selective 5HT3 receptor antagonist (ondansetron), bismuth agents, folic acid, anti-inflammatory (mesalazine), laxatives, gastroprotectors, and enteral nutrition.

During the patient's stay in the Gastroenterology Department, laboratory parameters improved slightly: WBC — 8.73×10^9/l, RBC — 3.59×10^{12}/l, hemoglobin — 107 g/l, platelets — 234×10^9/l, alkaline phosphatase — 478.74 U/l, lipase — 11.24 U/l, alpha-amylase — 23.36 U/l.

In connection with the diagnosed primary hyperparathyroidism with underlying parathyroid adenoma, which caused indomitable vomiting with secondary water-electrolyte disorders, the patient was transferred to the Surgical Department for surgical treatment of parathyroid adenoma.

On November 20, 2019, a right-sided parathyroidectomy was performed. According to biopsy results, no neoplasm elements were found.

The postoperative period was characterized by a significant decrease in levels of hemoglobin, calcium, potassium (laboratory test results from November 25, 2019: WBC — 7.80×10^9/l, RBC — 2.04×10^{12}/l, hemoglobin — 59 g/l, platelets — 140×10^9, total calcium — 1.37 mmol/l; potassium — 2.73 mmol/l).

Transfusion of RBC concentrate was performed, with positive effect. The decrease in calcium level to less than 1.9 mmol/l was an indication for intravenous administration of calcium gluconate [1]. After three days, blood calcium level increased to 2.25 mmol/l, along with the improved general state of the patient. Conservative treatment in the Surgical Department: infusion therapy, calcium gluconate, RBC concentrate, alfacalcidol. On day 14 after surgical treatment, the wound healed by primary intention, scar is competent. The patient was discharged for outpatient treatment.

Final clinical diagnosis: Primary hyperparathyroidism with adenoma of the right lower parathyroid gland (condition after right-sided parathyroidectomy), gastrointestinal type, newly diagnosed, complicated by gastropathy in the form of indomitable vomiting, secondary erosive-ulcerative enterocolitis with symptoms of transient dynamic small bowel obstruction. Nutritional deficiency grade 2. Water-electrolyte disorders of moderate severity. Background disease: Chronic biliary-dependent pancreatitis, parenchymal type, recurrent course, dyspeptic form, exacerbation phase. Exocrine pancreatic insufficiency grade 1. Postcholecystectomy syndrome (condition after laparoscopic cholecystectomy due to cholelithiasis from August 16, 2019). Duodenal ulcer, newly diagnosed, remission phase. Cicatricial deformation of the duodenal bulb with compensated pyloric-bulbar stenosis. Urolithiasis.

Diet recommendations (calcium-, potassium-rich) were given on discharge. Limited physical activity for 2–3 months. Alfacalcidol + calcium carbonate (0.25 μg + 500 mg) — 2 capsules in the morning and 1 capsule in the evening. Control of complete blood count, total and ionized calcium.

Discussion

In the presented clinical case, the patient suffered from nausea, indomitable vomiting, and epigastric pain persisting after cholecystectomy due to cholelithiasis. The treatment prescribed to relieve chronic biliary-dependent pancreatitis had no effect. During examination of the patient, parathyroid adenoma was found. Clinical manifestations corresponded to the picture of the visceral type of primary hyperparathyroidism, which was an absolute indication for surgical treatment. Surgical treatment is the most radical and effective method of managing this pathology [3]. The postoperative period can be characterized by hypocalcemia (up to 50% of cases), which is caused by long suppression of the normal function of parathyroid glands by active parathyroma, postoperative edema of the remaining parathyroid glands, or by "hungry bone" syndrome [2]. During the postoperative period, serum calcium level in this patient dropped to 1.37 mmol/l, which was an indication for intravenous administration of calcium gluconate [2]. The patient was discharged with a significant improvement during follow-up by a local therapist and endocrinologist, with recommendations to continue taking calcium and the active form of vitamin D on an outpatient basis.

Conclusion

The diagnosis of primary hyperparathyroidism with visceral signs is a challenging task for physicians of most specialties. Timely diagnosis and surgical treatment can significantly improve the prognosis and patient's quality of life. Analysis of clinical cases that are difficult to diagnose is important to improve the effectiveness of primary care physicians since they can bring the experience of clinical treatment of patients with rare pathologies into their practice [5].

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