A Case of Hyperparathyroidism due to a Large Intrathyroid Parathyroid Adenoma with Recurrent Episodes of Acute Pancreatitis

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1. Introduction

Primary hyperparathyroidism (PHPT) is a common endocrine disorder characterized by hypercalcemia and excessive secretion of parathyroid hormone (PTH) [1]. PHPT is most commonly caused by a single adenoma of the parathyroid gland. Patients with PHPT tend to develop complications such as reduction of bone mineral density, nephrolithiasis, and gastric ulcer, which may impair quality of life [1, 2]. In the management of PHPT, parathyroidectomy of the abnormal gland is the gold standard for effective treatment. Generally, most parathyroid adenomas remain relatively small, measuring under a few centimeters and weighing less than 1 g [3]. Large or giant parathyroid adenomas are seldom seen in patients with PHPT [4], and in such cases differential diagnosis is necessary to rule out malignancy.

Acute pancreatitis may be induced by cholelithiasis and alcohol abuse in adults; however, the incidence of pancreatitis in patients with hyperparathyroidism was reported to be only 1.5% [5]. Here, we report a case of hyperparathyroidism due to a large intrathyroid parathyroid adenoma with episodes of acute pancreatitis. She had been treated for acute pancreatitis twice. However, there was no episode of pancreatitis after the operation.
Table 1: General laboratory data.

|                         | Before operation | After operation | (normal values) |
|-------------------------|------------------|-----------------|-----------------|
| **Peripheral blood**    |                  |                 |                 |
| White blood cells (/μL) | 5690             | 6210            | (3500–8500)     |
| Red blood cells (/μL)   | 3.50             | 3.84            | (3.80–4.80 × 10⁶) |
| Hemoglobin (g/dL)       | 10.7             | 10.9            | (11.5–15.0)     |
| Hematocrit (%)          | 31.5             | 32.7            | (34.0–45.0)     |
| Platelets (/μL)         | 18.1             | 20.5            | (13.0–35.0 × 10⁴) |
| **Blood biochemistry**  |                  |                 |                 |
| Total protein (g/dL)    | 6.9              | 7.0             | (6.7–8.3)       |
| Albumin (g/dL)          | 4.0              | 4.0             | (3.9–4.9)       |
| Total bilirubin (mg/dL) | 0.8              | 0.6             | (0.2–1.1)       |
| Aspartate aminotransferase (U/L) | 28 | 25 | (10–35) |
| Alanine aminotransferase (U/L) | 20 | 16 | (7–38) |
| ɣ-Glutamyltranspeptidase (U/L) | 28 | 35 | (0–65) |
| Alkaline phosphatase (IU/L) | 263 | 213 | (104–340) |
| Urea nitrogen (mg/dL)   | 17               | 14              | (8–25)          |
| Creatinine (mg/dL)      | 0.81             | 0.89            | (0.40–1.10)     |
| Sodium (mmol/L)         | 145              | 143             | (137–146)       |
| Chloride (mmol/L)       | 112              | 107             | (99–110)        |
| Potassium (mmol/L)      | 4.4              | 4.0             | (3.5–4.9)       |
| Calcium (mg/dL)         | 12.4             | 9.6             | (8.3–10.3)      |
| Phosphorus (mg/dl)      | 2.4              | 3.3             | (2.4–4.7)       |
| Total cholesterol (mg/dl)| 215             | 182             | (115–220)       |
| Triglyceride (mg/dL)    | 185              | 215             | (20–150)        |
| Plasma glucose (mg/dL)  | 98               | 132             | (70–110)        |
| Hemoglobin A1c (%)      | 5.1              | 5.8             | (4.6–6.2)       |
| Intact PTH              | 253.0            | 59.3            | (8.7–79.5)      |

Left hemithyroidectomy was performed due to the clearly defined soft tissue mass within the left thyroid. Histopathology showed no signs of invasion, and this is consistent with parathyroid adenoma. The adenoma was composed mainly of chief cells and oxyphil cells, covered with a fibrous capsule (Figure 2(a)). Evaluation of chromogranin A expression showed positive chromogranin A immunostaining (Figure 2(b)). Evaluation for PTH expression showed positive PTH immunostaining (Figure 2(c)). Soon after surgery, the elevated calcium and iPTH were normalized. The patient has had no episodes of pancreatitis for one year after the operation.

3. Discussion

This is an unusual case of hyperparathyroidism due to a large parathyroid adenoma. This present patient had been treated for acute pancreatitis twice. Pooled clinical data suggest an association between PHPT and pancreatitis [6, 7]. Serum calcium levels in PHPT with pancreatitis were found to be higher than those in PHPT without pancreatitis [6, 8]. Acute pancreatitis may be caused by calcium-induced activation of intrapancreatic trypsinogen to trypsin. However, only a
majority of patients with PHPT would develop pancreatitis. Felderbauer et al. found that mutations in the serine protease inhibitor Kazal type I (SPINK1) and cystic fibrosis transmembrane conductance regulator (CFTR) genes increase the risk for pancreatitis, and mutations in the Chymotrypsin C gene (CTRC) modulate susceptibility for pancreatitis [9, 10]. Therefore, markedly elevated serum calcium may contribute to pancreatitis, together with additional genetic or environmental insults [6].

Parathyroid adenomas usually measure less than 2 cm and weigh less than 1 g. In parathyroid lesions larger than 2 cm, the differential diagnosis between giant parathyroid adenomas and parathyroid carcinomas would be considered [11]. Parathyroid cysts or cystic adenomas often show large parathyroid ones [12]. No signs of malignancy, such as presence of capsular invasion, angioinvasion, and invasion of the surrounding structures, were observed by morphological analysis in our case. The weight or size of the adenoma may have been correlated with the functional status of the gland and the severity of biochemical abnormalities. For example, larger adenomas may be associated with a more severe form of primary hyperparathyroidism [13]. Conversely, in some cases of giant adenoma, there was no correlation with clinical symptoms or functional status [14].

The incidence of intrathyroid parathyroid adenoma is rare: true one is 0.7%, and partial one is 1.9% [15]. Imaging may miss the pathologic gland [16]. Generally, different imaging techniques, such as high resolution ultrasonography, CT, arteriography, venous sampling, and magnetic resonance imaging, have been used for detection of the abnormal parathyroid glands [17, 18]. Radionuclide imaging has also been used in the detection and localization of parathyroid adenomas. $^{99m}$Tc-MIBI has been used for preoperative evaluation of PHPT [19], as demonstrated in our case.

Hypercalcemia may mediate the development of pancreatitis and our patient had earlier been treated for acute pancreatitis twice. However, during short-term follow-up, she had not experienced any episodes of pancreatitis after surgery. In a patient with recurrent episodes of pancreatitis, the possibility of complication with hyperparathyroidism should be considered.
In summary, we report an unusual case of hyperparathyroidism due to a large intrathyroid parathyroid adenoma with episodes of acute pancreatitis.

**Consent**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Conflicts of Interest**

None of the authors have any potential conflicts of interest associated with this research.

**Authors’ Contributions**

All authors contributed to the management of the patient and drafting of the manuscript, and all have approved the final submission.

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