

A case of multiple bone destruction due to parathyroid adenoma

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Abstract: Primary hyperparathyroidism (PHPT) is caused by an overproduction of parathyroid hormone (PTH.) The most common cause is parathyroid adenoma, and its main clinical manifestations may involve urinary stones, bone pain, osteoporosis, and pathologic fractures. The treatment of choice is surgery, and accurate diagnosis is essential for the treatment of this disease. This article reports a rare case of parathyroid adenoma and hyperparathyroidism leading to multiple bone destruction in an adolescent, aiming to raise clinicians' awareness of parathyroid adenoma leading to multiple bone destruction.

1. Introduction

Primary hyperparathyroidism (PHPT) is caused by excessive secretion of parathyroid hormone (PTH). The disease can occur at any age, the peak of the disease is 50-60 years old, and the incidence is rare in children and adolescents. The prevalence of PHPT in children/adolescents reported abroad is 2 to 5 per 100, 000, which is significantly lower than that in adults (1:500 to 2000). In general, the disease is more common in women, especially in postmenopausal women, with a male to female ratio of about 1:2.8. However, PHPT in children/adolescents did not show significant gender difference, with a sex ratio of 1:1.3 ~1.5 [1-3]. The most common cause is parathyroid adenoma, which accounts for about 85%. In recent years, it has been found that low dietary calcium intake and heavier body weight are risk factors for PHPT in women [4-5]. It has also been found in studies that PHPT in children and adolescents is related to mutations in MEN1 gene and CDC73 gene, with a mutation rate of about 31.2% [6]. Parathyroid adenomas not only occur in the parathyroid gland, but also sometimes in unexpected places. The most common atypical locations are the thyroid gland, thymus, upper mediastinum, and even in the posterior esophageal space, pericardium, supraclavicular fossus, etc., with an incidence of about 6%-10% [7-8]. The low incidence of PHPT in children/adolescents and the rare cases are one of the important reasons for the difficult diagnosis of this patient.

2. Clinical manifestation

The parathyroid gland secretes parathyroid hormone (PTH), and its main target organs are the

bones and kidneys. PTH can regulate the metabolism of calcium in the body and maintain the balance of calcium and phosphorus. It can promote the function of osteoclasts and release bone calcium into the blood, thereby increasing the level of blood calcium and blood phosphorus. When the concentration of PTH in the blood exceeds a certain threshold, it will be eliminated through urine, resulting in high urinary calcium and high urinary phosphorus. PTH can also inhibit the reabsorption of phosphorus by renal tubules, resulting in high urinary phosphorus and low blood phosphorus, as shown in Figure 1.

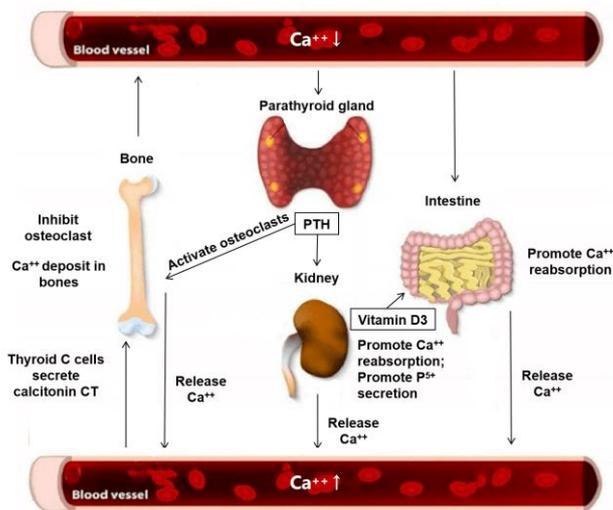


Figure 1: The Mechanism of PTH Regulating Blood Calcium

Primary hyperparathyroidism can involve multiple systems in clinical practice, including the skeletal system. The main manifestations are nonspecific osteoporosis, bone pain, bone malformation, and bone destruction. For urinary system, the main manifestations are polyuria, kidney stones, and kidney calcification. For the digestive system, it is mainly manifested as poor appetite, nausea, vomiting, abdominal pain, and so on. However, because children and adolescents are in the flourishing period of growth and development, the skeletal system is more sensitive to the concentration of parathyroid hormone, so the clinical symptoms of PTH in adolescents are more common and more severe than those in adults [3]. Therefore, it is particularly important to detect the levels of parathyroid hormone and alkaline phosphatase when osteoporosis, bone pain, and bone destruction occur in adolescents. Primary hyperparathyroidism is easily misdiagnosed clinically because the skeletal system manifestations of osteoporosis, bone pain, bone deformity, and bone destruction are similar to those caused by multiple myeloma. Multiple myeloma (MM), on the other hand, is a malignant hematologic disease caused by abnormal proliferation of clonal plasma cells, and ranks second in the incidence of lymphohematopoietic system. Multiple myeloma is prevalent in the elderly, and studies have shown that the age of prevalence in Europe and the United States is 65-70 years old [9-10]. In China, the incidence rate is slightly lower than that in Europe and the United States, and the age of prevalence is 55-60 years old [11]. The symptoms of multiple myeloma are varied and can involve multiple systems, tissues, and organs. However, 90% of patients with multiple myeloma develop osteolytic changes, i.e. multiple myeloma bone disease (MMBD) [12], and its main clinical manifestations are osteoporosis, hypercalcemia, bone pain, pathological fractures, and other skeletal lesions. The diagnostic criteria for multiple myeloma include, in addition to the clinical manifestations of target organ damage, a bone marrow clonal plasma cell ratio of $\geq 10\%$ or the presence of a plasma cell tumor (bone or extramedullary) confirmed by tissue biopsy.

3. Anatomical structure

Anatomically speaking, the parathyroid gland is closely attached to the left and right side of the thyroid gland, the neck examination is not easy to find abnormalities, as shown in Figure 2. Coupled with the lack of experience of non-specialist doctors, so it is easy to be misdiagnosed in the early stage. The early misdiagnosis of this patient is similar to that reported in recent years. Ding Jinyong et al. [13] conducted a retrospective analysis of 42 PHPT patients admitted to the First Affiliated Hospital of Guangzhou University of Chinese Medicine from November 2002 to January 2017, and found that the misdiagnosis rate was as high as 66.7% (28/42), and there were 9 kinds of misdiagnosed diseases, mainly osteoporosis, bone tumor, kidney stone, ankylosing spondylitis, and various types of arthritis, which were misdiagnosed as bone The probability of porosity is as high as 32.1% (9/28). The misdiagnosis time was from 1 week to 6 years, and the misdiagnosis time was more than 1 year in 12 cases (42.9%).

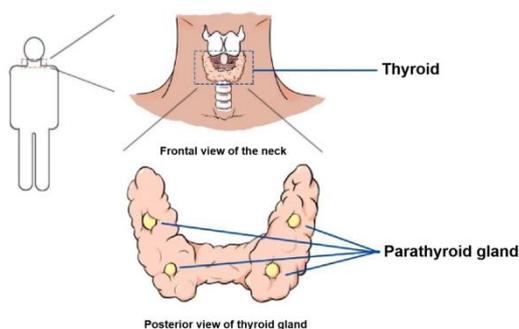


Figure 2: Thyroid anatomic structure

4. Diagnostic

The diagnosis of PTHT mainly includes two aspects: location diagnosis and qualitative diagnosis. In addition to symptoms and signs, the qualitative diagnosis is particularly important for blood calcium concentration, PTH and alkaline phosphatase. The location diagnosis is mainly made through neck B-ultrasound, mediastinal CT and radionuclide detection [14]. Clues for early diagnosis of PHPT in this patient include: unexplained bone and joint pain, and auxiliary examination suggests elevated parathyroid hormone, blood calcium, and alkaline phosphatase. B-ultrasonography indicated hypoechoic mass behind the right lobe of the thyroid, and CT scan + enhancement indicated slightly low density nodules behind the right lobe of the thyroid, considering parathyroid occupation. Parathyroid nuclide examination indicated that most of the lesions in the dorsal side of the right inferior lobe of the thyroid were parathyroid adenomas.

5. Treatment and care

The treatment principle of hyperparathyroidism caused by parathyroidoma is surgical resection, as shown in Table 1. In recent years, the surgical methods for parathyroid adenoma have evolved from open surgery to endoscopic surgery and microwave ablation. There are various surgical modalities, but the opinions on which treatment modality to choose do vary. Li Xia [15] et al. retrospectively analyzed 108 patients with parathyroid adenomas admitted to Yangjiang City Hospital of Traditional Chinese Medicine for surgical treatment from October 2015 to September 2017, and found that 56 patients with microwave ablation had shorter operation time, shorter hospital stay, and less intraoperative bleeding than 52 patients with traditional surgical treatment, and that postoperative levels of calcium, phosphorus, and parathyroid hormone decreased significantly in both groups. The

postoperative calcium, phosphorus and parathyroid hormone levels of the patients in both groups decreased significantly. That is to say, microwave ablation can achieve the same effect in the treatment of parathyroid adenoma with traditional open surgery, but microwave ablation has the advantages of shorter operation time and hospitalization time, less intraoperative bleeding and less trauma, which is worth to be popularized and applied in clinic in the author's opinion. Zhang Dongyan et al. [16] conducted a retrospective study on 1026 medical records of thyroidectomy patients from 2013 to 2014 and found that the incidence of postoperative hypoparathyroidism ranged from 1% to 32%, most of which were temporary hypoparathyroidism. In addition to temporary hypoparathyroidism, hypocalcemia is more common, which makes postoperative care especially important. Postoperative care mainly includes general care, daily care, psychological care and symptom care. General nursing care mainly includes close monitoring of patients' postoperative vital signs, and instructing patients to take more bed rest and reduce activities. Daily care includes eating a diet high in calcium and low in scale and rich in microbial D, such as vegetables, fruits, fish, lean meat, etc. Daily exercise encourages patients to get more sunshine and avoid strenuous activities. Psychological care mainly includes eliminating patients' postoperative nervousness, giving patients psychological support, so that patients maintain a positive mood, which will help patients to recover soon. The most common symptoms in postoperative patients include numbness of the mouth and face, twitching of the hands and feet, and in more severe cases, laryngeal muscle tension leading to dyspnea. The main reason is that after parathyroidectomy, parathyroid hormone secretion decreases, blood calcium concentration decreases, and neuromuscular excitability increases. Clinical manifestations include numbness in the face, mouth or limbs in mild cases, twitching of hands and feet in severe cases, and laryngeal muscle tension resulting in respiratory distress. Therefore, it is necessary to closely monitor the blood calcium level after surgery. And in order to avoid respiratory distress, it is especially important to closely detect the patient's respiration, pulse rate and oxygen saturation. Therefore, in addition to a high-calcium diet, oral medication can be used to replenish calcium in the postoperative period, but in order to prevent hypocalcemia in the clinic, 10% calcium gluconate is usually injected intravenously, and it is worth noting that the concentration and speed of calcium supplementation in the vein should be strictly controlled, and the concentration and speed of calcium supplementation in the vein can be too thick and too fast, which can cause cardiac arrhythmia and circulatory failure, etc [17-18].

Table 1: Surgical indications for parathyroidoma

Types of the patients	Surgical indications
PHPT Patients with clear symptoms	√
PHPT Patients without clear symptoms	The following points need to be met: (1) Patients with hypercalcemia have blood calcium levels higher than the normal upper limit of 0.25 mmol/l (1mg/dL); (2) Patients with kidney damage have a muscle clearance rate below 60ml/min; (3) Patients' partial bone density values are lower than the 2.5 standard deviation of peak bone mass (T-value<-2.5) and/or patients have brittle fractures; (4) Patients are less than 50 years old; (5) Patients can not receive routine follow-up
PHPT Patients	Patients don't have surgical contraindications and the lesion localization is clear

6. Cases

The patient is male, 16 years old, admitted to the hospital with "pain in both knee joints for half a month". Half a month ago, the patient had pain in both knees and weakness in both lower limbs during activities without any obvious triggers, and the pain could be relieved at rest. Because of the recurrence of the above symptoms, on 2023-02-15, he consulted a hospital in Dingxi City, and MRI of bilateral knee joints suggests "multiple abnormal mixed signal foci in bilateral tibia-fibular bones, bone cortical defects? Bone infarction?". CT of both knees showed "multiple fibrous cortical defects in the lower femur and upper fibula on both sides". The patient and his family visited a hospital in Shaanxi for further treatment. Admission: Clear consciousness, good spirit, normal diet, soreness and discomfort in both knee joints after activity, normal urination and defecation, no significant weight loss. Physical examination: temperature: 36.3°C, respiration: 16 times/min, pulse: 68 times/min, blood pressure: 110/60mmHg. Neck symmetry, no jugular vein irritation, soft neck no resistance, trachea centered, thyroid area no abnormal mass, neck no abnormal lymph nodes. There were no obvious abnormalities in the heart, lung and abdomen. The physiological curvature of the spine is present, lumbar tenderness, percussion pain (-), and motion is reasonable. The appearance of both knee joints showed no obvious deformity, no redness and swelling, skin temperature was not high, floating patella test (-), lateral test (-), drawer test (-), peripheral blood flow and sensorimotor of both lower limbs were good, muscle strength of both lower limbs was normal, and no obvious abnormalities were found in the remaining limbs. Admission diagnosis: "Bone mass to be investigated (Non-ossifying fibroma? Multiple myeloma?)".

After admission to the hospital, relevant examinations were completed: Hemoglobin 177g/L ↑, free-triiodothyronine 7.56pmol/L ↑, triiodothyronine 3.17nmol/L ↑, alkaline phosphatase 1775U/L ↑, glutamyl transpeptidase 46IU/L ↑, hydroxybutyrate dehydrogenase 187U/L ↑, total carbon dioxide 21.4mmol/L ↓, calcium 3.00mmol/L ↑, and total carbon dioxide 21.4mmol/L ↓. Calcium 3.00mmol/L ↑. Electrocardiogram: sinus bradycardia, heart rate: 54 beats/min, premature repolarization. Thoracic and abdominal CT showed: (1) Multiple bone destruction (multiple boundary clear bone destruction areas of varying sizes were found in the bilateral humerus, scapula, clavicle, bilateral ribs, T1, L4 vertebrae, L5, S1 vertebrae, left transverse process, symphysis pubis, bilateral ilium acetabulum, ischium, and left femoral neck, and soft tissue density was found inside. The larger one was located in the left ilium with a size of about 43mmx17mm, The CT value is about 39HU). (2) The density of the left lobe of thyroid decreased. (3) No clear anomaly was found. According to the results of the auxiliary examination, multiple bone destruction, white-to-spheroid ratio of 2.4, elevated alkaline phospholipase, elevated hemoglobin, and elevated red blood cell count were suggested for consultation in the Department of Orthopedics and hematology. The consultation opinions were as follows: bone marrow puncture and biopsy were recommended, radiological examination of the skull was improved, and bone tissue puncture and biopsy were performed if necessary. The patient and his family were informed, and the bone marrow puncture biopsy was performed on 2023-02-21 with the consent of the patient and his family. The results of the bone marrow puncture biopsy on 2023-02-23 showed no obvious abnormalities. Rule out multiple myeloma. Head CT showed no obvious abnormality in brain parenchyma and uneven bone density in skull. Thyroid function series indicated high levels of free triiodothyronine and triiodothyronine, CT indicated decreased density in the left lobe of thyroid, and laboratory examination indicated parathyroid hormone 658.0ng/L↑. Therefore, thyroid disease was suspected and relevant examinations were continued to be improved. B-ultrasound examination of the thyroid gland showed that the hypoechoic mass behind the right lobe of the thyroid gland (about 6.3x15. 9x24. 8mm hypoechoic mass with clear boundaries and uneven internal echo, no significant changes in the post-echo, CDFI showed visible blood flow signals). Thyroid cysts: Type 2 TI-RADS. Thyroid plain CT

scan + enhancement indicated: nodules in the rear of the right lobe of the thyroid (slightly low-density nodules with a size of about 1.3cmx3.1cmx0.8cm were observed in the rear of the right lobe of the thyroid, and the CT value was about 41HU. The enhancement in the arterial phase was significantly enhanced, and the enhancement in the venous phase and the delayed phase was weakened), considering the space occupying lesion, which may be from the parathyroid gland. Therefore, the revised diagnosis is: "(1) Parathyroid occupation (parathyroid adenoma? Hyperparathyroidism?). (2) Multiple systemic bone destruction." In order to further clarify the diagnosis and location of the lesions, and improve the parathyroid nuclide examination, SPECT/CT suggested that: two-phase parathyroid MIBI imaging and fusion tomography imaging: most of the lesions on the dorsal side of the right lobe of the thyroid were parathyroid adenomas. Definite diagnosis: "parathyroid adenoma, hyperparathyroidism, systemic multiple bone destruction".

7. Acupotomy Treatment

Bilateral parathyroid exploration and resection of right inferior parathyroid tumor were performed in the neck under general anesthesia at 14:00 on 2023-03-02. Intraoperative findings: A lump of about 2x2x1.5cm in size was seen on the dorsal side of the lower pole of the right lobe of the thyroid gland, soft and intact, and no abnormal parathyroid gland was detected on the upper pole and the dorsal side of the left lobe of the thyroid gland. Postoperative pathological examination indicated benign lesions.

After surgery, the patient experienced numbness, twitching, muscle spasm and restlessness in the mouth, face and limbs. Calcium gluconate was given 30mg once every 8h. Parathyroid hormone was found 83.15ng/L ↑, 1.85mmol/L ↓ on the 2nd day after surgery. Parathyroid hormone was found 172.5ng/L ↑, 1.91mmol/L ↓ on the 7th day, and was discharged from hospital on 2023-03-15. The patient was asked to periodically review the concentrations of blood calcium, blood PTH, and blood phosphorus.

On 2023-07-12, he came to the hospital for review, parathyroid hormone 122.6 ng/L ↑, and the rest did not show any significant abnormality. Frontal and lateral DR of the skull, hands and knees showed that the skull and hands were better than the previous film (2023-02-23), and the knees were better than the previous film (2023-02-23), and the knees were better than the previous film. DR of both knee joints showed better bone changes than the previous film.

8. Discussion

The clinical manifestations of PHPT are diverse, but its main target organs are bones and kidneys. The bone destruction and bone pain caused by PHPT are similar to those of multiple myeloma, but the diagnostic and therapeutic process is very different. Epidemiologic investigations of PHPT and MM do not occur well in 16-year-old adolescents, i.e., the incidence of PHPT in children/adolescents is low, which is one of the important reasons for the diagnostic difficulty of this patient. Therefore, clinicians should strengthen the understanding of PHPT, and should further perform blood PTH and thyroid ultrasonography in patients with unexplained bone pain, osteoporosis, multiple episodes of urinary stones and renal calcium deposition, accompanied by abnormalities of calcium, phosphorus, and alkaline phosphatase, as well as performing bone marrow aspiration to exclude the possibility of multiple myeloma. The parathyroid glands are closely attached to the back of the right and left thyroid lobes of the thyroid gland and are not easy to be touched, which is one of the reasons why this disease is easily misdiagnosed. This is the second reason why the disease is easily misdiagnosed. However, due to the abundance of modern medical diagnostic and therapeutic means, the disease can be diagnosed faster and more accurately with the help of auxiliary examinations. Once the disease is diagnosed, surgical treatment is the inevitable choice. Surgery is safe, effective and has a good prognosis, but the patient's calcium status needs to be closely monitored after surgery. Patients with

this disease require comprehensive care, which is combined with dietary calcium supplementation and medication calcium supplementation. Moreover, postoperative patients can also be given intravenous injection of 10% calcium gluconate solution for Calcium supplementation. Overall speaking, the incidence of adolescent parathyroid adenoma is low, and the first symptoms are not typical, but clinicians should strengthen the awareness, with the help of modern auxiliary examination, once the diagnosis is clear, and actively operate, the majority of patients have a good prognosis.

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