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ENDOCRINE SURGERY

Primary hyperparathyroidism due to ectopic parathyroid adenoma in an adolescent: a case report and review of the literature

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Abstract

Purpose Primary hyperparathyroidism (PHPT) is a common endocrine disorder and is usually diagnosed in adults. PHPT due to ectopic parathyroid adenoma in adolescents is rare.

Methods We describe the case of a 15-year-old boy with PHPT due to ectopic parathyroid adenoma. A review of the literature of PHPT in adolescents was performed, focusing on etiology, clinical presentation, preoperative localization methods, pathology, and treatment.

Results The patient was successfully treated with surgery and was followed up for 5 years with no signs or symptoms of hyperparathyroidism. By reviewing the literature, only seven cases of PHPT associated with ectopic parathyroid lesions in adolescents have been reported. Parathyroidectomy is the only known curative treatment. Accurate preoperative localization of the target lesion is critical.

Conclusions This study should raise awareness of the diagnosis and treatment of PHPT due to ectopic parathyroid adenoma/carcinoma in adolescents.

Keywords Primary hyperparathyroidism · Parathyroid hormone · Ectopic parathyroid gland · Parathyroidectomy · Adolescent

Introduction

Globally, primary hyperparathyroidism (PHPT) is a common endocrine disorder. PHPT is characterized by elevated serum calcium and serum parathyroid hormone (PTH) levels [1–3]. PHPT is usually caused by a single parathyroid adenoma. The parathyroid glands are generally located adjacent to the thyroid, but may be ectopic in an estimated 2% of individuals [4]. The standard treatment for PHPT is to remove the parathyroid adenoma. However, locating ectopic parathyroid adenomas preoperatively can be challenging [5].

PHPT affects approximately 1% of the population, occurring mainly in individuals aged 50–60 years; PHPT in adolescents is rare [4, 6–8]. Here, we present a case of PHPT caused by an ectopic parathyroid adenoma in an adolescent, and present a review of the literature in which less than ten similar cases have been reported [5, 7–13].

Case presentation

A 15-year-old boy was admitted to the Department of Endocrinology, at the First Affiliated Hospital of China Medical University, complaining of fatigue and ostealgia in all four limbs for the past 5 years. One and a half years ago, the patient suffered a right upper limb fracture while arm wrestling with a classmate, and 6 months later, a second fracture occurred in the same location due to overexertion. Two months ago, the patient fell and suffered a patellar fracture in the left knee. He experienced chronic pain and anxiety and lost his appetite. The patient subsequently lost

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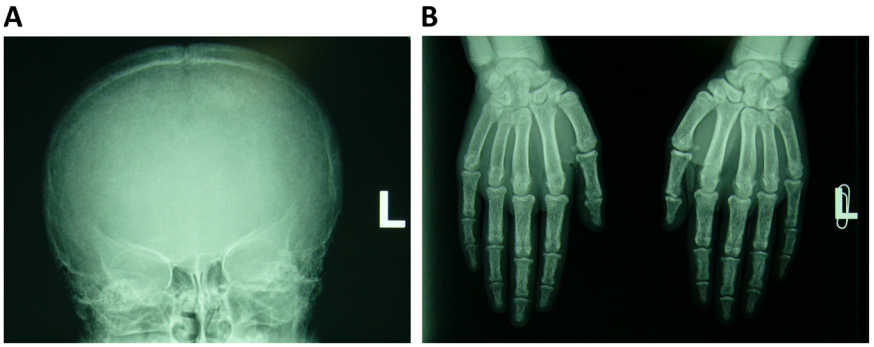

Fig. 1 X rays showed obvious osteopenia of the hands **a** and skull **b**

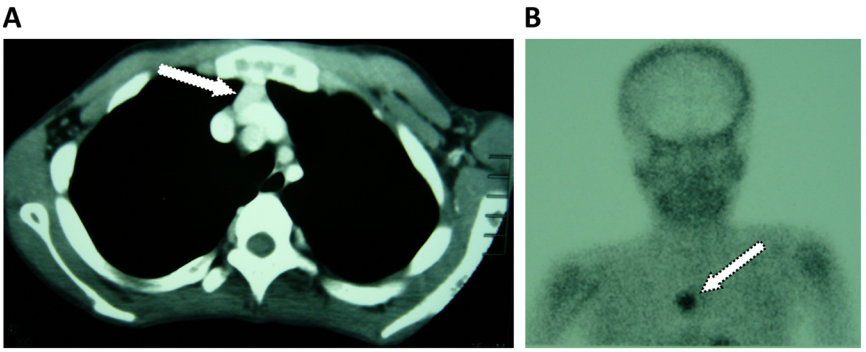

Fig. 2 **a** A hypervascular nodule in the superior mediastinum was noted on CT (arrow). **b** A nodule was visualized with high uptake on 99mTc-MIBI scintigraphy (arrow)

10 kg of body weight. His body mass index (BMI) on admission was 14.78 kg/m^2. There was no evidence of celiac disease.

Physical examination revealed the patient was slim and pale. There were no deformities or developmental abnormalities, and there was no palpable mass on the neck. Laboratory assessments after admission revealed a serum calcium level of 4.29 mmol/L (normal, 2.20–2.70 mmol/L), albumin level of 42.7 g/L (normal, 35–55 g/L), serum PTH level of 112 pmol/L (normal, 1.16–7.06 pmol/L), and serum alkaline phosphatase level of 1971 U/L (normal, 15–128 U/L).

X-ray of the hands, knees, and skull demonstrated obvious osteopenia (Fig. 1). The lumbar (L1–L4) bone mineral density (BMD) *Z* score was −2.9. Abdominal ultrasonography indicated multiple stones in both kidneys; the largest was 1.52 cm in diameter. Neck ultrasound was unremarkable. Three-dimensional computed tomography (3DCT) of the mediastinum showed a hypervascular nodule in the superior mediastinum, which was confirmed with Technetium-99 methoxy-isobutyl-isonitrile (99mTc-MIBI) scintigraphy (Fig. 2).

After a multidisciplinary team consultation among the departments of thoracic surgery, head and neck surgery, radiology, and endocrinology, the patient underwent transsternal surgery. A soft brown mass measuring 1.5 × 1 × 1 cm was found in the right lower thymus and was resected (Fig. 3). Postoperative pathologic evaluation indicated intrathymic ectopic parathyroid adenoma.

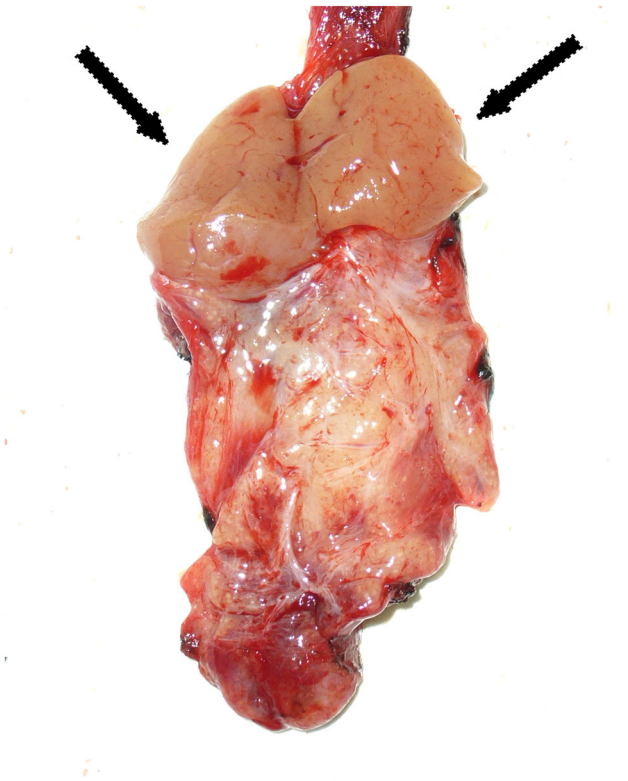

Fig. 3 Soft brown mass located in the thymus (arrows)

After surgery, the patient complained of severe numbness of the face and extremities, which was associated with a sharp drop in serum calcium from the preoperative level of 4.29 mmol/L to a postoperative level of 1.81 mmol/L (normal, 2.20–2.70 mmol/L) and albumin levels of 42.7 g/L and 47.9 g/L (normal, 35–55 g/L), respectively. Intravenous infusion of 10% calcium gluconate (2 g calcium in 20 mL) QD and oral administration of 600 mg caltrate BID effectively alleviated the symptoms. Both serum PTH and calcium levels returned to the normal range (3.83 mmol/L) at 1 week after surgery. The patient's BMI improved to 17.53 kg/m^2 and 18.51 kg/m^2 at 6 months and 1 year of follow-up, respectively. Outpatient examinations at 1 year of follow-up revealed that the lumbar (L1–L4) BMD *Z* score recovered to −0.8, and the renal calculus had disappeared. The patient was followed up for the next 4 years with no signs or symptoms of hyperparathyroidism.

Discussion

PHPT was first reported in the early 1900s, and diagnosis dramatically increased in the 1970s due to the development of automated clinical chemistry analyzers [14]. The estimated incidence of PHPT ranges from 4 to 820 cases per million, with a female predominance, and peak incidence occurring in middle-aged and elderly individuals [15, 16]. Cases in adolescents are rare [5, 7–12], probably because PHPT is usually asymptomatic [14], or adolescents do not recognize the non-specific signs and symptoms that characterize symptomatic PHPT, which leads to an inaccurate or delayed diagnosis. This case report should raise clinicians' awareness of the possibility of PHPT in adolescents.

PHPT is caused by a single adenoma in 80% of cases, multiple adenomas in 5% of cases, parathyroid hyperplasia in 10–15% of cases, and rarely parathyroid carcinoma (<1% of cases) [3]. Interestingly, in our literature review of PHPT in adolescents, we found approximately 30% of reported cases were associated with ectopic parathyroid carcinoma (2/7, 28.6%); both patients were 10 years old (Table 1). However, due to the limited number of reports, a causal relationship between young age and PHPT due to ectopic parathyroid carcinoma cannot be confirmed.

Parathyroid glands develop from the third and fourth pharyngeal pouches, descend with the thymus, and are located in the neck [17, 18]. The thymus is a specialized primary lymphoid organ that enlarges until puberty, plays a critical role in the immune system during childhood, and subsequently atrophies. Therefore, localization and resection of ectopic parathyroid adenomas are extremely challenging in young patients. Clinicians should be aware of the possibility of PHPT in adolescents due to ectopic

Table 1 Summary of previously reported cases of PHPT caused by ectopic parathyroid lesions in adolescents

Case	Sex	Age (years)	Clinical presentation	Preop PTH (pg/mL)	Preop calcium (mg/L)	Radiological studies	Organ damage	Surgical approach	Pathology	Reference
1	M	10	–	>3000	>150	^{99m}Tc-MIBI: negative findings	Renal calcinosis	Exploration of the neck and mediastinum	Carcinoma	Righi et al. [5]
2	M	12.5	Fatigue and muscle pains	140.8–316.7	↑	4DCT: hypervascular nodule in the left side of the mediastinum	Fracture of the hand	Exploration of the neck and mediastinum	Adenoma	Dhillon et al. [7]
3	F	17	Asymptomatic	208	123	^{99m}Tc-MIBI: focal uptake in the anterior mediastinum	Ureteral stone	Thoracoscopic surgery	Adenoma	Minamiya et al. [8]
4	–	<17	Asymptomatic	>2800	156	^{99m}Tc-MIBI: increased uptake on the left and in the mediastinum	Urolithiasis, bone involvement	–	Adenoma	Li et al. [9]
5	F	18	Back pain, fatigue, weakness, and vomiting	204	252	Half-dose ^{99m}Tc-MIBI: high uptake in the superior posterior mediastinum	Pyelonephritis	Right-side video-assisted thoracoscopy	Adenoma	Saad et al. [10]
6	M	16	–	3690	156	^{99m}Tc-MIBI: enhanced activity in the superior mediastinum	–	Right thoracoscopic exploration	Adenoma	Birdas et al. [11]
7	M	10.5	Anorexia, fatigue, and knee pain	300	155	^{99m}Tc-MIBI: negative findings	Invasion of the thymus	Exploration of the neck and mediastinum	Carcinoma	Fiedler et al. [12]

parathyroid adenoma and understand the guidelines for diagnosis and treatment of this condition [3, 14, 16, 19–21].

PHPT due to ectopic parathyroid adenoma/carcinoma is treated by parathyroidectomy. Surgical exploration should be minimized by accurate preoperative localization of the target gland. Detection methods include preoperative 99mTc-MIBI, which has a sensitivity of 68–86% [22, 23]. False-positive findings on imaging of the mediastinum may be due to lung cancer metastasis or mediastinal tumors such as thymoma, seminoma, and lymphoma. Negative results can be caused by multiple adenomas and hyperplasia [24, 25]. In our literature review of PHPT in adolescents, six of the seven case reports used 99mTc-MIBI to localize the target organ before surgery, with positive findings in 66.7% of cases (4/6). The remaining cases, which involved ectopic parathyroid carcinoma (2/6, 33.3%), showed negative findings on imaging (Table 1). Four-dimensional computed tomography (4DCT) can also be used to successfully localize ectopic parathyroid adenomas [7, 26].

Parathyroidectomy is recommended for all symptomatic PHPT patients and may be appropriate in most asymptomatic patients [3, 21]. The best surgical approach for resection of ectopic parathyroid adenomas remains controversial. A transcervical approach may be suitable for resection of most hyperfunctional mediastinal parathyroid adenomas [13, 27, 28]. Traditionally, median sternotomy was used for parathyroid adenomas located deeper in the mediastinum. More recently, thoracotomy is being applied as a less invasive procedure that minimizes morbidity and enhances cosmesis [29]. A cervical approach can be used for lesions localized preoperatively at the aortic arch or upper region [13].

Following successful resection of hyperfunctional parathyroid glands, PTH levels can drop >50% [19, 30] and patients are prone to hypocalcemia, with a rapid drop in calcium levels and/or cramps. In the present report, the patient experienced hypocalcemia 1 day after surgery, which was corrected with oral calcium supplementation for 1 week. Thus, it is necessary to closely monitor serum calcium for dynamic changes.

Long-term outcomes of resection of hyperfunctional parathyroid glands include a reduction in risk for fracture and nephrolithiasis during the 10-year postoperative period [16, 23].

In conclusion, we report a rare case of PHPT due to ectopic parathyroid adenoma in an adolescent, and present a review of similar previously published reports. Findings showed the incidence of PHPT due to ectopic parathyroid carcinoma is high in adolescent patients with PHPT. Accurate preoperative localization of ectopic parathyroid lesions is not only helpful but also necessary to minimize surgical exploration during resection. Monitoring of intraoperative PTH levels may be useful to confirm the adequacy of surgery.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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

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