



Primary Hyperparathyroidism due to Ectopic Intrathymic Parathyroid Adenoma in A Child: A Case Report

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Case Report

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Abstract

Primary hyperparathyroidism (PHPT) is a rare endocrine disorder in children and adolescents. Surgery is curative in most pediatric patients with PHPT. PHPT due to ectopic parathyroid adenoma (EPA) presents the difficulty of their exact topographic diagnosis and there is no consensus for the optimal imaging modality. The ^{99m}Tc-sestamibi (^{99m}Technetium -labeled methoxy-isobutyl-isonitrile) scintigraphy appears to be the best exam to establish a topographic diagnosis of parathyroid adenoma. Herein, we present the case of a 14-year-old girl with the diagnosis of PHPT with bone involvement. Parathyroid scintigraphy (dual-phase and dual tracer subtraction imaging), has shown an abnormal tracer uptake in the anterior mediastinum. Computed tomography (CT), has confirmed the mediastinal seat of the adenoma, measured 40 x 24.6 mm, repressing the thymus. An adenectomy was performed using video-assisted mini-thoracoscopic surgery. Histological findings have shown intrathymic ectopic parathyroid adenoma. After surgery, the patient had profound and persistent hypocalcemia as a result of extensive remineralization in a relation to Hungry Bone Syndrome (HBS). Through this clinical report, we insist on the importance of preoperative localization of parathyroid adenoma to select the surgical approach and to avoid failed cervicotomy especially in cases of ectopic adenomas.

Keywords: Primary Hyperparathyroidism; Ectopic Parathyroid Adenoma; Sestamibi Scintigraphy; Mini- Invasive Surgery; Children

Abbreviations: PHPT: Primary Hyperparathyroidism; EPA: Ectopic Parathyroid Adenoma; CT: Computed Tomography; HBS: Hungry Bone Syndrome; SPECT: Single-Photon Emission Computed Tomography; MEN: Multiple Endocrine Neoplasia.

Introduction

Primary hyperparathyroidism (PHPT) is rarely described in children and may be misdiagnosed. PHPT is

caused by a solitary parathyroid adenoma in 65%-70% of children [1,2]. Ectopic parathyroid adenoma (EPA) is a rare entity, accounting for 6%-16% of all parathyroid adenomas and the most common ectopic location is the thymus, which accounts for 38% of EPA [3]. In all pediatric PHTP patients, surgical removal is the only curative option [4]. Thus, accurate preoperative localization of parathyroid adenomas is essential. Advanced imaging techniques provide a more precise localization, and it is now possible to consider a minimally invasive mediastinal approach in children. On this

basis, ^{99m}Tc -sestamibi single-photon emission computed tomography (SPECT) and ^{99m}Tc -sestamibi SPECT/CT may be the optimal imaging modality [5]. Here, we report a rare case of PHPT due to ectopic mediastinal parathyroid adenoma in a 14-year-old girl to highlight the importance of ^{99m}Tc -sestamibi scintigraphy in the surgical management of PHPT.

Case Description

A 14-year-old girl with no previous medical or surgical history was admitted for a pathological fracture of the right femoral cervix complicating PHPT. Laboratory evaluation showed hypercalcemia (3,2mmol/l; reference range, 2,2-2,6mmol/l), hypophosphatemia (0,7mmol/l; reference range, 1,3-1,85mmol/l), elevated parathyroid hormone (2490pg/mL; reference range ,15-65pg/mL), elevated alkaline phosphatase (3682U/L ; reference range , 100-400U/L), elevated 24-hour urine calcium (10,36mmol/L; reference range, 0,05-0,1mmol/kg/24 hours) and vitamin D deficiency (25-OH-vitamin D level of 3,49ng/mL; reference range, 30-80ng/mL). Radiological findings have shown low bone density and multiple, variable-sized osteolytic lesions of the axial and peripheral skeleton consistent with metabolic osteodystrophy. Renal ultrasonography has shown no signs of nephrocalcinosis. Neck ultrasonography was normal. Parathyroid scintigraphy (dual-phase and dual tracer subtraction imaging), revealed a large area of increased tracer uptake in the anterior mediastinal region correlating with an EPA (Figure 1). The patient underwent a neck computed tomography (CT) with contrast injection that

confirmed the mediastinal seat of adenoma, measured 40 x 24.6 mm, repressing the thymus gland, in direct contact with the pericardium, the right atrium and the left brachio-cephalic vein trunk, and at a distance from the large mediastinal vessels (Figure 2). There was no evidence of multiple endocrine neoplasia syndrome, familial hyperparathyroidism- jaw tumor syndrome, or family history of endocrinopathies. Magnetic resonance imaging (MRI) of the pituitary gland was normal and thoraco-abdomino-pelvic CT was unremarkable. Subsequently, the child was referred to the thoracic surgery department after treating the hypercalcemia and the femoral fracture. She underwent a video-assisted right lateral mini-thoracotomy. During the act, the ectopic parathyroid gland was found to be within the thymus. A right thymectomy was performed (Figure 3). The anatomopathological study concluded to an intrathymic parathyroid adenoma. It showed a well circumscribed nodule with a thin fibrous capsule, composed of rounded monomorphic cells with granular eosinophilic cytoplasm and regular central nuclei. Areas of hemorrhagic degeneration and calcifications were observed. The nodule was surrounded by residual thymic parenchyma. There was no evidence of lymphovascular invasion, perineural invasion or invasion into adjacent structures. During the postoperative period, the patient had persistent hypocalcemia and hypophosphatemia as a result of extensive remineralization in a relation to Hungry Bone Syndrome (HBS). She required prolonged oral calcium and calcitriol supplements. At the 6th month follow-up, serum calcium, phosphate, parathyroid hormone, alkaline phosphatase values were completely normal.

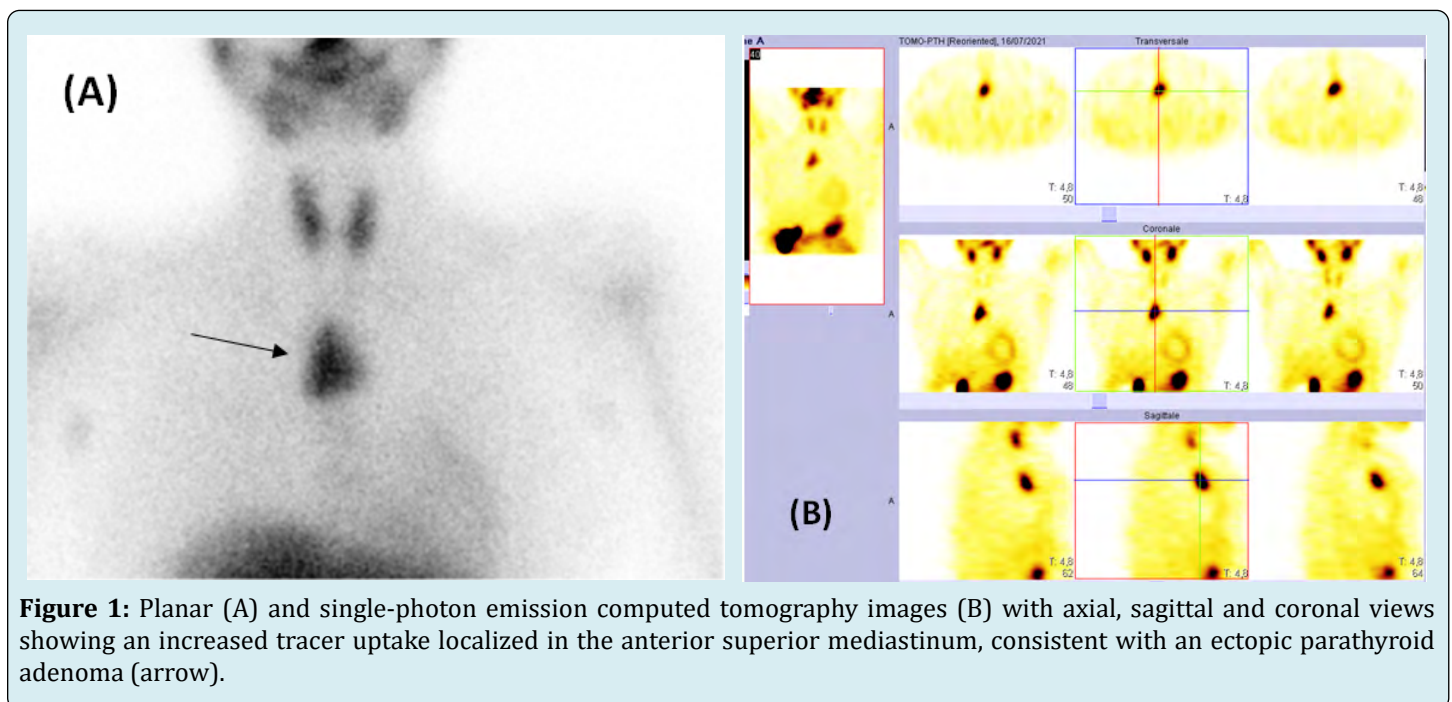


Figure 1: Planar (A) and single-photon emission computed tomography images (B) with axial, sagittal and coronal views showing an increased tracer uptake localized in the anterior superior mediastinum, consistent with an ectopic parathyroid adenoma (arrow).

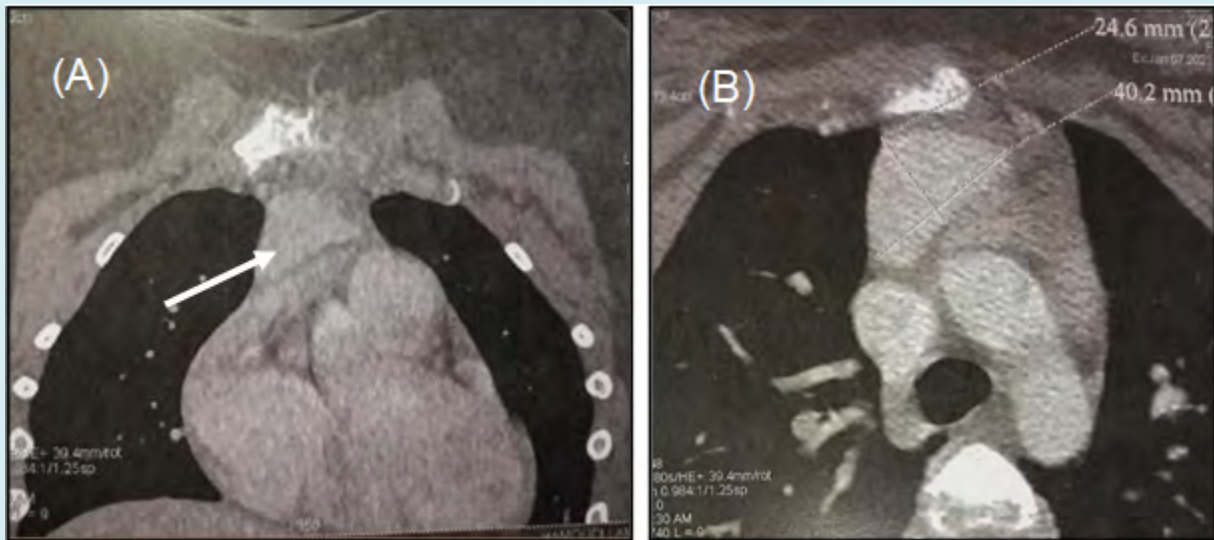


Figure 2: Coronal (A) and axial (B) views of chest computed tomography demonstrating the ectopic parathyroid adenoma (arrow) in the mediastinum.

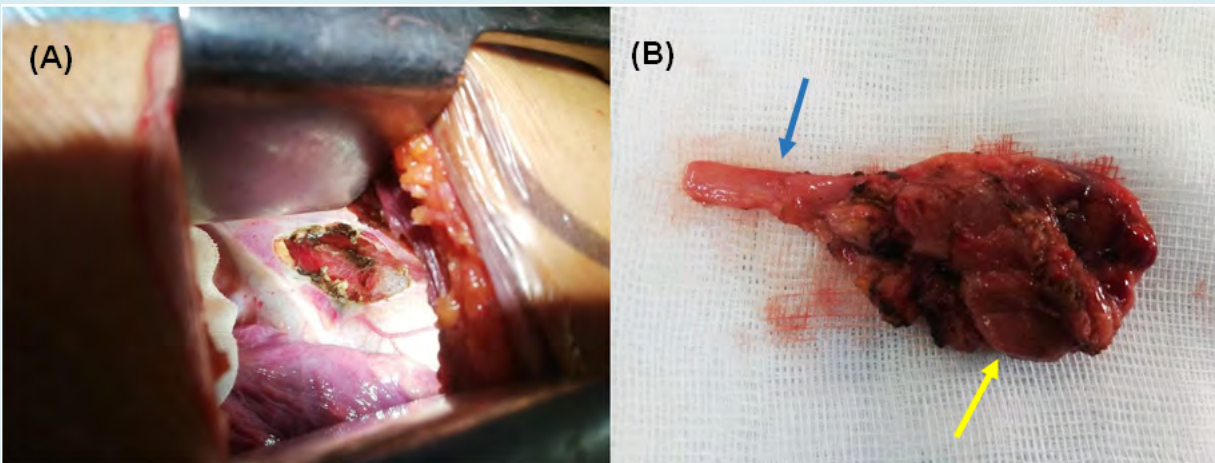


Figure 3: Intraoperative view, by right video-assisted mini-thoracotomy, after the resection of the ectopic parathyroid adenoma (A). Macroscopic appearance of the resected specimen (B): parathyroid adenoma (yellow arrow) and right thymic horn (blue arrow).

Discussion

PHPT is uncommon in the pediatric population. Unlike adult patients, children with PHPT can present with nonspecific symptoms; therefore, diagnosis may be delayed. In our case, the patient presented with a right femoral fracture complicating severe bone involvement. Most cases of PHPT are caused by sporadic isolated adenomas. However, autosomal dominant hyperparathyroidism and familial syndromes such as Multiple Endocrine Neoplasia (MEN) type I and IIA, and hyperparathyroidism jaw tumor syndrome,

may also present with a single parathyroid adenoma in a child [6]. Genetic screening in children diagnosed with hyperparathyroidism is essential, as genetic mutations are observed in 24% to 46% of children with PHPT [7]. Detailed family history along with careful explorations did not suggest any evidence of MEN in our case.

PHPT due to EPA is a rare entity. The lower parathyroid glands develop from the third pharyngeal pouch in close association with the thymus. As a result, they may be found commonly within the anterosuperior mediastinum making

the thymus the most common ectopic site for a parathyroid gland [2]. The curative treatment of PHPT in children is surgical removal. The traditional surgical approach has been bilateral neck exploration, a trans-sternal or transthoracic approach in cases with deep mediastinal parathyroid lesions. However, the improved sensitivity of imaging techniques has encouraged the use of less invasive surgical procedures in adults. Nowadays, recent studies have shown that minimally invasive mediastinal ectopic parathyroidectomy is safe and feasible if the anatomical position of any lesions is well determined, even in children [8-10]. Locating EPA preoperatively can be challenging. Both ^{99m}Tc-sestamibi scintigraphy and neck ultrasonography (US) are considered as the first-line preoperative imaging modalities in patients with PHPT [11]. In a meta-analysis of 43 preoperative localization technique studies, Cheung et al. have demonstrated that ultrasound and ^{99m}Tc-sestamibi-SPECT have comparable accuracy, with pooled sensitivities of 76.1% and 78.9%, respectively, and positive predictive values of 93.2% and 90.7%, respectively [12]. Thus, ^{99m}Tc-sestamibi-SPECT is recognized as the most sensitive imaging method in PHPT (sensitivity per adenoma, 95%) [13]. In fact, tomographic three-dimensional reconstruction improves separation between the activity in the thyroid gland and a parathyroid adenoma situated behind the thyroid. False-negative results can be caused by a small parathyroid adenoma, multiple adenomas, and hyperplasia. Recently, the emerging of ¹⁸F-fluorocholine positron emission tomography/computed tomography may play a role as a second-line imaging in patients with PHPT and can also improve the localization of the hyperparathyroid glands [14]. In our case, ^{99m}Tc-sestamibi SPECT scanning had successfully detected EPA and the patient required a preoperative thoracic CT for more precise anatomic information.

Conclusion

In sum, PHPT in children is unusual. Surgical removal is the only curative treatment for children with PHPT. Accurate preoperative localization of the target lesion is critical. Detection methods include preoperative ^{99m}Tc-sestamibi scan, which has the advantage of detecting ectopic adenomas, thus allowing a minimally invasive therapeutic approach.

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

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