Case Report

Ectopic Parathyroid Adenoma in an 11-Year-Old Girl: Case Report and Literature Review

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Abstract

Objective: Primary hyperparathyroidism secondary to an ectopic parathyroid adenoma is rare among children and adolescents. Methods: We describe the case of an 11-year-old girl with incidentally diagnosed primary hyperparathyroidism secondary to an intrathymic parathyroid adenoma and performed a review of the related literature. Results: 99mTechnetium sestamibi single-photon emission computed tomography/computed tomography and 4-dimensional computed tomography confirmed the ectopic location of the adenoma. The patient underwent thoracoscopic thymectomy and remained normocalcemic with elevated parathyroid hormone showing a downward trend. Parathyroid hormone normalized 18 months after successful parathyroidectomy. Conclusion: We review the case of a rare mediastinal parathyroid adenoma in a pediatric patient and summarize the epidemiologic profile, diagnosis, and management of similar pediatric cases.

Introduction

Primary hyperparathyroidism secondary to an ectopic parathyroid adenoma is a rare entity, especially among the pediatric population.1,2 The only curative option is surgical removal.3 Accurate preoperative localization of parathyroid adenomas is essential to the success of minimally invasive parathyroidectomy. Ectopic adenomas may be located anywhere in the trajectory from the tongue to the mediastinum, usually in close association with the thymus.4 Identifying ectopic parathyroid adenomas can be challenging, and there is no consensus for the optimal imaging modality in this population. 99mTechnetium sestamibi scintigraphy (MIBI), neck ultrasound, computed tomography (CT), and magnetic resonance imaging have been traditionally used to locate parathyroid adenomas.4 The use of combinations of imaging techniques, such as single-photon emission computerized tomography (SPECT)/CT and positron emission tomography/CT, have been increasingly reported in the literature, particularly when other modalities have initially failed to reveal the source of ectopic production of parathyroid hormone (PTH).5,6

We present the case of an 11-year-old girl incidentally diagnosed with primary hyperparathyroidism who underwent the removal of an intrathymic parathyroid adenoma. Medical record review of this patient was approved by the New York Presbyterian Brooklyn Methodist institutional review board. We also performed a review of the literature of ectopic parathyroid adenomas among pediatric and adolescent patients aged up to 18 years old.

Case Report

An 11-year-old girl with no previous medical or surgical history presented to the emergency room with symptoms of sore throat, nasal congestion, and fever. She was not taking any medications or supplements. There was no family history of endocrinopathies. Her
physical examination result was normal, except for right peri-
tonsillar inflammation. She was admitted to the pediatric unit for
intravenous antibiotics in the setting of peritonsillar cellulitis.
During this time, a complete metabolic panel was drawn as
part of the initial assessment of infection. The calcium level was
14.1 mg/dL (normal 8.5-10.1 mg/dL), and ionized calcium level was
1.90 mmol/L (normal 1.09-1.3 mmol/L). On further investigation,
the PTH level was 230 pg/mL (normal 14-72 pg/mL), vitamin
25(OH)D level was 28.6 ng/mL (normal 30-100 ng/mL), phosphorus
level was 1.8 mg/dL (normal 2.5-4.9 mg/dL), and alkaline phos-
phatase level was 181 U/L (normal 42-141 U/L). The patient un-
derwent a neck CT without contrast as part of a peritonsillar
abscess work up, which showed normal parathyroid anatomy.
On follow-up, she continued to be asymptomatic. The PTH level
continued to rise to 839 pg/mL, and calcium level ranged between
12.2 and 14.1 mg/dL. Neck and upper chest MIBI showed a small
focal area of moderately increased tracer uptake in the anterior
mediastinal region slightly above the level of the heart, with
suspicion for parathyroid adenoma. Genetic testing was negative
for pathogenic variants or deletions/duplications in the CASR,
CDC73, CDKN1B, MEN1, and RET genes (Hyperparathyroidism
Panel, Invitae). No imaging studies to evaluate bone density were
performed.

Because of suspicion of ectopic adenoma, MIBI SPECT/CT
was performed, which showed abnormal focal uptake in the
anterior mediastinum measuring 1.9 × 1.0 × 1.4 cm, correlating
with an enhancing intrathymic nodule (Fig. 1). This finding was
confirmed by 4-dimensional (4D) CT (Fig. 2). She underwent
thoracoscopic thymectomy 5 months after her initial emergency
room visit. The pathologic specimen revealed a 2.1 × 1.6 × 1.1
cm well-circumscribed, unencapsulated nodule consistent with
parathyroid adenoma inside an otherwise normal thymus.
Intraoperative PTH level dropped to 99 pg/mL. On discharge, the
calcium level was 9.3 mg/dL. She was discharged with a pre-
scription of 1000 mg of elemental calcium twice daily for 16
days. Approximately 1 year after the surgery, she remained
asymptomatic and was normocalcemic. The PTH level remained
elevated but showed a downward trend under close monitoring
with regular serum draws every few months in increasingly
spaced intervals for 11 months (range 115.9–216 pg/mL).
Eventually, the PTH level normalized 19 months after the
operation. The vitamin 25(OH)D level ranged from 24.1 to 37.6
ng/mL in the same postoperative period.

Discussion
Our 11-year-old girl is one of the youngest cases of ectopic
parathyroid adenoma in the limited pediatric literature. In this
case, the initial MIBI located an abnormal uptake in the anterior
mediastinum that was confirmed by MIBI SPECT/CT and 4D CT.
Correlation with a second scan is sometimes necessary to verify
the ectopic location of an adenoma, to map the relationships

Fig. 1. Coronal (A), sagittal (B), and axial (C) views of 99mtechnetium sestamibi with SPECT/CT demonstrating the ectopic parathyroid adenoma.
with surrounding anatomic structures, and to guide the surgical localization, especially for minimally invasive procedures.\(^7\)

Of note, the PTH level remained elevated for approximately 1 year after surgery before returning to normal levels. The patient remained asymptomatic and normocalcemic during this period. The PTH level was elevated postoperatively for years in a case of a 16-year-old patient with normocalcemia, reflecting the effect of hyperparathyroidism secondary to persistent vitamin D deficiency.\(^8\) In our case, vitamin 25(OH)D levels remained above 24 ng/mL during the follow-up period. This persistent elevation has been previously described in the literature among adult populations. In a review published in 2017, 33 studies reported data on this phenomenon, with a mean prevalence of 23.5% among postoperative cases.\(^9\) There is no reported association with primary hyperparathyroidism recurrence.\(^9\) Its etiology is not fully understood, and it is considered to be multifactorial. Vitamin D deficiency, a decrease in the glomerular filtration rate, the relative drop in postoperative calcium, the presence of hungry bone syndrome, and altered peripheral sensitivity to PTH have been proposed as possible mechanisms.\(^9\) In a recent study by Caldwell et al,\(^10\) approximately one third of the adult patients who underwent parathyroidectomy had persistent elevation of PTH level. Interestingly, this was associated with lower, but not abnormal, preoperative vitamin 25(OH)D levels compared with the group with normal postoperative PTH levels (26 ± 15 pg/mL vs 36 ± 11 pg/mL). There were no available postoperative vitamin 25(OH)D data reported. In our case, the vitamin 25(OH)D level was 29 ng/mL preoperatively, normalized without supplementation in the postoperative period, and subsequently dropped to 28 ng/mL 19 months after the surgery, when the PTH level normalized. Further studies evaluating the association of vitamin D insufficiency with this phenomenon are warranted.

Primary hyperparathyroidism in the pediatric population has been estimated to occur in 1 in 200 000 to 300 000 patients and is caused by a single adenoma in majority of cases.\(^2,11-14\) In a recent retrospective study of 86 pediatric patients by Rampp et al,\(^12\) 22 cases of ectopic parathyroid adenomas were identified in 3 tertiary care facilities over the span of 20 years. In pediatric cohorts, the prevalence of ectopic adenomas among diagnoses of primary hyperparathyroidism ranges between 5% and 26%.\(^2,11-14\) Our literature review for studies, including case reports, case series, and cohorts, of pediatric patients aged 18 years and below with ectopic parathyroid tumors yielded individual data for 33 cases (Table 1 and Supplementary Table). Two of the 33 cases were parathyroid carcinomas.\(^17,22\) There was no sex predominance. In approximately half of the cases, the localization of the adenoma was reported to be associated with the thymus, similar to ours. Our patient was asymptomatic at presentation and remained asymptomatic postoperatively. Among the 30 reports that included relevant medical history for the cases, a minority (5 of 30, 17%) of patients were diagnosed incidentally. Bone and renal involvement were the most commonly described end-organ pathologies. In only 1 of the cases, the patient was reported to have known multiple endocrine neoplasia 1 syndrome.\(^7\)

The diagnostic challenge of ectopic parathyroid adenomas is highlighted by the fact that in 11 cases, the patient underwent more than 1 procedure until cure. Most patients underwent 2 or more different imaging modalities preoperatively, with half of the reports providing results on 3 or more imaging modalities (Table 1). The most commonly reported imaging modality was MIBI in 24 (including the current) of the cases, with a sensitivity of 71% (Table 2). Neck ultrasound results localized 2 intrathyroidal adenomas,\(^29,41\) an adenoma located in the suprasternal fossa,\(^21\) and an entopic adenoma in a patient with multiple gland etiology (but not the ectopic adenoma of the same patient).\(^12\) From studies in adult populations, the sensitivity of both ultrasound and MIBI regarding ectopic parathyroid adenomas is highly variable (US, 27%-89% and MIBI, 54%-100%).\(^4\) In the pediatric literature, Rampp et al\(^11\) report a sensitivity of 10% for MIBI among ectopic cases. SPECT/CT identified the ectopic adenoma in 5 of 6 cases (including the current study) (Table 2). Notably, 4D CT has been increasingly used and is even used as a first-line imaging choice in some centers.\(^12\) Its use in pediatric cases may be limited to a secondary role due to high radiation exposure.\(^11\) To date, the pediatric literature on 4D CT has been limited to case reports, and future studies should investigate its role in diagnosing parathyroid adenomas in this population. Finally, the emerging 18F-fluorocholine positron emission tomography/CT, used in 1 of the cases, may play a role in complex cases when all other studies are negative.\(^5\)
Table 1: Cases of Ectopic Parathyroid Adenoma and Carcinomas

| Author                  | Year | Age | Sex | Presenting symptoms, medical history, end-organ damage signs                                                                 | Imaging related to adenoma localization                  | Location of adenoma                    | Number of procedures |
|-------------------------|------|-----|-----|-----------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|----------------------------------------|---------------------|
| Schmidt et al           | 2001 | 8 M | M   | Open tibial fracture secondary to trauma                                                                                  | US: neg, MRI: ND, MIBI: neg (FPos)                      | Intrathyric                           | 1                   |
| Çelik et al             | 2014 | 9 F | F   | Mental retardation                                                                                                         | US: neg, MIBI: neg                                      | Close to common carotid artery         | 3                   |
| Righi et al             | 2008 | 10 M| M   | Renal calcinosis                                                                                                           | US: neg, MIBI: neg                                      | Adjacent to thymus                    | 1                   |
| Wu et al                | 1985 | 10 M| M   | URI, malaise, mandibular pain (dental abscess), polyuria                                                                  | US: neg, MIBI: neg, second MIBI: neg (FPos), second US: neg, MRI: neg, CT: neg, PET/CT: neg, MIBI SPECT/CT: pos, second MRI: pos | Dorolateral to left common carotid artery | 2                   |
| Libanský et al          | 2008 | 10 F| F   | Fatigue, decreased appetite and muscle strength, decreased bone density, subperiosteal brown tumor lesions, bilateral genu valgum deformities | US: FPos, MIBI: neg, second US: neg, MRI: ND, MIBI: neg (FPos) | Dorsolateral to left common carotid artery | 2                   |
| Baird et al             | 2011 | 10 M| M   | Abdominal pain, acute pancreatitis                                                                                        | US: pos, MIBI: pos                                     | Adjacent to thymus                    | 1                   |
| Zhang et al             | 2010 | 10 F| F   | Extremity pain, polydipsia, anorexia emesis                                                                           | US: pos, MIBI: pos                                     | Suprasternal fossa                    | 1                   |
| Fiedler et al           | 2017 | 12 M| M   | Fatigue, muscle pains, h/o hand fracture                                                                             | US: neg, MIBI: neg, second MIBI: neg (FPos)             | Within the carotid sheath             | 3                   |
| Bauman et al            | 2017 | 13 F| F   | Anxiety, headaches, lethargy, muscle fatigue, impaired concentration                                                   | US: neg, MIBI: neg, second US: neg, MRI: ND, 4D CT: pos | Intrathyric                           | 2                   |
| Morimoto et al          | 2018 | 13 M| M   | Abdominal pain, hydroelectrolysis, nephrocalcinosis                                                                       | CT/3D CT: pos, MIBI: pos, MIBI: pos, SPECT: pos        | Intrathyric                           | 1                   |
| Kordahi et al           | 2019 | 13 M| M   | Fever, sore throat, difficulty swallowing, h/o chronic constipation, h/o painful gast Brown tumors in the posterior parietal and occipital bone | MIBI: neg, 4D MRI: pos, CT: pos | Left retropharyngeal space            | 1                   |
| Pituchcheewanont et al  | 2008 | 14 M| M   | Abnormal gait, bilateral foot pain Flat feet, valgus deformities of knees, osteopenia, osteodystrophy (vitamin D deficiency rickets) | MIBI: pos, CT: pos                                      | Intrathyric                           | 1                   |
| Tonelli et al           | 2016 | 15 M| M   | MEN1 gene mutation, h/o pituitary microadenoma, h/o hyperprolactinemia                                                 | US: FPos, MIBI: pos, MRI: pos, CT: pos                | Near the tracheal bifurcation          | 1                   |
| Liu et al               | 2019 | 15 M| M   | Chronic fatigue & limb ostealgia, anorexia, weight loss, Recurrent fractures, osteopenia                               | US: neg, MIBI: pos, 3D CT: pos                         | Intrathyric                           | 1                   |
| Girard et al            | 1982 | 15 M| M   | Anemia, growth delay Osteopenia                                                                                        | US: neg, MIBI: pos, 3D CT: pos, MIBI: pos             | Intrathyric                           | 1                   |
| Lawson et al            | 1996 | 15 M| M   | Renal colic, Osteopenia, nephrocalcinosis                                                                              | US: pos, CT: neg, MRI: pos, thallium/Tc: pos          | Mediastinum                           | 2                   |
| Bender et al            | 1992 | 16 F| F   | Nephrocalcinosis                                                                                                          | US: neg, MRI: neg, MIBI: pos, CT: pos                 | Intrathyroidal                        | 2                   |
| Birdas et al            | 2005 | 16 M| M   | Anterior to the junction of R atrium & superior vena cava                                                                | US: neg, MIBI: pos, CT: pos, MIBI: pos                | Anterior to the junction              | 1                   |
| Li et al, Heller et al  | 2012 | 16 F| F   | Urolithiasis, bone involvement Nephrocalcinosis                                                                           | US: neg, MRI: neg, MIBI: pos, CT: pos                 | Infrathyric                           | 1                   |
| Minamiya et al          | 2009 | 17 F| F   | Urolithiasis, Nephrocalcinosis                                                                                           | US: neg, MIBI: pos, CT: pos                           | Infrathyric                           | 1                   |
| Daruwalla et al         | 2013 | 17 F| F   | Urolithiasis, Nephrocalcinosis, Fatigue, flat affect                                                                       | US: neg, MIBI: pos, CT: pos, MIBI: pos                | Intrathyric                           | 1                   |
| Dhiwakar et al          | 2016 | 17 F| F   | Bony growths in mandible & hard palate Giant cell reparative granuloma of mandible, lytic bone areas                   | US: neg, MIBI: pos, CT: pos, MIBI: pos                | Intrathyroidal                        | 1                   |
| Boccalatte et al        | 2018 | 18 M| M   | Hypertension, asymptomatic                                                                                               | US: neg, MIBI SPECT: neg, MRI: neg, 18F-choline PET/CT: pos | Infrathyric                           | 1                   |
| Wells et al             | 1991 | 18 F| F   | Nephrocalcinosis                                                                                                          | US: neg, MIBI: pos, CT: pos, MIBI: pos                | Infrathyric                           | 2                   |
| Martinez et al          | 1995 | 18 F| F   | Nephrocalcinosis                                                                                                          | US: neg, MIBI: pos, CT: pos, MIBI: pos                | Under the arch of the ascending aorta | 2                   |
| Deeb et al              | 2001 | 18 F| F   | Nephrocalcinosis                                                                                                          | US: neg, MIBI: pos, CT: pos, MIBI: pos                | Infrathyric                           | 2                   |
In conclusion, we report the case of a mediastinal parathyroid adenoma in a pediatric patient and highlight appropriate methods of diagnosis, cure, and follow-up of this rare disease, supplementing with a review of reported pediatric and adolescent cases. In our case, monitoring of the PTH level for 18 months postoperatively showed persistent elevation of the PTH level without any signs of recurrence of hyperparathyroidism or concurrent vitamin D deficiency. This phenomenon, described in adult cases, has not been adequately studied in the pediatric population.

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Table 1 (continued)

| Author       | Year | Age | Sex | Presenting symptoms, medical history, end-organ damage signs | Imaging related to adenoma localization | Location of adenoma | Number of procedures |
|--------------|------|-----|-----|---------------------------------------------------------------|----------------------------------------|---------------------|---------------------|
| Spinelli et al17 | 2012 | 18  | F   | Asymptomatic                                                 | US: neg, thallium: neg, MIBI: pos, SPECT: pos, CT: pos, live labeling of erythrocytes, Tc-pyroscent:- SPECT: pos, MRI: neg | Infrathyroidal       | 1                   |
| Saad et al42  | 2014 | 18  | F   | Chronic weakness, fatigue, polyuria, vomiting, pregnancy at 23 weeks of gestation | Half-dose MIBI: pos                    | Superior posterior mediastinum | 1                   |
| Wang et al41  | 2014 | 18  | M   | Pain in right shoulder                                       | US: pos, CT: pos, MIBI: pos            | Infrathyroidal       | 1                   |
| Ruanpeng et al42 | 2017 | 18  | F   | Fatigue, depression                                          | MIBI SPECT/CT: pos, CT: pos            | Infrathyroidal       | 1                   |

Table 2

Imaging Data From 31 Cases of Ectopic Parathyroid Tumors

| Author             | Year | US | MIBI | CT | 4D CT | MRI | SPECT/CT | PET/CT |
|--------------------|------|----|------|----|-------|-----|----------|--------|
| Wells et al16       | 1991 | ...| ...  | ...| ...   | ... | ...      | ...    |
| Bender et al29      | 1992 | ✓  | ✓    | X  | ...   | ... | ...      | ...    |
| Martinez et al18    | 1995 | X  | ✓    | X  | ...   | ... | ...      | ...    |
| Lawson et al32      | 1996 | X/X| ...  | X  | ...   | ... | ...      | ...    |
| Schmidt et al19     | 2001 | X  | X    | X  | ...   | ... | ...      | ...    |
| Deeb et al38        | 2001 | ... | ✓    | ✓  | ...   | ... | ...      | ...    |
| Birdás et al30      | 2005 | ... | ✓    | ...| ...   | ... | ...      | ...    |
| Righi et al37       | 2008 | X  | X    | ...| ...   | ... | ...      | ...    |
| Libánský et al19    | 2008 | X/X| X/X  | X  | ...   | X✓ | ✓        | X      |
| Pituńchewanont et al8 | 2008 | ...| ✓    | ✓  | ...   | ... | ...      | ...    |
| Fiedler et al31     | 2009 | X  | X    | ...| ...   | ... | ...      | ...    |
| Yeşilkaya et al18   | 2009 | X  | ✓    | ...| ...   | ... | ...      | ...    |
| Minamiya et al12    | 2009 | ...| ✓    | ✓  | ...   | ... | ...      | ...    |
| Zhang et al21       | 2010 | ✓  | ✓    | ...| ...   | ... | ...      | ...    |
| Baird et al30       | 2011 | ...| ...  | ...| ...   | ... | ✓        | ...    |
| Spinelli et al19    | 2012 | X  | ✓    | ✓  | ...   | ... | ...      | ...    |
| Li et al12          | 2012 | X  | ✓    | ...| ...   | ... | ...      | ...    |
| Dhillon et al34     | 2013 | X/X| X    | ...| ✓    | ✓  | X        | ...    |
| Çelik et al16       | 2014 | X  | X    | ...| ...   | ... | ...      | ...    |
| Saad et al38        | 2014 | ...| ✓    | ✓  | ...   | ... | ...      | ...    |
| Wang et al34        | 2014 | ...| ✓    | ✓  | ...   | ... | ...      | ...    |
| Tonelli et al33     | 2016 | X  | ✓    | ✓  | ...   | ... | ...      | ...    |
| Daruwala et al31    | 2015 | X  | ✓    | ...| ...   | ... | ...      | ...    |
| Dhivakar et al36    | 2016 | ...| ✓    | ...| ...   | ... | ...      | ...    |
| Bauman et al40      | 2017 | X  | ...  | ...| ...   | ... | ✓        | X      |
| Morimoto et al15    | 2018 | ...| ✓    | ✓  | ...   | ... | ...      | ...    |
| Ruanpeng et al42    | 2017 | ...| ✓    | ✓  | ...   | ... | ...      | ...    |
| Boccalatte et al15  | 2018 | X  | ...  | ...| ...   | ... | ✓        | ...    |
| Kordahi et al36     | 2019 | ...| X    | ✓  | ...   | ... | ...      | ...    |
| Liu et al27         | 2019 | X  | ✓    | ✓  | ...   | ... | ...      | ...    |
| Flokas et al (current case) | ... | ✓  | X    | ✓  | ...   | ... | ✓        | ...    |

Abbreviations: CT = computed tomography; MIBI = 99Tc technetium sestamibi scintigraphy; MRI = magnetic resonance imaging; SPECT = single-photon emission computed tomography; X = negative; true positive results; ✓ = true positive results; 4D MRI not depicted.

Conflict of Interest: None

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Disclosure

The authors have no multiplicity of interest to disclose.

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