Preoperative multiple endocrine neoplasia type 1 diagnosis improves the surgical outcomes of pediatric patients with primary hyperparathyroidism


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A B S T R A C T

Background: Primary hyperparathyroidism (PHPT) is uncommon in children. The surgical management of PHPT in children has evolved over the past two decades.

Methods: A retrospective study of patients who underwent parathyroidectomy for PHPT diagnosed at age <18 years and managed at a tertiary referral center for endocrine and familial disorders.

Results: Thirty-eight patients met eligibility criteria (1981–2012). Median age at PHPT diagnosis was 15 years. Two-thirds of patients were symptomatic (68%, n = 26), most commonly from nephrolithiasis. Twenty-six (68%) patients underwent a standard cervical exploration while 32% underwent a focused unilateral parathyroidectomy. Multiple endocrine neoplasia type 1 (MEN1) was diagnosed preoperatively in 22/26 patients. Patients with a preoperative diagnosis of MEN1 were more likely to undergo a complete initial operation (≥3 gland parathyroidectomy with transcervical thymectomy, 13/22, 59% vs. 0/4, 0%; P = 0.03) and less likely to have recurrent disease (10/22, 45% vs. 3/4, 75%; P < 0.001) during follow up than patients diagnosed postoperatively.

Conclusions: Children with PHPT should raise suspicion for MEN1. Preoperative MEN1 evaluation helped guide the extent of initial parathyroidectomy and was associated with lower rates of recurrence in sporadic and familial PHPT in pediatric patients. Management should occur at a high volume center with experienced clinicians and genetic counseling services.

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1. Background

Primary hyperparathyroidism (PHPT) occurs at an incidence of 100,000 cases annually in the United States. Sporadic disease accounts for the majority of cases; it typically presents in the seventh to eighth decades of life, is caused by a single benign adenoma, and affects women more frequently than men (4:1 ratio) [1]. In children, PHPT is rare (1% of PHPT cases) [2], more evenly affects females and males [3–5], and is commonly associated with classic symptoms at diagnosis [3–6].

Regardless of age at presentation, approximately 3% to 5% of PHPT cases are hereditary and may represent the initial clinical manifestation of multiple endocrine neoplasia type 1 (MEN1) (OMIM 613733) [7]. Initially described in 1954 [8], MEN1 is the most common cause of hereditary PHPT [7]. Unlike sporadic disease, MEN1-associated PHPT manifests at a younger age (onset between 20 and 25 years with nearly 100% diagnosed by age 50), is associated with 4-gland parathyroid hyperplasia, frequently with supernumerary glands, and affects men and women equally [7]. Following parathyroidectomy, persistence and late recurrence are more common in MEN1 patients than in sporadic PHPT [9]. Modern genetic testing detects approximately 70%–95% of patients with MEN1 [9,10]; a clinical diagnosis of MEN1 in a patient presenting with PHPT requires a family history of MEN1 in a first degree relative and/or the occurrence of ≥2 MEN1-related tumors in the same individual [11].

Current guidelines for the treatment of PHPT in MEN1 patients call for standard cervical exploration (SCE) with resection of ≥3 parathyroid glands and transcervical thymectomy [11–13]. Thus, preoperative clinical or genetic diagnosis of MEN1 is essential to performing the appropriate operation and achieving cure.

This manuscript describes the clinical features, operative management, and outcomes of PHPT in a pediatric cohort referred for primary treatment or follow up to a tertiary referral center specializing in the treatment of sporadic and familial endocrine disorders. Due to the abundance of MEN1 patients in this cohort, we used this opportunity to evaluate the role of a preoperative MEN1 diagnosis on the surgical outcomes of parathyroidectomy in children with PHPT.

2. Methods

After obtaining institutional review board approval, we retrospectively analyzed the records of patients who underwent parathyroidectomy for PHPT diagnosed at age ≤18 years. Institutional and research databases were queried to identify pediatric patients treated with initial
parathyroidectomy at The University of Texas MD Anderson Cancer Center as well as those referred for follow up, and/or evaluation of recurrent PHPT after initial parathyroidectomy off-site. The surgeons at our institution were high-volume surgeons with extensive experience in endocrine surgery. Clinical, pathological, operative, and genetic testing data were abstracted from the electronic medical records.

At our institution pediatric patients are defined as patients 18 years or younger. MEN1 was a clinical and/or genetic diagnosis. A clinical diagnosis of MEN1 was made if a patient had a family history of MEN1 in a first degree relative and/or the occurrence of ≥2 MEN1-related tumors in the same individual [11]. A genetic diagnosis was made based on identification of a pathogenic mutation using standard methodology [12,14,15]. While genetic testing is now a criterion for the clinical diagnosis of MEN1, for the purposes of this manuscript, a clinical diagnosis of MEN1 did not include genetic testing. Genetic testing was performed through federally certified Clinical Laboratory Improvement Amendments laboratories. At our institution, a research protocol established in 2002 allows for MEN1 genetic testing when clinical testing is unavailable to patients.

SCE refers to a bilateral neck exploration, but does not refer to the number of glands actually excised. Minimally invasive parathyroidectomy (MIP) refers to a focused, unilateral parathyroidectomy guided by preoperative imaging and intraoperative parathyroid hormone (PTH) monitoring. A complete operation for MEN1 patients was defined as SCE with ≥3 parathyroid glands excised and concomitant transcervical thymectomy [10,12,13]. Persistent PHPT was defined as normocalcemia for at least 6 months, followed by recurrent hypercalcemia detected >6 months. Cure was defined as eucalcemia for >6 months without documented recurrence. Permanent hypoparathyroidism was defined as PTH <10 pg/mL at more than 6 months postoperatively and continued daily calcium and/or calcitriol requirements.

Descriptive statistics were used to evaluate clinical and operative factors. Subgroup analyses were performed to evaluate for differences in outcomes based on a known MEN1 diagnosis preoperatively. Differences between groups were calculated using Pearson’s χ² coefficient or Fisher’s exact test, where appropriate. A p value of 0.05 or less was regarded as statistically significant. Analyses were carried out using IBM® SPSS© Statistics, Version 19.0.0, Armonk, NY: IBM Corp.

3. Results
3.1. Patient characteristics

Thirty-eight pediatric patients who underwent parathyroidectomy for PHPT from 1981 to 2012 were included in this study. The median age at initial diagnosis of PHPT was 15 years (range 11–18), and median age at initial operation was 18 years (range 12–34). The male to female ratio was 1:1.2. The majority of patients (n = 26, 68%) were symptomatic. Of those with symptoms, 73% had nephrolithiasis (n = 19). Other documented symptoms (n = 11) included difficulty concentrating, poor performance in school, and headaches; 7 patients exclusively reported this type of symptoms. One-third of patients (n = 12, 32%) had no objective symptoms documented. Nearly two-thirds (n = 24, 63%) of patients reported a family history of hypercalcemia and/or MEN1. The median follow-up after parathyroidectomy was 4.3 years (range 0–29 years).

3.2. Preoperative evaluation for MEN1

Three-fourths of patients in this study ultimately were diagnosed with a hereditary cause of PHPT (n = 28, 74%). The most common familial etiology of PHPT was MEN1 (26/28 patients with familial PHPT, 68% of total population) followed by hyperparathyroidism–jaw tumor

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Fig. 1. Timing and method of diagnosis of familial primary hyperparathyroidism in 38 pediatric patients who underwent parathyroidectomy. Of the patients with known MEN1 preoperatively, 16/26 were diagnosed based on clinical guidelines. Six patients were diagnosed by genetic testing, of whom 3 underwent genetic testing based solely on age at diagnosis.
syndrome (2/28 with familial PHPT, 5% of total population). Most MEN1 patients in this series met clinical diagnostic criteria at initial evaluation for PHPT (n = 16/26, 62%, Fig. 1). Only 10/26 (38%) MEN1 patients underwent genetic testing preoperatively; 6 of these patients were diagnosed solely by preoperative genetic testing. Of these, 3 patients had seemingly sporadic PHPT and genetic testing was initiated solely due to age at diagnosis; the other 3 patients had a suggestive but not definitive family history at the time of genetic testing. For the other 16 patients with MEN1, 8 had a clinical diagnosis and did not undergo genetic testing during the study period. A clinical diagnosis was confirmed in 4 patients who had genetic testing after initial parathyroidectomy. Finally, 4 patients without initial suspicion for MEN1 had positive results in diagnostic genetic testing carried out postoperatively—3 had testing prompted by family members developing PHPT or MEN1, and 1 patient had testing prompted by recurrence of PHPT.

3.3. Operative technique and outcomes of parathyroidectomy

Over half of patients underwent initial parathyroidectomy at our tertiary care center (n = 22, 58%), while the remainder underwent initial parathyroidectomy pre-referral. Table 1 summarizes operative management for this cohort. Eleven (29%) patients underwent MIP, nearly all of which were performed during the second half of the study. Of 16 transcervical thymectomies performed, 3 (19%) occurred before the year 2000. Overall, 15 patients (40%) had recurrent PHPT and median time to recurrence was 5.1 years. Recurrence was lower in patients whose initial parathyroidectomy occurred at our institution (5/22 vs. 10/16, P = 0.013). The median follow-up for MEN1 patients was 9 years (range 0–29 years).

Perioperative complications, such as transient hypocalcemia or transient recurrent laryngeal nerve palsy were not recorded consistently for all patients. There were no documented permanent injuries to the recurrent laryngeal nerve. Permanent hypoparathyroidism occurred in 5 (13%) patients, all of whom had a preoperative diagnosis of MEN1, and all required >1 procedure for PHPT (range 2–3). Of these patients, 3 had an incomplete initial operation and 2 required autograft debulking for their recurrent disease.

3.4. Outcomes of parathyroidectomy in MEN1 patients

Definitive preoperative delineation of MEN1 versus sporadic PHPT improved appropriate operative management and decreased recurrence in this series (Table 2). Of the 26 pediatric patients with a final diagnosis of MEN1, those who had a definitive clinical or genetic diagnosis preoperatively were more likely to undergo a complete initial operation (10/22, 45% vs. 3/4, 75%; P < 0.001) during follow up than those patients with MEN1 who were not identified preoperatively. Nine MEN1 patients who met the diagnosis criteria preoperatively, underwent an incomplete operation with a recurrence rate of 67% (6/9); none of the four patients with the postoperative MEN1 diagnosis underwent a complete initial operation (SCE and bilateral transcervical thymectomy). Those with a known preoperative diagnosis of MEN1 had a longer median time to persistence/recurrence than those without a known MEN1 preoperative diagnosis (59 vs. 48 months). Patients undergoing initial parathyroidectomy at our institution were more likely to have a preoperative diagnosis of MEN1 (13/13, 100% vs. 9/13, 69%; P = 0.030), and complete initial operation (10/13, 77% vs. 3/13, 23%; P = 0.006) compared with those who underwent initial operation pre-referral. On pathologic analysis, parathyroid tissue was present in 6/14 (43%) of the thyrmic specimens excised from MEN1 patients.

3.5. Outcomes of parathyroidectomy for patients with sporadic PHPT

Negative results on preoperative genetic testing that supported sporadic etiology (performed in 5/10 patients with an ultimate diagnosis of sporadic PHPT) allowed for an appropriate, focused operation (MIP) in the 5 patients tested preoperatively with 100% cure. In addition, patients underwent genetic testing to rule out MEN1 after initial parathyroidectomy for recurrence (2) and a new diagnosis in a family member (1). One patient with low suspicion for MEN1 did not have results available at time of operation, and another did not undergo genetic testing.

Table 1
Management and surgical outcomes of 38 pediatric patients with primary hyperparathyroidism who underwent parathyroidectomy.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>38</td>
<td>100</td>
</tr>
<tr>
<td>Etiology of PHPT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sporadic</td>
<td>10</td>
<td>26</td>
</tr>
<tr>
<td>MEN1</td>
<td>26</td>
<td>68</td>
</tr>
<tr>
<td>HPT-JT</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Extent of operation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIP</td>
<td>11</td>
<td>29</td>
</tr>
<tr>
<td>SCE</td>
<td>27</td>
<td>71</td>
</tr>
<tr>
<td>Thymectomy</td>
<td>16</td>
<td>42</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td>15</td>
<td>40</td>
</tr>
<tr>
<td>Persistent PHPT</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Patients who underwent reoperation</td>
<td>14</td>
<td>37</td>
</tr>
<tr>
<td>Permanent hypoparathyroidism</td>
<td>5</td>
<td>13</td>
</tr>
</tbody>
</table>

MIP, minimally invasive parathyroidectomy; SCE, standard cervical exploration; PHPT, primary hyperparathyroidism; HPT-JT, hyperparathyroidism–jaw tumor syndrome.

Table 2
Operative outcomes in patients with primary hyperparathyroidism (PHPT) and multiple endocrine neoplasia type 1 (MEN1). Most patients were diagnosed preoperatively. Preoperative diagnosis of MEN1 was associated with greater likelihood of complete operation and lower recurrence of PHPT. A complete operation for MEN1 patients was defined as standard cervical exploration (SCE) with >3 parathyroid glands excised and concomitant transcervical thymectomy.

<table>
<thead>
<tr>
<th>Outcome of parathyroidectomy</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No recurrence at last follow-up</td>
<td>13</td>
<td>50</td>
</tr>
<tr>
<td>Recurrence</td>
<td>12</td>
<td>46</td>
</tr>
<tr>
<td>Persistent disease</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Operative failure by timing of MEN1 diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete operation if preoperative diagnosis</td>
<td>13/22</td>
<td>59</td>
</tr>
<tr>
<td>Complete operation if postoperative diagnosis</td>
<td>0/4</td>
<td>0</td>
</tr>
<tr>
<td>Operative failure by operative approach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If preoperative diagnosis</td>
<td>10/22</td>
<td>45</td>
</tr>
<tr>
<td>If postoperative diagnosis</td>
<td>3/4</td>
<td>75</td>
</tr>
<tr>
<td>Operative failure by operative approach if preoperative MEN1 diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If complete operation</td>
<td>4/13</td>
<td>31</td>
</tr>
<tr>
<td>If incomplete operation</td>
<td>9/13</td>
<td>69</td>
</tr>
</tbody>
</table>

1 P = 0.03.
2 P < 0.001; includes 1 patient with persistent PHPT.
3 P = 0.05.
4 P = 0.096.
Two patients with sporadic PHPT had recurrent PHPT within one year after MIP (7 and 9 months). One patient had an intrathyroidal parathyroid gland at reoperation (missed single adenoma). The second patient had a single gland excised with pathology revealing parathyroid hyperplasia (presumed multigland disease), and was pending reoperation at last follow-up. Finally, one patient underwent successful SCE with resection of >3 glands, with final pathology revealing hypercellular parathyroid tissue. Thus, the incidence of multigland disease in this series in sporadic PHPT patients was 20%.

### 3.6. Patients with hyperparathyroid-jaw tumor syndrome

Two patients in this series were diagnosed with hyperparathyroid-jaw tumor syndrome. One patient had a family history of PHPT and underwent genetic testing for MEN1, which was negative. The preoperative diagnosis was cystic parathyroid adenomatosis. The patient initially underwent SCE with resection of 2 parathyroid glands and forearm autograft. Genetic testing of CDC73 (formerly HRPT2) was pursued after the patient’s PHPT recurred, and results were positive for a mutation. The second patient was diagnosed clinically after having multiple ossifying fibromas removed from the mandible. Hypercalcemia was noted incidentally, and PHPT from a single adenoma was treated successfully with MIP. Genetic testing for a mutation in CDC73 was negative in this patient.

### 3.7. MEN1 follow up

After a diagnosis of MEN1 and initiation of standard biochemical and imaging screening protocols, 23 (88%) MEN1 patients were found to have another neuroendocrine site of disease during follow up—12 pituitary adenomas, 16 pancreatic neuroendocrine tumors, and 3 bronchial carcinoid tumors. Two deaths occurred during follow up in patients with bronchial carcinoid tumors; both patients initially presented at age 16 and underwent SCE without transcervical thymectomy. One patient had MEN1 clinical diagnosis at initial operation and expired 21 years later. The second patient had initial operation at age 39, but did not have an MEN1 diagnosis until age 55 and metastatic carcinoid was identified through screening for MEN1-related tumors.

### 4. Discussion

This large series of pediatric patients undergoing parathyroidectomy for PHPT confirms that pediatric PHPT patients present with specific symptoms of hypercalcemia, with males and females represented equally, unlike their adult counterparts. Nephrolithiasis was the leading cause of objective symptoms in this series, consistent with previous reports that have suggested that young patients are more likely to be symptomatic than adult patients [16]. Nonetheless, one-third of our patients had no documented evidence of disease. This may reflect the increased finding of incidental hypercalcemia on laboratory assays collected for another indication. We believe that it also reflects early implementation of biochemical screening when family history of hereditary syndromes is present. Additionally, the true rate of symptoms may be underestimated based on reliance of documentation by the providers and the retrospective nature of this study.

Approximately two-thirds of young patients referred to our institution had an ultimate diagnosis of familial PHPT, most commonly MEN1. Our tertiary care center serves as a national and international referral base for diagnosis and treatment of sporadic and hereditary endocrine syndromes. Nearly half of patients in this series (n = 16, 42%) were referred to our center after initial parathyroidectomy, likely secondary to suspicion of a familial disease. Thus, while most series of pediatric PHPT report a rate of familial disease at approximately 15% [4,17], referral bias is the likely cause of familial disease in 2/3 of patients in our study. Nevertheless, this cohort of pediatric PHPT predominantly caused by MEN1 offers us the unique opportunity to study the influence of preoperative disease classification (sporadic or familial) on surgical management and outcomes.

The incidence of multigland disease in PHPT patients presumed to represent sporadic disease in this study was 20%. MEN1 affects all parathyroid tissue and is by definition a multigland disease. Others have suggested that multigland disease in pediatric patients with sporadic PHPT is less common than previously thought and may be similar to that in the adult population [17], perhaps due to an increased recognition of familial disease in children. Most series report approximately one-fourth of pediatric patients have multigland disease, although these studies have included familial PHPT cases [3–6,18]. A review of young adults with PHPT found that family history of nephrolithiasis or hypercalcemia, even without a diagnosis of hereditary syndrome, was associated with multigland disease [16]. Our data corroborate the recommendation that children whose clinical evaluation suggests sporadic PHPT and who have localizing studies suggesting a single adenoma may be considered for a focused parathyroidectomy, as the vast majority of these patients are unlikely to recur. However, the interpretation of imaging requires experience as presumed solitary concentrated isotope uptake does not confirm single gland disease. A recent study of an adult population found that 17% of patients whose operation required conversion from MIP to SCE had concordant imaging suggesting single gland disease [19].

Over the 31-year study period, testing and diagnosis of familial PHPT have changed considerably. While the genetic basis of MEN1 was described by Wermer in 1954, causative mutations in the MEN1 gene encoding the menin protein were not identified until 1997 [14,15]. Thus, patients undergoing parathyroidectomy earlier in the study were diagnosed with MEN1 through clinical or family history only. In contrast, a current research protocol at our institution supports routine MEN1 testing for pediatric patients with PHPT. This testing strategy in pediatric patients without a definitive clinical history suggesting familial disease identified 6 patients with MEN1 who would not have been diagnosed based on clinical criteria alone. Using genetic testing as the gold standard, the use of clinical diagnostic criteria for MEN1 was only 62% sensitive. Previous reports have found that family history is unreliable because many patients do not report a positive diagnosis of MEN1 in a family member [20]. In fact, this lack of reliability led to the development of screening questionnaires for patients with PHPT to alert the clinician about a potential underlying MEN1 diagnosis and need for referral to genetic counseling services. The 6-question screening tool was more sensitive (83%) when compared to medical history (45%) [20]. Nonetheless, genetic testing is reported to miss 5–30% of MEN1 cases [9,10]. A cost–benefit analysis of routine versus selective genetic testing for MEN1 in pediatric patients who present with PHPT will be worthwhile.

The approach to parathyroidectomy has also evolved over the past few decades. Parathyroidectomy with SCE, the approach used routinely at the beginning of the study period, was routinely recommended for all young patients with PHPT by some authors [3]; it may have helped identify the nodular hyperplasia common to MEN1 parathyroid glands even in the absence of a preoperative MEN1 diagnosis. While bilateral cervical thymectomy is not routinely performed as part of SCE for sporadic PHPT, it is recommended as part of standard parathyroidectomy in MEN1 patients [11,12]. This may also explain why some of the MEN1 patients who underwent SCE did not undergo concomitant thymectomy. Given that nearly half of patients with MEN1 who underwent cervical thymectomy had parathyroid tissue in their thymic specimens, preoperative knowledge of an MEN1 diagnosis and performance of a complete initial operation may decrease or substantially delay recurrence. Conversely, we routinely use a focused operative approach (MIP) for parathyroidectomy in appropriate patients whose well-localized imaging study suggests a single adenoma. Negative preoperative genetic
testing in children with suspected sporadic PHPT increases our confidence that MIP is an appropriate procedure.

In this series, recurrent PHPT occurred in nearly half of children with MEN1 with a median follow-up of 8 years; this is slightly lower than the 67% recurrence rate at 8 years reported by Burgess et al. following subtotal parathyroidectomy (without thymectomy) [21]. Operative failure was associated with an unknown preoperative diagnosis of MEN1 (3/4 patients) and an incomplete initial operation (excision of <3 glands and/or without cervical thymectomy, 4/4 patients). This is consistent with previous reports that preoperative identification of MEN1 is essential to plan the most appropriate operative procedure as well as to screen for MEN1-related tumors. Repeated operations were associated with permanent hypoparathyroidism, which occurred after reoperation in 5 patients with MEN1 and recurrent PHPT. Although all 3 met criteria for clinical diagnosis of MEN1 preoperatively, none of these patients had preoperative genetic testing, and 3 underwent an incomplete initial operation.

Now that genetic testing for MEN1 is readily available and accurate, we have adopted an approach of testing nearly all pediatric patients for MEN1 prior to elective parathyroidectomy. In addition to assisting with operative planning and diagnosis of some patients missed by clinical screening, genetic testing also helps identify patients who need routine clinical screening for MEN1-related manifestations and may identify at-risk relatives who may benefit from predictive testing. In our series, the majority of MEN1 patients had a positive finding on a subsequent screening test, most commonly an asymptomatic non-functional pancreatic neuroendocrine tumor. Early identification of MEN1 for future screening may be lifesaving in some patients, as evidenced in one of our patients whose metastatic carcinoid tumor was found after MEN1 diagnosis nearly 40 years following initial PHPT presentation. A small European series that screened MEN1 children with cross-sectional imaging identified 2/12 patients harboring nonfunctional pancreatic neuroendocrine tumors greater than 2 cm in size [22]. In fact, when genetic testing was used in a study of MEN1 families to promote adherence to screening guidelines, subclinical disease was identified as many as 10 years before clinical manifestations of disease [23]. Pieterman et al. found that MEN1 patients diagnosed by genetic testing had significantly fewer manifestations of disease than patients with a clinical diagnosis did, and the use of genetic testing was associated with less morbidity at follow-up [24]. Therefore, early diagnosis of MEN1 by genetic testing may lead to improved outcomes if patients properly follow surveillance guidelines.

This study has several limitations. Its retrospective nature and inclusion of a population treated at a referral center for familial endocrine disease introduced both selection and ascertainment bias. However, given the rarity of both pediatric PHPT and MEN1, this descriptive study is informative despite these inherent biases. Given that the study spans 3 decades, there are clear differences in availability of genetic testing and operative approach based on the period of initial parathyroidectomy. Whereas early in the study MEN1 was a clinical diagnosis, the modern era of genetic testing enabled identification of several patients with MEN1 who had no identifiable family history of disease.

In conclusion, at a tertiary care referral center for endocrine neoplasia, the vast majority of pediatric patients with PHPT have an underlying familial cause—chiefly MEN1. Preoperative diagnosis, by clinical criteria or genetic testing, of MEN1 in young patients with PHPT helps the surgeon plan the most appropriate initial operation, which appears to decrease recurrence and subsequent complications associated with reoperation. Furthermore, the identification of MEN1 in a pediatric patient is expected to facilitate the presymptomatic screening for other MEN1-related clinical manifestations and improve long-term outcomes as related to these other neoplastic processes. Our data support the benefit of testing for MEN1 in young patients with PHPT, although future studies should address the cost-effectiveness of such an approach. Young patients with PHPT should be managed at a high-volume center with experienced clinicians and genetic counseling and testing services.

References