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Review article

Characterization of hyperparathyroidism in youth and adolescents: A literature review

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ABSTRACT

Objectives: To systematically review the preoperative diagnostic modalities, surgical treatments, and glandular pathologies associated with primary hyperparathyroidism in children and adolescents under 20 years of age.
Methods: We searched PUBMED, Cochrane databases, OVID, Web of Science (SCIE and SSCI), CINAHL, and Health Source: Nursing academic for articles involving surgical management of primary hyperparathyroidism in the pediatric population on 5/2012. Selection Criteria: Literature review, database review, and retrospective review studies date were used from 1986 until 2012. Ages ranged for 0–19 years old.
Results: Of the 230 cases of pediatric primary hyperparathyroidism reported since 1987, solitary adenomas (SA), multiple gland hyperplasia disease (MGHD), double adenomas (DA), and normal parathyroid gland pathology occurred in 80%, 16.5%, 0.9%, and 2.6% respectively. Of the MGHD patients (38 pts), 1/2 (19 pts) of the cases were attributed to MEN I, MEN II, or familial non MEN hyperparathyroidism. Tc^{99m}-sestamibi and ultrasound were 86% (37/43) and 74.5% (70/94) sensitive, respectively for localizing parathyroid disease.
Conclusions: Limited data exists on pediatric and adolescent patients with primary hyperparathyroidism. Sufficient data exists demonstrating single adenomas are most common and young patients are usually more symptomatic than adults. One may conclude that spontaneous primary hyperparathyroidism may be approached and managed similarly to adults. The incidence of primary hyperparathyroidism in this population may be under appreciated and a lower threshold for ordering a screening serum calcium should be considered.

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1. Introduction

Primary hyperparathyroidism (PHPT) is a rare disease in adolescents with an incidence of 2–5 in 100,000 [1,2]. This compares to an adult incidence of 1:500–2000 [2]. The causes of

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PHPT in the adolescent population include parathyroid adenomas, multi-glandular disease (MGD), and parathyroid carcinoma. The latter is relatively rare and will not be discussed further. Also neonatal hyperparathyroidism has been well established to be its own distinct disease entity and will also not be described [3]. MGD in younger patients is generally due to hereditary family disorders including multiple endocrine neoplasia type 1 (MEN 1), MEN 2a, or familial isolated hyperparathyroidism. Historically, pediatric PHPT was believed to be due largely to the disproportionate representation of MGD in small series [4]. However, more recently it has been established that PHPT in the majority of adolescents is due to a single adenoma, just as in adults [5]. This paradigm shift in understanding PHPT has led to changes in surgical management.

Typically, PHPT in an adolescent or pediatric population has been managed with a standard bilateral neck exploration with identification and biopsy of the parathyroid glands. This approach is appropriate for MGD and should continue to be its standard of care. However, with the discovery that PHPT is mostly due to single adenomas, the surgical management may be modified to parallel that of many adults, focused parathyroid exploration and excision of single gland disease utilizing intraoperative parathormone assay (IOPTH).

The advent of successful preoperative localization scans, most notably Tc^{99m}-sestamibi, has allowed a minimally invasive technique to be developed. First described by Norman et al. in 1998, minimally invasive radioguided parathyroidectomy (MIRP) has emerged as a leading method of treatment for PHPT. The evolution from a bilateral neck exploration to unilateral neck exploration then to minimally invasive parathyroidectomy (MIP) has many documented benefits including decreased operative time and expense, decreased hospital time and expense, and fewer operative complications [6].

Currently, there exist sparse literature supporting MIP in the adolescent population. It should be considered given the similarities between adult and adolescent disease. In fact, preoperative sestamibi localization scanning may be more beneficial in the adolescent population due to the higher percentage of ectopic parathyroid adenomas in this group. [7] Sestamibi scans can image adenomas in the chest not detectable by ultrasound. The sensitivity of Tc^{99m}-sestamibi in the adult population is 88% with a probability of surgical cure with MIP of 96.6% [8].

Hyperparathyroidism should be suspected in patients with intermittent or persistent hypercalcemia in the absence of other pathology such as malignancy, immobilization, milk alkali syndrome, etc. A patient's parathyroid hormone (PTH) level should be drawn with matching total and ionized calcium levels. The diagnosis of PHPT is confirmed by normal (which is inappropriate in the setting of hypercalcemia) or elevated PTH levels. A 25 OH vitamin D level should also be drawn to look for the very prevalent vitamin D deficiency.

The purpose of this paper is to improve the understanding of this rare condition in the pediatric and adolescent population by gathering relevant literature, performing systematic analysis, and adding those results to the contemporary medical literature.

2. Methods

This study was a systematic retrospective literature review. We searched PUBMED, Cochrane databases, OVID, Web of Science (SCIE and SSCI), CINAHL, and Health Source: Nursing academic for articles involving surgical management of primary hyperparathyroidism in the pediatric population on 5/2012. Selection criteria included: Literature review, database review, and retrospective review studies from 1986 until 2012. Search terms included: "hyperparathyroidism, surgery, humans, English, children, pediatric, young adult, infant, child, toddler, preschool, "tween", teen, or adolescent". Ages ranged for 0–19 years old.

We included retrospective review studies, case series, and database reviews that were only written in English (Table 1). We excluded case series of less than 3 patients. Several studies included patients over the age of 19, but were only included if they gave individual data for those patients under 20 years of age so they could be separately analyzed. We specifically looked at the parathyroid pathology and diagnostic modalities if reported (Table 2). Other parathyroid pathology including parathyroid carcinomas and neonatal hyperparathyroidism articles were excluded.

The results of the search yielded 287 total journal articles. After careful reading and filtering with our criteria only 13 articles of this

Table 1
Summary of pediatric and adolescent primary hyperparathyroidism literature.

Study (year[a])	Study type (country)	No. patients	Age range (years)	M:F ratio	Predominant pathology	Presence of symptoms
Lawson (1996)	Retrospective Review (USA)	11	12.3–17.7	0.8:1	Single adenoma (100%)	Bone disease (73%) nephrolithiasis (45%)
Harman (1999)	Database Review (USA)	33	9–19	1.1:1	Single adenoma (94%)	Nephrolithiasis (42%) bone disease (27%)
Kollars (2005)	Retrospective Review (USA)	52	4–18.9	0.67:1	Single adenoma (65%)	Fatigue and lethargy (35%) headache (35%) Nephrolithiasis (33%) nausea (29%)
Venail (2007)	Case Series (France)	4	7–14	0.33:1	Single adenoma (100%)	Bone disease (50%)
Libansky (2008)	Retrospective Review (Czech Republic)	10	10–17	1:1	Single adenoma (100%)	Urolithiasis (50%) bone impairment (30%)
Durkin (2010)	Retrospective Review (USA)	12	10–18	0.09:1	Single adenoma (75%)	Nephrolithiasis (25%) fatigue (12%)[b]
Cronin (1996)	Prospective (USA)	8	13–18	1.7:1	Single adenoma (75%)	Gastrointestinal symptoms (87.5%)
Loh (1997)	Retrospective Review (USA)	7	15–18	2.5:1	Single adenoma (86%)	Fatigue (86%) joint pain (29%) nausea (29%) polyuria (29%)
Rapaport (1986)	Case Series (Israel)	7	15–22[c]	1.33:1	Single adenoma (100%)	Nephrolithiasis (71%) bone disease (71%) polyuria (71%) polydipsia (71%)
Hsu (2002)	Retrospective Review (USA)	13	10.5–18	1.17:1	Single adenoma (69%)	Nephroltihiasis (38%)
George (2010)	Retrospective Review (India)	18	13–19	0.29:1	Single adenoma (100%)	Bone impairment (89%) nephrolithiasis (39%)
Mallet (2008)	Retrospective Review (France)	44	6–18	0.69:1	Single adenomas (66%)	Nephrolithiasis (41%) weakness (39%) weight loss (32%)
Bhadada (2008)	Retrospective Review (India)	11	5–18	0.57:1	Single adenomas (91%)	Bone impairment (91%)

[a] Year study was published.
[b] Symptomatic presentations include patients up to 25 (not given individual statistics for pts <20 years old).
[c] One patient is 22 years old at time of surgery, but had documented symptoms for 12 years.