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Original Articles

# Surgical treatment of children with hyperparathyroidism: Single centre experience☆,☆☆

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ABSTRACT

*Background:* Hyperparathyroidism (HPT) in children is rare and surgical management is supported only by limited evidence.
*Methods:* Retrospective case series of all children under the age of 16 years who underwent parathyroidectomy (PTx) between 1978 and 2012.
*Results:* We identified 29 children who had surgery for HPT. Six were neonates with neonatal severe hyperparathyroidism (NSHPT) and 23 older children (age range 7–16 years) with sporadic (16) or familial (7) HPT and 93% were symptomatic. Accuracy of ultrasound and MIbi in localising solitary parathyroid adenomas was 96%, but less helpful in hyperplasia and neonates.
Children with NSHPT underwent 5 curative total and 1 subtotal PTx (no reoperations). Children with familial HPT underwent 3 total and 4 subtotal PTx. One child with subtotal PTx required a reoperation. Children with sporadic HPT underwent subtotal PTx prior to 1980 (2), exploration and removal of enlarged glands 1980–2002 (5) and minimally invasive PTx since 2002 (9) and all cured by the first operation.
*Conclusions:* Our study documents that HPT in children is predominantly symptomatic on presentation and genetically determined in 46% of cases. Imaging is accurate in localising parathyroid adenomas, but not hyperplasias. Total PTx for familial HPT was curative and minimally invasive PTx is the operation of choice for older children with sporadic HPT.



Hyperparathyroidism (HPT) affects both children and adults but it is rare in the former and common in latter [1–5]. In sharp contrast to only a handful of small case series of children with HPT described in the literature [2,4–6], there is a significant body of evidence about HPT in adults concerned with its epidemiology, symptoms, accuracy of imaging and surgical outcomes [7,8]. Management of hyperparathyroidism in adults has seen a sea of change in the last two decades [7,8]. Main drivers of this transformation were more precise and faster biochemical assays, increased ability to detect genetic mutations and more accurate preoperative imaging. Clarity of biochemical, genetic and radiological diagnosis allowed for the introduction of 'key hole' parathyroidectomy done through smaller incisions and resulting in better cosmesis, less pain and reduced hospital stay [6,9].

The impact of these new technologies on the management of children with HPT is not well documented. Published case series describe children managed over many decades and this long time frame, when constant advances move goal posts in biochemistry, genetics, radiology, pharmacology and surgery, is a challenge when formulating a coherent management strategy. There is a need to explore whether lessons learnt from treating adult patients with HPT could be applied to younger patients and this requires the differences between HPT in children and adults to be well understood. This study reviews our 35 years' experience of treating children with HPT, highlights clinical aspects of this condition in different age groups and documents the impact of the evolving laboratory testing, imaging and surgical techniques on their management.

## 1. Methods

We have performed a retrospective review of all children under the age of 16 years diagnosed with HPT who had parathyroidectomy

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at our institution between 1978 and 2012. Demographic data collected were gender, age at diagnosis and age at the time of surgery. Fisher's exact test was used to assess gender distribution and the independent sample t-test for age differences.

Causes of HPT were classified as genetically determined (familial) or sporadic and, wherever possible, details of the mutations were reported. The clinical presentations were classified in the following categories: gastrointestinal, skeletal, renal, neurological/psychological or as asymptomatic. The laboratory measurements reviewed were serum calcium and parathyroid hormone concentration at presentation and after the operation.

Pre-operative localisation studies reviewed were ultrasonography (US), technetium 99m sestamibi parathyroid scintigraphy (MIBI) and parathyroid venous sampling (PVS). Their value was expressed as sensitivity, specificity and overall accuracy of their ability to identify firstly the laterality of the abnormal glands (left/right), and secondly to predict the precise quadrant position of abnormal glands (i.e. left/upper and right/lower). Accuracy of US and MIBI in distinguishing single from multiple gland disease was also calculated. Findings of the imaging were compared to findings at surgery and histology, which were considered 'gold standard'.

Operations were classified either as minimally invasive parathyroidectomy (MIP) or bilateral neck exploration (BNE). Minimally invasive parathyroidectomy was defined as an operation during which a single abnormal parathyroid gland was removed through a small lateral incision without an attempt to visualize other glands. Bilateral neck exploration was performed through a skin crease collar incision, which allowed direct visualisation of all and removal of abnormal glands. Histology of the removed glands was reported as adenoma, hyperplasia or normal. Surgical outcomes were determined by postoperative complications classified as bleeding, infection, voice change, hypocalcaemia and the need for re operation. Length of follow up was recorded.

## 2. Results

### 2.1. Demographics and diagnosis (Table 1)

Twenty-nine children (15 boys, 14 girls) underwent surgery for HPT at our institution. Six children (3 boys, 3 girls) had neonatal severe hyperparathyroidism (NSHPT) and presented in infancy [3 days–4 months (median 2 weeks)] and 23 children (12 boys, 11 girls) presented later in childhood with familial [7–6 years (median 13 years)] and sporadic HPT [8–16 years (median 15 years)]. Seven children had familial [4 MEN1, 1 MEN2a, 1 hyperparathyroidism jaw tumour syndrome, (HPT-JT) 1 X linked hypophosphataemia, XLHP] and sixteen sporadic HPT. The age at presentation, sex differences and the age at the time of surgery between children with familial and sporadic HPT were not significantly different [$p = 0.64$ (gender), $p = 0.99$ (age), $p = 0.83$ (age at operation)].

### 2.2. Clinical presentation

The symptoms involving gastrointestinal, renal, skeletal and neurological systems were not mutually exclusive.

Four neonates presented with gastrointestinal symptoms of poor feeding/vomiting and two with jaundice. Skeletal abnormalities were noted in three neonates, including one with multiple rib fractures, flail chest and respiratory failure requiring mechanical ventilation on the intensive care unit. Neurological symptoms identified in four neonates included developmental delay (3) and lethargy (2).

In the older group, gastrointestinal symptoms were the commonest presenting complaint affecting eight children and included abdominal pain (6), vomiting (3), constipation (2) and diarrhoea (1). Three children had skeletal abnormalities, one child had deformity of the knees and two had osteomalacia. Two children had acute renal colic owing to calculi and two children presented with CNS symptoms of depression with suicidal ideation (1) and lethargy (1), both in conjunction with gastrointestinal symptoms. Incidental diagnoses were made in two asymptomatic children; one child diagnosed on a preoperative blood test for a cochlear implant and the other child was investigated for premature adenarche.

### 2.3. Biochemical and genetic findings

Calcium and PTH concentrations on presentation in the neonatal group ranged from 3.03–8.10 mmol/l (median 4.02 mmol/l) and from 15.8 to 360 pmol/l (median 56.9 pmol/l) respectively (Table 1). Four neonates tested positive for mutations of the CaSR gene encoding the calcium sensing receptor. [two neonates—2nd degree relatives: homozygous p.Q164X, one homozygous p.C570, one compound heterozygote p.R680C (paternal) and one p.C60F (maternal)].

Older children had calcium and PTH concentrations ranging from 2.75 to 4.09 mmol/l (median 3.10 mmol/l) and from 9.4 to 62 pmol/l (median 16.4 pmol/l) respectively. Differences between serum calcium and PTH levels in children with the familial and sporadic HPT were not statistically significant [$p = 0.80$ (calcium), and $p = 0.37$ (PTH)].

### 2.4. Localisation studies

Ultrasonography was performed as a solitary investigation in two neonates and in combination with MIBI scanning in two; the remaining two patients did not have any imaging carried out. None of the scans identified abnormal glands.

In older children, ultrasonography was performed in 17 (14 sporadic and 3 familial HPT) and this was in conjunction with MIBI scanning in 16 children (13 sporadic and 3 familial HPT). The ability of US and MIBI imaging to distinguish solitary from multiple glands disease and to accurately predict the laterality of the abnormal solitary gland was 100%. In children with sporadic HPT, the accuracy of US and MIBI for precise quadrant localisation of abnormal gland

**Table 1**
Demographics, calcium and PTH levels.

| | Neonates with NSHPT | Older children with sporadic HPT | Older children with familial HPT [a] |
|---|---|---|---|
| Number | 6 neonates | 16 children | 7 children |
| Gender—M:F | 3 boys: 3 girls | 7 boys: 9 girls | 5 boys: 2 girls |
| Age at diagnosis | 3 days–4 months (median 2 weeks) | 7–16 years (median 13 years) | 8–16 years (median 15 years) |
| Age at operation | 3 weeks–3 years (median 5 months) | 9–16 years (median 14 years) | 10–16 years (median 15 years) |
| Calcium levels at diagnosis (mmol/l) | 3.03–8.10 (median 4.02)<br>Normal: 2.37–2.74 | 2.75–4.09 (median 3.07)<br>Normal: 2.15–2.55 | 2.86–3.57 (median 2.95)<br>Normal: 2.15–2.55 |
| PTH levels at diagnosis (pmol/l) | 15.8–360 (median 56.9)<br>Normal: 1.1–5.4 | 9.4–62 (median 16.4)<br>Normal: 1.3–7.6 | 9.4–44.9 (median 16.7)<br>Normal: 1.3–7.6 |

[a] 4, MEN1, 1 MEN2a, 1 HPT-JT, 1 X linked H.