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Surgical treatment in hyperparathyroidism in children (about 3 cases)

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Abstract
Hyperparathyroidism is a rare condition in children, mainly primary school rarely, may be complicated by renal, musculoskeletal digestive and cardiovascular systems.
The contribution of biology (calcium and phosphate and parathyroid hormone assay) of modern imaging (ultrasound, scintigraphy) and histopathology at diagnosis is essential.
The cure is surgery. It is within this context that our retrospective study of three patients admitted in the pediatric surgery department of Hospital A child of Rabat.
There were three patients' two girls and one boy, mean age 10 years, divided into a primary hyperparathyroidism with nephrolithiasis, a case of primary hyperparathyroidism with osteoarticular complications and a lack of hyperparathyroidism chronic kidney. Our three patients had received a good cervicotomy with removal of a parathyroid adenoma; the postoperative course was unremarkable except for one patient, who had a crisis of hypocalcemia.
The evolution was marked by an improvement in clinical symptoms and normalization of calcium and phosphate and PTH levels.
The cure rate is organic over 95%.

Keywords: parathyroid, hyperparathyroidism, child, surgery, adenoma

Introduction
The hyper functioning of parathyroid glands may be related to a primary condition of these glands (adenoma, primary hyperplasia) or reaction secondary to various pathologies that may lead to excitatory hypocalcemia (rickets and renal failure).
Discovered in 1880 by Sandtrom, the parathyroids will wait a few more years to be assigned a pathological role.
Since the first parathyroidectomy performed in 1925, and until very recently, parathyroid surgery was a "find me if you can!" Surgery. "(" Find me if you can! "), Indeed, the surgeon operated his patient by bilateral transverse cervicotomy, without preoperative imaging, and was looking for the pathological gland (s) in the course of a complete exploration of the upper cervical and mediastinal region [1], based on the anatomy and embryological evolution of the glands. In the hands of surgeons who have gained extensive experience in the treatment of primary hyperparathyroidism, there is little failure with more than 95% of patients cured by a single cervicotomy. Under these conditions, morbidity and mortality are almost nil [2].
In 1938 Duken describes an almost certain case of HPT in a 14-year-old girl.
In 1930 Pemberton reported the first successful parathyroid adenoma observation.
In 1945 Bickeld wrote the first case with urolithiasis.
In 1947 Prat reported the first case of proven hyperplasia in infants.
In 1973 Daum reported the first case of secondary pancreatitis.
In 1974 Leclerc Macabeo Rober and Talwalker describe the ultra-structure under the electron microscope in a case of neonatal hyperplasia.
Primary HPT occurs at any age, from infancy to very old people. However, the incidence of the disease increases gradually into adulthood.
The disease is sporadic in the vast majority of situations. The factors that condition the usually monoclonal proliferation of primary cells and the formation of adenomas are poorly understood.
In 5 to 10% of situations, primary HPT is familial. The frequency of primary hyperparathyroidism is 90 to 100% of patients with multiple endocrine neoplasia type 1.

Materiels & Methods
This is a retrospective study that focused on all patients with hyperparathyroidism who were hospitalized in the Surgery A department of the Rabat Children's Hospital.
We treated 3 cases including two cases of parathyroid nodule and one case of hyperparathyroidism on chronic renal failure.

Results
1st case
This is a 14-year-old girl, with no particular personal or family history, who consults for a right valgum genu whose history of her illness dates back a year before her hospitalization by the appearance of pain at the level of the right ankle with lameness, without any notion of trauma and evolving in a context of apyrexia.
4 months later, the parents noticed a deformity of the right knee which worsens progressively with accentuation of the lameness which becomes more and more disabling. In addition, after minimal trauma to the left shoulder causing total functional impotence, the child consulted with us.

The objective clinical examination is an asthenic child, with difficult autonomic walking and lameness. Genu valgum right at 45 ° with a bi-malleolar distance of 18cm without amyotrophy or shortening. The exam also notes a zero shoulder abduction and very painful.

Radiologically

The standard radiographs note an aspect of the geodes with the punch on the skull, images of lysis of the extremities of the two clavicles, an important demineralization of the upper extremity of the left humerus with pathological fracture, a bone demineralization of the two hands with phalangeal micro-geodic images, sub-chondral erosion with phalangeal tussock resorption, bilateral epiphysiolysis with chondral symphysis erosion responsible for pseudo-enlargement of the pubic symphysis, and a right valgus genu with diffuse demineralization of the tibia and fibula.

These radiological features were strongly suggestive of hyperparathyroidism and led to a phosphocalcic assessment that corroborated this hypothesis and a CT scan that confirmed the diagnosis.

However, the diagnosis of primary HPT seems more likely especially as there is no vitamin D intoxication, or Burnett syndrome (milk drinker) and that complementary exams are not in favor. sarcoidosis, nor paraneoplastic syndrome and that they do not allow any suspicion of neoplastic bone lysis.

CT showed a straight, homogeneous, hypo-dense parathyroid mass with respect to the surrounding thyroid tissue, which is located at the dihedral angle formed by the lateral thyroid margin and the esophagus and is 2 cm in diameter.

The child was operated after cervicotomy Kocher tie with discovery of a 4 cm nodule developed at the expense of the right lower parathyroid. The right upper parathyroid is also hypertrophied and nodular, all adhering to the right lobe of the thyroid

Straight lobectomy with both parathyroid glands is performed following identification of the recurrent nerve. The left parathyroids are of normal appearance.

The postoperative course was marked by the appearance of tetanic signs and a sign of Chvostek, the serum calcium fell to 77 mg / l.

The patient was put on calcium by oral perfusion, which brought the serum calcium to normal levels without the use of vitamin D. Calcium was stopped very gradually in stages.

Anatomo-pathological examination confirms that the nodule corresponds to a parathyroid adenoma essentially to main cells. The nodule is well encapsulated and has no evidence of malignancy.

On the orthopedic plane, she was treated with a varus osteotomy maintained by a crampo-pedal plaster, 4 months after the plaster was removed and the patient was allowed to walk.

Currently, she is walking well with good overall evolution.

2nd case

He is a 14-year-old child with a family history of renal lithiasis in his paternal uncle and notions of frequent nephritic colic in the father; as a personal history, a hospitalization for meningitis treated, several episodes of urinary infection whose etiological diagnosis returned to a polylithiasis kidney destroyed which led to the realization of a right nephrectomy and a right valgum genu which he has benefited from a varative osteotomy.

The general examination finds a child in fairly good general condition, with difficult autonomic walking and lameness, a left valgum genu (contralateral side of the operated side), with sensitivity to palpation of the shoulder blades, pelvis and lumbosacral spine.

Radiographically, standard radiographs show lysis of the two outer extremities of the clavicles, an eroded and flared appearance of the metaphyseal epiphyseal regions distal to the radius and ulna with resorption of the phalangeal tussles, as well as a calcium image of approximately 1 cm in projection of the left renal air and masses of small calcifications in projection of the lower pole of the same kidney.

An abdominal ultrasound shows that the left kidney is increased in size (130 mm) with multiple lithiases, the largest of which are pyelic (24mm) and lower polar, with a discreet dilation of the calyx cavities.

Cervical CT and parathyroid scintigraphy with Thalium and Technetium show the presence of a zone of right medio-lobar parathyroid hyperplasia, which disappears at the TI-TC subtraction.

The phosphocalcic balance being disturbed.

This clinical, biological and radiological picture is very much in favor of hyperparathyroidism, the diagnosis of primary HPT seems more likely.

The patient is operated by cervicotomy Kocher tie with the discovery of a 2.5 cm nodule developed at the expense of the upper right parathyroid. The lower right parathyroid is also hypertrophied and nodular, adhering to the right lobe of the thyroid. Straight lobectomy was performed with the two right parathyroid glands after identification of the recurrent nerve. The left parathyroids are of normal appearance.

Histologically: two nodules included in totality

a. The large nodule corresponds to a parathyroid tissue seated in two territories, one central made of small cells with a small cytoplasm and a rounded nucleus without atypia and without mitosis on an endocrinoid background. On the periphery parathyroid parenchyma with clear cytoplasm is recognized around a central regular nucleus. Both ranges are separated by a discontinuous fibrous tissue.
   The capsule in place is peeled without being able to confirm its invasion after several cuts.
b. The right inferior parathyroid nodule is without abnormality.

Concluding as a parathyroid adenoma.

Postoperatively, the child reports a sudden deformity of the left leg with complete functional impotence without trauma

The clinical examination shows a left leg in external rotation.

A radio in the left leg shows a fracture of the two bones of the leg.

The patient was operated with intramedullary nailing by double approach with immobilization by a crampo-pedal plaster. The fracture consolidated and the material is removed with good evolution.

3rd case

A 13-year-old child with a personal history of several urinary tract infections (3 to 4 episodes per year), the etiological diagnosis being a bilateral vesico-ureteric reflux requiring bilateral reimplantation, as well as spontaneous bone pain, especially of the lower limbs, with no notion of trauma. This uropathy, being neglected until its appointment at the consultation, led to chronic terminal renal failure. The patient subsequently developed a 40 ° left valgus genu with total functional impotence.

Radiographically, standard radiographs show lysis of the outer end of the left clavicle, an eroded and flared appearance of the metaphyso-epiphyseal regions distal to the radius and ulna with resorption of phalangeal tussocks, and a left valgum genu with diffuse demineralization of the tibia.

Cervical ultrasound returned to a right parathyroid adenoma.

A phosphocalcic assessment is disturbed with hypocalcemia, hyperphosphoremia and a hyperreal PTH.

The diagnosis of tertiary hyperparathyroidism on chronic renal failure secondary to neglected uropathy was retained.

The patient was operated on with a transversal cervicotomy and demonstrated a right parathyroid nodule measuring 1 cm × 0.5cm with resection of this nodule by sparing the right recurrent nerve.

The postoperative course was without particularities. The patient is on hemodialysis at the rate of 3 sessions per week with substitution treatment.

Discussion

The study we conducted showed that hyperparathyroidism is infrequent in children, only about 100 cases were described in the literature while our survey allowed us to collect:

- Two cases of primary hyperparathyroidism on parathyroid adenoma.
- A case of secondary hyperparathyroidism.
- No cases of primary hyperplasia.

While the results found in the literature: 90.7% adenoma against 9.3% hyperplasia.

The shape of the big child is especially seen between 10 and 14 years. The distribution between the two sexes shows a slight female predominance (sex ratio = 0.79%) [3]. (In our study, we note the female predominance with 2 girls and a boy).

In the literature, most cases of hyperparathyroidism are white children, but there are also cases of yellow and black children. (In our study, the three cases are Caucasian)

The family history of renal lithiasis is present only in 4.76% of cases in the literature, the nature of this lithiasis is not known, but if they are of calcium origin, one can wonder about the existence of an undiagnosed HPTP or a physicochemical context favoring lithiasis, and thus of predisposing family terrain. As a result, these antecedents remain insignificant despite their presence in one of our 3 patients. The HPTP clinic is mainly attributable to the direct and indirect effects of excess PTH on the skeleton, kidney and gastrointestinal tract, as well as the consequences of hypercalcemia. It is usually an alteration of the general state with asthenia which can be physical or psychic. Anorexia responsible for severe weight loss up to cachexia, and therefore a significant delay in weight and pallor.

- The osteo-articular lesions are met with in the child in 33 to 58% [4] according to the data of literature thus one finds the following signs
- A pain syndrome. : related to a demineralization, mechanical type and most often affecting the long bones, the spine, the pelvis and the ribcage
- Deformities: varied according to the evolutionary stage of the disease [5].
- It is
  - Genu valgum which is particularly common (17% of cases).
  - Thorax in carina anomalies of the spinal axes.
  - In the spine, it is scoliosis, kyphosis or kyphoscoliosis.
- Pathological fractures: Spontaneous or caused by minimal trauma especially in the limbs or spine.
- Bone swellings: rare and must be searched systematically for the limbs, fingers, jaw, skull. They are regular of small volume, little painful.
- Renal involvement with lithiasis is currently observed in only 15 to 20% of PTNP, whereas before 1965 it was found in more than 50% of cases [6].

HPT accounts for 5 to 10% of etiologies of kidney stones. The polyurea-polydipsic syndrome due to nephrogenic diabetes insipidus associated with hypercalcemia is exceptional, as is nephrocalcinosis.

Two circumstances impose the systematic measurement of the calcemia: The discovery of a renal lithiasis and that of a beginning IR.

In the presence of renal impairment, the risk of new lithiasis or progression to IR is proportional to the degree of hypercalcemia and hypercalciuria. The reduction in the risk of lithiasis after parathyroidectomy is questioned by Mollerup [7] who shows a risk similar to that of a lithiasis disease without HPT.

In our study, the signs of discovery of the disease are bone manifestations in 2 cases and renal manifestations in one case.

Digestive signs are suggestive in 10% of cases, we distinguish

Functional signs related to hypercalcemia

Abdominal pain, usually poorly defined and not very localized, is a complaint sometimes revealing in a small percentage of patients with HPT. Abdominal examination is often normal

Nausea and vomiting associated with anorexia, are responsible for weight loss

Constipation

Organic signs

The peptic ulcer: is rarely seen in children, it is characterized by its early onset in the course of the disease and by its frequent situation in the duodenum.

Its presence must make search for a Wermer syndrome [8].

Acute or chronic pancreatitis: its pathogenesis is discussed.

Some authors think that it is secondary to a direct action of the PTH on the parenchyma.

Pancreatic, others make hypercalcemia the fundamental factor by canalicular lithiasis. Indeed, it has never been demonstrated that there is a direct relationship between HPT and pancreatitis [9].

Cardiovascular signs are mainly based on arterial hypertension found in 17% of hyperparathyroidism, it can be moderate or severe during an acute attack of hypertension that is found in 17% of cases of hypercalcemia [8].

It seems to be due either to the specific action of hypercalcemia or to renal involvement and is therefore of poor prognosis.

Subjective muscular involvement is difficult to quantify [10]. It seems to improve after para thyroidectomy [11].

It is manifested mainly by weak muscular fatigability, cramps.

Osteo-tendinous hyper-reflex can be revealed by examination (which is most often normal).

Other, rarer attacks may occur. Arterial calcification, especially of the aorta, of the visceral arteries inducing their induration, without narrowing of their caliber.

Many other organs can be affected by excess calcium and be the seat of calcium precipitation; at eye level, there are conjunctival or corneal inflammations secondary to calcification.

Ear level describes calcium precipitation in the eardrum and sometimes deafness. Calcifications can also be observed in the soft tissues.

Biologically; the phosphocalcic balance is disturbed.

Hypercalcemia greater than 2,625 mmol / l reported in 98% of cases in the literature is verified in the first 2 cases of our study.

The hypophosphoremia lower than 1.28 mmol / l reported in 99% of cases in the literature is verified in the cases of our study.

Hyper calcification is verified in the cases of our study.

Hyper-phosphaturia is very inconsistent, thus being a much less reliable sign.

Elevation of plasma levels of alkaline phosphatase is often found in HPTP, but is not specific for the disease.

Dynamic explorations (calcium perfusion test, cortisone test) can prove the autonomy of the HPTP and make the differential diagnosis with hypercalcemia of other origins. These two tests are little used in children and their results are not always convincing.

The positive diagnosis of HPTP is based on the radioimmunoassay of circulating PTH.

Radiologically, standard radiography can be specific and evocative, showing:

- Sub periosteal bone resorption, regardless of its location
- Subchondral resorption
- Diffuse or localized demineralization
- The presence of incomplete image and opaque metaphyseal bands.

Ultrasound and 99mTc-Sestamibi scintigraphy (MIBI: methoxyisobutyl-isonitrile) are the two imaging tests routinely performed in the diagnosis of localization of primary hyperparathyroidism. These examinations will guide the type of surgery used (bilateral cervical exploration, unilateral or minimally invasive surgery). Indeed, we recall that the primary hyperparathyroidism is related to the presence of a single adenoma, a diffuse hyperplasia of the parathyroid glands, a double adenoma or a parathyroid adenocarcinoma in, respectively, 88.9%, 5.74%, 4.14% and 0.74% of cases [12].

The CT scan of the thyroid gland for primary hyperparathyroidism requires 5 mm contiguous sections and iodine injection. The sensitivity is 54 to 81% according to the authors, the interpretation remaining difficult for glands weighing less than 500 mg.

MRI allows a good exploration of the basi-cervical region and the mediastinum; the detection threshold is 5 mm, and its interpretation requires a great deal of experience [13].

Therapeutically, the goal is to correct the condition of HPT by removing the pathological gland (s) that is (are) responsible (s). Only surgical treatment is curative.

Medical treatment aims at preparing the patient for surgery, and thus for the urgent management of parathyroid attacks with a serum calcium exceeding 140 mg / l. This medical treatment can be used also symptomatic HPTP in patients who refuse to be operated on or in whom surgery is an absolute contraindication. [14, 15] Patients who are not operated on should be followed every six months in the first year and then every year.

However, surgical treatment, aimed at the removal of the gland (s) responsible, is indicated in all primary hyperparathyroidism (parathyroid adenoma, primary parathyroid hyperplasia, multiple endocrine neoplasia and parathyroid intra-thyroid) and some cases of secondary hyperparathyroidism.

Parathyroid adenoma is the most common cause of sporadic HPTP in children. In the Thampson series (63 patients whose symptoms appeared in adolescence) 51 patients had an adenoma and 11 patients had hyperplasia [16]. It is always necessary to locate the 4 glands, before doing the excision of the adenoma or any enlarged gland. This excision should be completed by a biopsy of at least one parathyroid that appears macroscopically normal, with extemporaneous examination. If the removed gland has the histological features of an adenoma and the biopsied gland is normal, the performed gesture may be considered sufficient. If the biopsy of the macroscopically normal gland shows signs of hyperplasia, subtotal parathyroidectomy is recommended [8].

Primary parathyroid hyperplasia is the primary cause of neonatal HPTP.

The main problem is that of its intraoperative diagnosis because there is no clinical distinction between HPTP linked to adenoma or hyperplasia.

On the other hand, the extemporaneous histological examination is not always conclusive, and the parathyroids are not always increased in volume. In the majority of cases there are at least two large parathyroids. Treatment is therefore discussed [17].

- Exercise the only hypertrophied glands which allows the return to normo-calcemia in the majority of patients.
- If the 4 glands are hyperplastic, either a subtotal para thyroidectomy is performed leaving only half a parathyroid (having the size of a normal parathyroid), or a

total para thyroidectomy with subcutaneous heterotopic auto transplantation. a parathyroid fragment [18].

Multiple endocrine neoplasia

In NEM type 1, parathyroid glands should be operated before excision of the pancreatic tumor or sometimes during the same procedure, but the procedure will be cumbersome for the child. The recommended approach is to perform a subtotal parathyroidectomy and a cervical-accessible thymus excision due to the non-neglected frequency of accessory parathyroid glands at this level (15%). A more economical excision exposes the inescapable risk of recurrence. The risk of postoperative hypoparathyroidism seems low. An alternative to this attitude is total para thyroidectomy with auto-transplantation of parathyroid tissue, but the risk of hypoparathyroidism is higher (5-10%) [19].

In the NEM type II: Parathyroidectomy is usually performed at the same time as thyroidectomy. It must be more economical, limited to (or only) the hypertrophied gland because of the low risk of recurrence. Subtotal parathyroidectomy leads to a high rate of definitive postoperative hypoparathyroidism [19].

In the case where the parathyroid is in the intra-thyroid position, the authors propose the blind thyroid lobectomy considered as the ultimate and reasonable step of a complete cervical exploration defeated by the certain or very probable presence of an inferior parathyroid pathological and not individualizable.

Intraoperative use of ultrasound tracking can guide cervical exploration [20].

In most cases, secondary hyperparathyroidism is controlled by appropriate dietetics with a hypophosphoremic diet and medical treatment including calcium, phosphorus chelators and active metabolites of vitamin D [21]. However, the use of surgery may be necessary in case of failure of medical treatment or severe form with very high levels of serum PTH associated or not with bone deformities or pathological fractures [22].

Regarding surgical techniques; currently three techniques share the favor of surgeons in the world:

- The traditional cervicotomy under general anesthesia keeps the preference of some. It is essential in cases of secondary hyperparathyroidism and in complicated forms, not or poorly documented.
- The unilateral surgery that allows to operate one patient in two under local anesthesia, initiated by Tibblin in 1983, is valued by other centers. This technique, currently conducted as an outpatient, now seems to be favored by many teams around the world considering the leaning towards minimally invasive surgery [23].
- The videoscopic procedures, which appeared after the publications of P. Mouret and F. Dubois in 1987, were developed by several French and Italian teams [24].
- Discussed in principle at the cervical level, videosurgery, on the other hand, finds a remarkable field of application in the treatment of mediastinal forms.

In light of these data, it is concluded that traditional bilateral cervical exploration is still relevant in the surgery of familial hyperparathyroidism or secondary hyperparathyroidism. For patients with solitary adenomas, many studies agree to promote unilateral cervical approach, arguing an effectiveness identical to that of the systematic bilateral approach with fewer complications. Its legitimacy and development depend only on the increasing sensitivity of pre- and intraoperative screening results with the advent of Sestamibi double phase scintigraphy.

Based on data from the literature [25].

A strategic surgical plan can be proposed allowing, when the preoperative imaging report shows a single adenoma, to perform unilateral surgery at lower risk (Figure). However, it is important to remember that this surgical attitude requires the collaboration of a doctor pathologist trained in the extemporaneous analysis of the parathyroid glands, the collaboration of nuclear medicine specialists and ultra-sonographers experienced in the exploration of these glands, with a material performance, and of course, the perfect knowledge of this pathology by the surgeon.

Immediate postoperative monitoring is carried out with the aim of diagnosing and avoiding post-operative complications that remain rare, namely a possible hematoma of the thyroid compartment, which can progress to a compressive hematoma and require emergency evacuation.

The drains are removed on the second postoperative day

Laryngoscopy is routinely performed postoperatively to confirm good laryngeal motricity indicative of non-involvement of the recurrent nerve.

Biological monitoring involves a daily determination of serum calcium during the 3 or 4 days that will last the hospitalization and this in search of hypoparathyroidism-hypocalcemia.

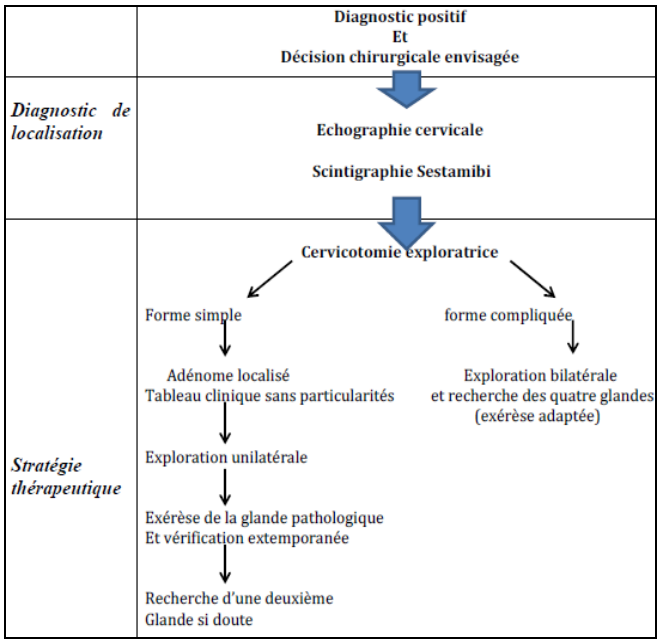

Fig 1: Therapeutic strategy for the surgical management of hyperparathyroidism

Conclusion

Hyperparathyroidism is an infrequent condition in children, often not very symptomatic and should be considered in any patient with hypercalcemia.

In clinical evaluation, multi-system manifestations of hyperparathyroidism can alter the function of the kidney, bone metabolism, digestive system, nervous system and cardiovascular system.

Diagnosis of this condition is based on serum calcium, parathyroid hormone and calciuria.

The treatment of hyperparathyroidism is surgical.

The conventional approach under general anesthesia, with exploration of all cervical parathyroid sites, has proved its effectiveness.

Recent advances in ultrasound imaging and MIBI scintigraphy currently make it possible to locate a single adenoma in the majority of cases. As a result, a "minimal" surgical strategy can be proposed, either by unilateral approach under local anesthesia or by videos copy.

Conflict of interest

All authors declare that they have no conflict of interest.

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