

Parathyroidectomy in Chronic Haemodialysis in the Nephrology and Haemodialysis Department at the University Hospital Center of Point G in Bamako, Mali

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Abstract

Introduction: Secondary hyperparathyroidism is a common complication in chronic hemodialysis patients. It is characterized by hypersecretion of parathormone by the parathyroid glands to maintain phosphocalcium homeostasis in response to hypocalcemia, lowering of 1.25 dihydroxy vitamin D3 and hyperphosphatemia. **Objective:** To analyze the results of parathyroidectomy (PTX) in cases of secondary hyperparathyroidism (HPTS), report the post-operative course and early and late complications. **Patients and Methods:** We conducted a retrospective study of ten (10) patients with chronic renal failure operated on at the CHU of Point G over a 32-month period, from January 1, 2016 to August 31, 2019. We analyzed the clinical, biological, radiological and histological parameters of the thyroid glands. **Results:** We have collected 33 cases of secondary hyperparathyroidism. Ten (10) patients met the inclusion criteria. They were 45 years old on average, seven (7) women and three (3) men, in dialysis for an average of 6.8 years before parathyroidectomy. Half of the initial kidney disease was of vascular origin (HTA). No cases of diabetic nephropathy were identified. Symptoms were in order of frequency: bone pain (60%), paresthesia (50%), functional impotence of the lower limbs (50%). Radiological signs included demineralisation (5 out of 6 cases) and brown tumour associated with a fracture (1 out of 6 cases). The most frequent indication for parathyroidectomy (100%) was persistence

despite treatment of a serum PTH concentration above 1000 pg/ml. Subtotal PTX (7/8) was performed after cervical ultrasound in all patients. Histological analysis of the parathyroid glands showed adenoma (60%) and hyperplasia in 40% of cases. The evolution was marked by a progressive reduction of the parathormone level over twelve (12) months, without achieving normalization. This could be related to sub-dialysis (generator failure with reduction of dialysis time). There were no cases of complications or mortality. **Conclusion:** Parathyroidectomy is an effective treatment to curb hypersecretion of parathyroid hormone. Despite this satisfactory result, the management of phosphocalcic abnormalities in renal failure remains an ongoing concern.

Keywords

Chronic Renal Failure, Secondary Hyperparathyroidism, Dialysis, Parathyroidectomy

1. Introduction

Secondary hyperparathyroidism is a common complication in chronic hemodialysis patients. It is characterized by hypersecretion of parathyroid hormone by the parathyroid glands to maintain phosphocalcium homeostasis in response to hypocalcemia, decreased 1.25 dihydroxyvitamin D3 and hyperphosphatemia [1] [2] [3]. Parathyroidectomy, which consists of the resection of three and a half (7/8) glands leaving a hyperplasia stump in place to prevent true permanent hypoparathyroidism [4], becomes necessary in 5% - 10% of cases when medical treatment is no longer sufficient to maintain the progressive rise in parathyroid hormone levels and the accompanying symptoms, including bone pain [5] [6] [7]. This surgery is problematic, because it requires an available, trained team as well as dialysis (anesthesia, surgery, pre and postoperative dialysis). The sequelae are marked by hypocalcemia and hypophosphatemia related to bone remineralization, as well as a predominant osteoblastosis that allows bone tissue to be reconstructed, which also explains the postoperative increase in serum alkaline phosphatase concentration [8]. For several years now, this parathyroidectomy has been performed at the UHC of Point G in Mali. The aim of the present work was to analyze the results of parathyroidectomy performed in our hemodialysis patients.

2. Patients and Methods

This was a retrospective, prospective and descriptive study of (10) chronic hemodialysis patients operated on for secondary hyperparathyroidism (HPTH) over a period from January 1, 2016 to August 31, 2019;

We have analyzed in these patients parameters:

- Socio-demographic data: age, gender, occupation, marital status, education level.
- Clinical data: session length, hemodialysis duration at the time of parathy-

roidectomy, causal nephropathy and clinical signs of HPTS (osteoarticular pain, hypertension, paresthesia, functional impotence, lower limb deformity and fractures).

- Biological data: blood levels of calcium, phosphorus, total alkaline phosphatase (TAP), vitamin D (25-(OH) D2, D3) and intact parathyroid hormone (PTHi), albuminemia, protidemia, blood count.
- Radiological data: bone demineralization, fractures, cardiovascular and valvular calcifications, parathyroid nodule or diffuse glandular hyperplasia, bone resorption (pepper-like skull, gaps, vertebral settlements, resorption of phalangeal tufts).

We also specified:

- Indications for parathyroidectomy
- The various surgical operations performed
- Local and metabolic post-operative complications and their management
- Anatomopathological study of the resected parathyroid tissue.

HPTS was defined as a blood level of PTHi greater than 585 pg/ml. Hyperphosphatemia, hypercalcaemia and increased total alkaline phosphatase are defined by blood levels of calcium phosphorus and vitamin D above the upper limit of the target levels recommended by Kidney Disease Improving Global Outcome (KDIGO 2009) (see **Table 1**) [9].

The data entry and statistical analysis was done using Word 2007 and SPSS version 20. The Chi-square test was used for the entire study, values of $p < 0.05$ were considered significant.

3. Results

We collected 33 cases of secondary hyperparathyroidism out of 123 chronic renal failure patients who underwent the assessment, *i.e.* a frequency of 26.3%. Of the 33 cases of secondary hyperthyroidism, 10 met the inclusion criteria.

The mean age of the (10) chronic hemodialysis patients operated on during the study period was 45 years (extremes 30 and 64 years) with a sex ratio of seven females to three males. The mean duration of hemodialysis at the time of the intervention was 6.8 years (extremes 3 and 10 years). The initial nephropathy was hypertensive nephropathy (5 cases), polycystic renal disease (2 cases), post-partum renal failure (2 cases) and nephropathy of undetermined cause (1 case).

Table 1. Kidney Disease Improving Global Outcome (KDIGO) recommended biological targets for phosphocalcium balance (6).

| Settings | |
|-----------------------------|--|
| Calcemia | Laboratory standards(2.1 - 2.55 mmol/l) |
| Phosphoremia | To standard (0.8 - 1.45 mmo/l) |
| Parathormone (PTH) | 2 to 9 times the upper limit (130 - 585) |
| Total alkaline phosphatases | Lab standards (40 - 129 ui/l) |
| 25 hydroxy vitamin D2 or D3 | 30 - 50 ng/l |

The clinical picture was varied, dominated by bone pain in 100%, paresthesias in 60%, myopathy (50%) and functional impotence of the lower limbs 50% (Cf. **Table 2**).

Radiological signs of diffuse bone demineralisation were observed in the majority of patients (83.33%), the association of a brown tumour and fracture (16.67%) (Cf. **Table 3**). Our study was characterized by the presence of certain lesions indicative of severe and advanced hyperparathyroidism: brown tumour (1 case), fracture (1 case) and lower limb deformity (1 case). The diagnosis was confirmed by the biology showing a disturbance of the phosphocalcic balance and an elevation of the parathormone with a mean value of 2381.6 pg/ml, 10% and 20% had respectively hypercalcemia and hypocalcemia at the time of parathyroidectomy (PTX) with a mean total calcium level of 2.184 mmol/l and 60% of the patients had a phosphorus level higher than 1.45 mmol/l (Cf. **Table 4**). All patients had cervical ultrasonography which revealed a parathyroid nodule (50%), multiple parathyroid nodules (20%), diffuse parathyroid hyperplasia associated with multi-nodular goiter (20%) and a parathyroid nodule associated with thyroid isthmus nodule (10%). Medical treatment prior to parathyroidectomy included calcium salts, non-calcium phosphorus binders, calcimimetics,

Table 2. Demographic and clinical characteristics of patients prior to surgery.

| Settings | N = 10 |
|---|----------------------|
| Age | Forty-five years old |
| Sex | 7F/3H |
| Dialysis seniority | 6.8 years |
| Dialyse \geq 6 years | 90% |
| Hypertension | 90% |
| Initial nephropathy | |
| • Vascular nephropathy | 50% |
| • Polycystosis kidney | 20% |
| • Post partum renal failure | 20% |
| • Undetermined nephropathy | 10% |
| Length of weekly session | 8 hours |
| Vascular approach | |
| • Arteriovenous fistula | 100% |
| Calcium dialysate 1.75 mmol/l | 100% |
| Joint pain | 100% |
| Paresthesia | 60% |
| Myopathy | 50% |
| Functional impotence of the lower limbs | 50% |
| Heart rhythm disorder | 40% |
| Lower limb deformity | 10% |

Table 3. Medical imaging.

| result | staff | percentage |
|---|-------|------------|
| Bone radiography bone demineralization | 5 | 83.7 |
| (N = 6) Brown tumor on fracture | 1 | 16.7 |
| Parathyroid ultrasound an isolated parathyroid nodule | 5 | 50 |
| (N = 10) Multiple parathyroid nodule | 2 | 20 |
| Diffuse hyperplasia multi-nodular goiter | 2 | 20 |
| Parathyroid nodule + thyroid nodule | 1 | 10 |
| Anatomical Pathology Hyperplasia | 4 | 40 |
| Adenome | 6 | 60 |

Table 4. Pre-surgical biological data.

| N° | PTH (130 - 585 pg/ml) | Vitamin D 30 - 50 ng/ml | Phosphoremia 0.85 - 1.45 mmol/ | Calcemia 2.1 - 2.55 mmol/l |
|---------|--------------------------|----------------------------|-----------------------------------|-------------------------------|
| 1 | 3250.12 | 35.35 | 3 | 2.61 |
| 2 | 1793 | 33.26 | 2.28 | 2.46 |
| 3 | 2020 | 37.2 | 1.3 | 2.25 |
| 4 | 1257 | 54.04 | 1.09 | 2.29 |
| 5 | 3351 | 37.78 | 1.63 | 2.31 |
| 6 | 3325 | 28.94 | 3.15 | 2.36 |
| 7 | 1984 | 28.31 | 1.24 | 2.19 |
| 8 | 1264 | 46.12 | 3.03 | 2.18 |
| 9 | 2269 | 46.18 | 2.10 | 1.28 |
| 10 | 3303 | 33.30 | 1.36 | 1.91 |
| Average | 2368.61 | | | |

biphosphate and vitamin D derivatives. The annual incidence of parathyroidectomy in our study was 2.5 cases/year. The most common indication for parathyroidectomy was persistent serum PTH concentration greater than 10 times the upper KDIGO standard and an abnormal thyroid gland on cervical ultrasound.

Parathyroidectomy was indicated in these ten (10) patients due to failure of medical treatment. The planned surgical procedure in all patients was a subtotal 7/8 parathyroidectomy. An anatomopathological study of these glands revealed a hyperplasia of the parathyroid cells in 40% of the cases, and a parathyroid adenoma in 60% of the cases. Among the ten (10) patients operated on, four underwent procedures associated with parathyroidectomy:

- Two patients have had subtotal thyroidectomies
- A patient with a left isthmolobectomy
- A removal of the ectopic glands.

The biological evolution of the post-operative parameters (Cf. **Table 5**), was marked in the immediate aftermath by the occurrence of hypocalcemia in 5 patients, *i.e.* 50% with an average serum calcium level of 1.92 mmol/l (Cf. **Table 6**).

Table 5. Evolution of biological parameters after parathyroidectomy (PTX).

| Patient no. | PTH before intervention | 1 month | 6 months | 9 months | 12 months |
|-------------|-------------------------|---------|----------|----------|-----------|
| 1 | 3250.12 | 986.10 | 739.30 | NF | 621.20 |
| 2 | 1793 | NF | 753.4 | 714.5 | 821.90 |
| 3 | 2020 | 1300 | 1009 | 970 | 700 |
| 4 | 1257 | NF | 876 | 740 | 802 |
| 5 | 3351 | NF | NF | 768.10 | 1666 |
| 6 | 3325 | 2504 | 2673 | NF | NF |
| 7 | 1984 | NF | NF | NF | NF |
| 8 | 1264 | 300 | 102.6 | NF | 698.40 |
| 9 | 2269 | NF | 1711 | 1675 | 698.40 |
| 10 | 3303 | 2370 | 2327 | NF | 698.40 |
| AVERAGE | 2381.612 | 1492.02 | 1273.912 | 1256.766 | 775.78 |

NF = not done.

Table 6. Calcaemia before and after surgery.

| No. Patients | Pre-operative blood glucose | Post-Operative Calcaemia |
|--------------|-----------------------------|--------------------------|
| 1 | 2.61 | 1.7 |
| 2 | 2.46 | 2.2 |
| 3 | 2.25 | 2.5 |
| 4 | 2.29 | 1 |
| 5 | 2.31 | 2.2 |
| 6 | 2.36 | 2.3 |
| 7 | 2.19 | 2.1 |
| 8 | 2.18 | 1.4 |
| 9 | 1.28 | 1.9 |
| 10 | 1.93 | 1.9 |
| Average | 2.184 | 1.92 |

One out of five patients who underwent a PTH control had a normal level at the time of surgery. Twelve months after the parathyroidectomy, the PTH level was more than nine (9) times the upper norm, *i.e.* 585 pg/ml in all patients who underwent control. The mean PTH level at 12 months after surgery was 775.78 pg/ml (>9 times the upper norm).

4. Discussion

HPTS is a common complication of chronic kidney failure. It is characterized by excessive parathyroid hormone synthesis and secretion, hyperplasia of the parathyroid glands, and abnormalities of phosphocalcic metabolism with bone and visceral involvement. [10] [11]. Treatment of HPTH should be primarily pre-

ventive by restricting phosphate-rich dietary intake, the use of phosphorus binders, native vitamin D and active vitamin D derivatives [12] [13]. In Mali new phosphorus binders such as sevelamer, lanthanum carbonate and nicotina-mide are not available. The control of HPTS is one of the main targets in the management of chronic hemodialysis patients because it is responsible for cardiovascular mortality and impaired quality of life [14] [15]. The incidence of severe HPTS in Mali could be reduced with therapeutic means provided it is managed early and detected by more frequent PTH testing in the IRC. The management of this complication relies on slowing down the hypersecretion of parathyroid hormone by medication and dialysis agents. This treatment available to us is expensive, and the bioassay is not widely available, expensive and unreliable in our context. Parathyroidectomy is performed on 1% - 2% of dialysis patients each year [16]. The incidence of parathyroidectomy increases from 0.3% if the duration of dialysis was less than five years to 3% if the duration was more than ten years. None of our patients have a hemodialysis duration of more than 10 years. The average duration of hemodialysis is 6.8 years with extremes of 3 and 10 years [17]. The annual incidence of parathyroidectomy is 2.5 cases per year in our study. The average age of our patients operated on for PTX is 45 years (extremes 30 and 64 years). This is consistent with the results in the literature. Indeed, the average age of patients treated surgically for HPTS varies between 40 and 50 years of age depending on the series [17] [18]. This can be explained by the fact that surgical treatment is avoided in the elderly because of the risk of anesthetic [17] [18]. No cases of diabetic nephropathy were identified in our study. This is consistent with the results in the literature. Indeed, it has been found that non-diabetic nephropathy is more associated with secondary HPTS [17] [19].

The most common indication for parathyroidectomy in the literature was the persistence of serum PTH levels greater than 800 g/mL after several weeks of treatment with calcitriol or an analogue associated with hypercalcemia and/or hyperphosphatemia [12] [20]. This was the most common incidence and all patients operated on had a PTH greater than 1000 pg/ml (mean 2381.6 pg/ml) of which 40% had a PTH greater than 3000 pg/ml. When the clinical-biological diagnosis is established, it is necessary to confirm that the parathyroid glands are enlarged or hyperplasia. The first-line morphological examination is the ultrasound examination of the parathyroid glands, which was pathological in all our patients. The surgery allowed a progressive reduction of the average PTH level over the 12 months of monitoring without achieving normalization. This slow normalization is due to patients under dialysis due to generator failure but also to inadequate dialysis. The rate of normalization of PTH varies from study to study [21] [22]. In our series no re-intervention was performed, although the indication was often for persistent hyperparathyroidism.

Limitations of the study: small sample size due to the low socio-economic standard of living of some patients, limiting the performance of certain complementary tests (serum calcium, phosphorus, vitamin D, bone imagery) because

of their high cost.

5. Conclusion

Surgical parathyroidectomy is an effective treatment to curb hypersecretion of parathyroid hormone with fairly satisfactory clinical, biological and radiological results. However, this technique must be carried out carefully with a bilateral exploration that allows a precise evaluation of the four glands to prevent possible persistence or recurrence of hyperparathyroidism. Despite these satisfactory results, the management of phosphocalcic anomalies in chronic renal failure remains essential.

Conflicts of Interest

The authors declare that they have no conflicts of interest in relation to this article.

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