

Primary Hyperparathyroidism in Algerian Population: About 38 Cases

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Abstract: Primary hyperparathyroidism (PHPT) is a disease whose incidence has increased considerably. The systematic and automated assay of serum calcium since the 70's has allowed a major evolution of the clinical picture of classical form with asymptomatic forms which represent 80% of cases diagnosed in industrialized countries. In poor countries, primary HPT continues to be diagnosed at the stage of complications. 38 cases of PHPT were recorded in 18 years with an average incidence of two cases per year. The average age of patients was 50.7 years (16 -75 years). 68% were aged over 46 years and 82% were female with a sex ratio (female / male sex ratio 4.4). The classic form involving bone and kidney complications, is present in 40%. Bone symptoms are predominant, it is found in over 80% of cases. Nephrolithiasis is found in 26.3%. The asymptomatic form was seen in less than 6% of patients. Cervical ultrasound showed a parathyroid adenoma in 90%. It is characteristic and located in the lower poles in all cases. A parathyroid hyperplasia was mentioned in other patients. The MIBI parathyroid scintigraphy performed in 60% confirmed the ultrasound findings in all the cases. The PHPT was sporadic in 81.6% and familial in 18.4%. The treatment was surgical in all patients. It consisted of the removal of the parathyroid by conventional surgery. The postoperative evolution was marked by hypocalcemia (90%) and tetany (20%). In 4 cases, failure of surgery was observed requiring further surgery. In these cases, it was hyperplasia (n: 3) and multiple adenomas (n: 1)

Keywords: Primary hyperparathyroidism, hypercalcemia, PTH, sporadic, genetics

I. Introduction

Primary hyperparathyroidism (HPT) is a common disease. Its incidence is estimated at 27 new cases per 100,000 people and its prevalence is about 1 in 1000.¹ It is twice more common in women than in men and occurs at any age with increased frequency after fifties.² The clinical presentation is highly polymorphic. The systematic and automated assay of serum calcium since the 70's has allowed a major evolution of the clinical picture of classical form with asymptomatic forms which represent 80% of cases diagnosed in industrialized countries.³ In poor countries, primary HPT continues to be diagnosed at the stage of complications. The objective of this study was to report the frequency of HPT and its diagnostic and therapeutic characteristics.

II. Population, Methodology

This is a retrospective descriptive and analytical study referred over a period from 1st January 1996 to 31st December 2014. The study population consisted of patients followed for primary HPT. The diagnosis was made on clinical osseous, renal, neuromuscular symptoms. To confirm the diagnosis, bioassays were performed (Serum Calcium, parathormone assay) and radiological examination (parathyroid ultrasound and sometimes scintigraphy of the Parathyroid). Serum calcium was considered high when it was greater than 105mg / l, parathyroid hormone was pathological for a high concentration, or "high normal" in presence of hypercalcemia. Exclusion criteria were secondary hyperparathyroidism, bone pain and fractures of other origins. After conducting an assessment of visceral impact of hypercalcemia, a therapeutic decision (medical or surgical) was indicated. Patients were re-evaluated and monitored after treatment.

Statistically, after entering the data into the software SSPS / PC Epi Info, comparisons were performed with the Pearson Chi squared test. A difference was considered significant when P <0.05.

III. Results

38 cases of PHPT were recorded in 18 years with an average incidence of two cases per year. The average age of patients was 50.7 years (16 -75 years). Two thirds of them (68%) were aged over 46 years and 82% were female with a sex ratio (female / male) of 4.4. The classic form of PHPT, involving bone and kidney complications, was present in almost half of cases (40%). Bone symptoms are predominant, it is found in over 80% of cases (Table I). Nephrolithiasis is found in nearly a third (26.3%). The asymptomatic form concerned less than 6% of patients.

Table I: spécifique clinical signs of PHPT in our patients		
Clinic	Number (n=38)	%
Bone manifestations		
- Bone pain	36	94,7
- Arthralgia	30	78,9
- Pathological fractures	10	26,3
Renal manifestations		
- Nephrolithiasis	10	26,3
- Polyuropolydypsique syndrome	15	39,5
- Nephrocalcinosis	2	5,3
Other manifestations		
- Digestive	5	13,2
- Neuropsychic	8	21,05

On the paraclinical level, the laboratory tests confirmed the diagnosis of PHPT in the majority of cases (80%) (Table II). Hypercalcemia is the most common sign with an average value of 115,4 mg / l (105-145) and a mean PTH was 82.2 mg / l (60-146). In 3 cases, a malignant hypercalcemia was observed

Table II: Biological Results

Biological test	Number of cases	Percentage (%)
Calcemia :		
- Hypercalcemia	30	78,9
- normal calcemia	8	21,05
Phosphoremia :		
- Hypophosphoremia	30	78,9
- normal Phosphoremia	8	21,05
Calciuria :		
- hypercalciuria	10	26,3
High PTH1-84	38	100
Elevated alkaline phosphatase	35	92,1

Cervical ultrasound showed a parathyroid adenoma in 90% of cases. It is characteristic and located in the lower poles in all cases. A parathyroid hyperplasia was mentioned in other patients. The MIBI parathyroid scintigraphy performed in 60% of cases confirmed the ultrasound findings in all the cases.

The PHPT was sporadic in 81.6% and familial in 18.4 % occurring in the course of a type 2 NEM (7 cases), type 1 NEM (1 case) and coexisting with a tumor Jaw syndrome in a case. In these genetic forms, the average age at diagnosis is 38 years (32-43).

The treatment was surgical in all patients. It consisted of the removal of the parathyroid by conventional surgery. The postoperative evolution was marked by hypocalcemia (90%) and tetany (20%). In 4 cases (10.5%), failure to surgery was observed requiring further surgery. In these cases, it was hyperplasia (n: 3)

and multiple adenomas (n: 1). Exploration during surgery of all parathyroid glands was not performed. The parathyroid adenoma was the predominant histopathological lesions (84.2%). Parathyroid carcinoma was observed in one case (Table III).

Table III: Results of the histological study

Histological results	Number of cases	Percentage (%)
Adenoma	32	84,2
Multiple adenomas	1	2,6
Hyperplasia	1	2,6
Adenoma + hyperplasia	1	2,6
Carcinoma	1	2,6

IV. Discussion

Due to systematic determination of serum calcium, the clinical presentation of PHPT has totally changed in recent decades. Conventional symptomatic forms have become rare and are only present in less of 20% of patients. Bone signs that were present in 23% of cases before 1965 are no more than 2% after 1986. Similarly, the incidence of kidney stones, which was 57% before 1965 rose to less than 20% after 1986.^{4,5,6} Currently over than 80% of patients are asymptomatics or paucisymptomatics at diagnosis.⁷

But contrary to what is observed in developed countries, PHPT continues to be diagnosed in its classical form in our country. Bone and kidney complications are found too significantly and make all the severity of this condition. They are explained by the ignorance of the disease and the delay of diagnosis. It has always been, and still based on the finding of hypercalcemia.

In the beginning stages, there may be a time of hyper alternating with normal serum calcium: these transient biological fluctuations may persist for months or years and should evoke the existence of "normo - calcémiques hyperparathyroidism".⁸ Also it should be noted that, a vitamin D deficiency, may mask hypercalcemia.⁹ Its research must be systematic in these cases but the retrospective nature of this study did not allow us to do it. However the high frequency of vit D deficiency currently found in our country could make it a systematic test.

Current immunometric assays can measure PTH (1-84) or its biologically active fragments. With the exactitude of these assays, it is possible to find any coexistence of hypercalcemia and minor high or even inappropriate value ("abnormally normal") of the PTH induced biological diagnosis of PHPT¹⁰ Radiologically, all the techniques currently used have the advantage of being non- invasive. They aim to demonstrate a parathyroid adenoma, with the only purpose is to guide the surgical procedure. The most commonly used and most efficient are ultrasound (60 to 80% detection) and Sesta MIBI scintigraphy (85% detection), with almost 100% in value localization of the adenoma when the both are concordant in the presence of a biological diagnosis. However, in no case the imaging results should not interfere in the positive diagnosis of HPT, which remains a biological diagnosis. A positive imagery should not influence a biologically contentious diagnosis; also a negative imaging should not question a certain biological diagnosis. The current pre-surgical imaging is a method of location and should remain so.¹¹

Preoperative exploration by the present imaging methods is essential if considering a minimally invasive lateralized surgical approach. In this case it is preferable to have two concordant pictures of adenoma. Conversely, if the diagnosis of PHPT imposes an exploration of all parathyroid (eg in case of multiple endocrine neoplasia) or if the surgical team prefers conventional surgery as was the case in our study, preoperative imaging does not appear necessary for first surgery.^{11,12} In the absence of recovery after the first cervicotomy (4 cases in our series), all imaging means must be implemented to try to locate the remaining pathological glands in normal or ectopic position.¹³

Isolated PHPT represents 98% of PHPT, whether a single adenoma (96%), multiple adenomas (2 adenomas in 2% of cases, exceptionally 3 or 4), or of rare cancers parathyroid (less than 1%) manifested by an array of malignant hypercalcemia.¹⁴

In 1% of cases, PHPT are part of a NEM1 where it's présent in over 95% of cases, of which it is the first event in about two thirds of cases.¹⁵ Other achievements of MEN1 are primarily pancreatic endocrine tumors and pituitary adenomas, which must be systematically sought. The MEN1 are due to mutations in the *menin* gene. In 1% of cases PHPT is part of a MEN2A, where the PHPT is present in 25-50% of cases.¹⁶ The

MEN2A is characterized by the successive development of medullary thyroid cancer (first attack in the natural history of the disease, diagnosed by calcitonin dosage), with a multiglandular PHPT and a bilateral pheochromocytoma. The MEN2A are caused by activating mutations of the RET proto-oncogene.¹⁷ The PHPT-Jaw Syndrome (PHPT associated with fibrous bone tumor of the mandible) is due to a mutation in the HRPT2 gene.¹⁸

Unlike sporadic PHPT that preferentially occur in individuals over 60 years, genetically determined PHPT occur in a younger population. It should be checked in any PHPT occurring before the age of 40 years.²

V. Conclusion

PHPT is common condition which is important to recognize. The delay in diagnosis is a serious cause for concern in our country. Early and effective diagnosis is based on the systematic determination of serum calcium in every subject with suggestive symptoms and especially in postmenopausal women.

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