

RESEARCH ARTICLE

THE PARATHYROID ADENOMAS CLINICAL AND THERAPEUTIC STUDY.

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Manuscript Info

Abstract

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Manuscript History

Received: 11 September 2017 Final Accepted: 13 October 2017 Published: November 2017

Key words:-

Parathyroid adenomas, ultrasound, surgery, biology.

..... The purpose of our study was the evaluation of epidemiological profile, the diagnosis, the therapeutic management and post-operative complications for patients suffering from parathyroid adenomas. This work is based on a retrspective study. Its purpose is to discuss the results found of 26 patients operated for parathyroid adenoma at the department of visceral surgery at the Ibn Rochd University hospital of Casablanca, during a period of 07 years, from January 2010 to December 2016, based on the data collected from the clinical files of the patients. The average age of our patients was 53 with a female predominance. The circumstances of discovery for disease were various: like the etiological assessment of a bone tumor and the fortuitous discovery at the time of a cervical surgery. The clinical signs of hypocalcemia were found among 61,54% of patients (asthenia, vomiting, polyuriapolydipsia syndrome, headache, and weight loss), while bone signs were found in 19,23% of patient and renal events were found in 7,69% of patient either. The value of blood-calcium among our patients was between 94 and 176mg /l with an average of 121,81 mg /l. All of our patients presented high levels of parathormone with an average to 115,06 pg/ml and extremes with 94 and 2897 pg/ml. The ultrasound revealed the parathyoid adenoma in 84,62% cases while i twas not decisive in 15,38% cases. On the other hand, the scintigraphy was decisive for all the patients having benefited from this examination. All our patients benefited from a parathyroidectomy of pathological gland. Extemporaneous examination revealed an appearance of parathyroid adenoma in 65.38% of cases, and parathyroid hyperplasia in 34.62% of cases. Nevertheless, conventional pathological examination revealed a parathyroid adenoma in all of our patients. Two of our patients developed a transitory hypocalcemia. The evolution was marked by a normalization of the bloos-calcium of all our patients.

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Introduction:-

Primary parathyroid pathology is represented by four types of glandular lesions: isolated adenoma (87% of cases), hyperplasia (9% of cases), multiple adenomas (3% of cases), and carcinomas 1% of cases). Primary hyperparathyroidism is defined by an inadequate increase in parathyroid hormone secretion (PTH) relative to serum calcium associated with an increase in the number and function of parathyroid cells and results in a disruption of the regulation mechanisms of serum calcium (1). Parathyroid adenoma is generally fortuitous in that it is mostly asymptomatic (1) but can be revealed by osteo-articular affections such as fibrocystic osteitis (3), renal lithiasis or even salivary lithiasis (4) or symptomatic or malignant hypercalcemia (5). Isolated adenoma is the most common glandular lesion found in HPTP and is responsible for hyperparathormaemia in 90% of cases (1). Its treatment is surgical and is not the subject of a consensus. Surgical success is directly related to the number of diseased pathological glands. 2 we shall not deal here with the question of the surgical indication before hyperparathyroidism, but that of its management as soon as an operative indication is retained.

Observation:-

This is a retrospective study spread over 7 years; from January 2010 to December 2016, covering 26 patients in the department of visceral surgery Wing 3 of the CHU Ibn Rochd of Casablanca for parathyroid adenoma. In our series we observe a clear female predominance of 69.24%. The mean age was 53 years with extremes ranging from 19 to 77 years.13 cases were hypertensive, ie 50%, 5 cases were diabetic, 19.23%, 9 cases of nephropathy, 34.61%, 3 cases of cardiac disease or 11.54%. In addition, the surgical history found the mandibular tumor and the varus equin in 1 case or 3.83%, the notion of chronic smoking was found in 5 patients. As for the circumstances of discovery, the signs of hypercalcaemia are the most frequently discovered mode (61.54%), followed by bone lesions (20% of cases). The predominant clinical manifestations are asthenia in 76.92%, headache in 46.15%, and anorexia in 30.77%. In our series, renal insufficiency was observed in 26.92% of patients, while lithiasis was observed in 15.38% of patients, bone pain in 42.30% of patients, arthralgia in 30, 77%, on the other hand, of the digestive manifestations represented by the abdominal pains were observed in 5 of our patients, that is to say 19,23%. The serum calcium varies between 94 and 176 mg / l with an average of 121.81 mg / l. Hypocalcaemia was found in 22 patients (84.62%). All of our patients had hyperparathormaemia with an average of 1115.06 pg / ml and extremes ranging from 92 to 2897 pg / ml, 11 patients were doused with phosphate. It was found to be low in 9 patients, whereas it was normal in 2 patients, a deficiency of vitamin D was found in 5 patients. An increase in TSH was observed in 2 patients, the rest of the patients in our series were euthyroid. All our patients underwent a cervical ultrasound, which showed a single parathyroid image in 12 cases (46,15%), a double parathyroid image in 10 cases (38.46%), a triple parathyroid image in 1 case 3.84%), whereas it was inconclusive in 4 cases (15.38%). In addition, thyroid nodules were individualized in 7 patients (26.92%). 3 of our patients underwent subtraction scintigraphy using 2 isotopes 99mTc-sestamibi and 123I. 4 of our patients (15.38%) benefited from ultrasound-guided cytopnesis, which returned benign in 3 patients, whereas it was inconclusive in 1 patient. 4 cases received CT. In our series, 1 patient received a thoracic radiograph demonstrating thoracic deformation with demineralization. 9 patients underwent rehydration to correct preoperative hypercalcemia (34.61%), 4 patients were treated with diuretics (15.38%), 4 patients were treated with HSHC (15.38%), a hemodialysis was performed in the patient (3.84%). All our patients were resected by adenomatous formations found during surgical exploration. Associated total thyroidectomy was performed in 4 patients. Associated loboisthmectomy was performed in 2 patients. A second time totalization was performed in 1 patient. Extemporaneous examination revealed an aspect of parathyroid adenoma in 17 patients (65.38%), and parathyroid hyperplasia in 9 patients (34.62%). The anatomopathological study has demonstrated parathyroid adenomas in all our patients, whose cell type was not specified on the anatomopathological report. In addition, thyroid heteronodular dystrophy was found in 4 patients and a papillary thyroid carcinoma of the vesicular variant in 3 patients. In our series the mortality was zero, transient hypocalcaemia was found in 8 patients (30.77%).

Discussion:-

The prevalence of parathyroid adenoma in the general population is estimated at 1 to 7 cases per 1,000 persons (14). The prevalence of this disease reaches 21/1000 people in women aged 55 to 75 years. The average age at diagnosis is in the sixth decade in North America and Europe (9, 15, 16,17). According to a study conducted by the team of the Mayo Clinic in Rochester during the period from 1965 to 2001 showed a significant increase in the incidence of parathyroid adenoma which quadrupled practically between the period 1965-1974 and the period 1974- 1982, where it rose from 15.8 per 100,000 population-year to a peak of 82.5 per 100,000 population-year, and then decreased with a change to an incidence of about 29.1 per 100,000 inhabitants year during the period 1983-1992, and

stabilization during the period 1993-2001 with an incidence of 21.3 per 100000 inhabitants-year (9,17). Suggestions for an explanation of the peak incidence of this disease during the period 1974-1982 were proposed such as the widespread use of therapeutic irradiation for the head and neck in childhood during the years 1930-1940 for for benign reasons, as well as for Japanese survivors of atomic explosions (7, 17). The parathyroid adenoma is singular by its clinical polymorphism without specification of symptoms (6) the common symptoms are: asthenia, constipation, polydipsy polyuria and bone pain (18, 9). Calcium lithiasis is a classic manifestation of this disease. It is actually much less frequent than initially appreciated, since the prevalence of lithiasis does not exceed 20%. The calculations are generally of oxalocalcic or phosphocalcic nature (9, 10, 18, 19). Nephrocalcinosis is only 7% and results from the renal parenchyma deposition of the calcium phosphate complex (9, 18). The occurrence of renal insufficiency during parathyroid adenomas is explained by nephrocalcinosis (9, 10). In our series the history of renal lithiasis was found in 15,38% of the cases, as for renal insufficiency was found in 26.92%, in these patients, renal insufficiency precedes parathyroid involvement, so the occurrence of parathyroid adenomas in these patients is rather in the context of tertiary hyperparathyroidism (HPTT). That is to say the importance of the delays of diagnosis in the renal insufficiency. In addition, none of our patients had nephrocalcinosis. In the majority of cases, the effects on the bone of the prolonged excess of PTH are less visible and relate mainly to the cortical bone (11, 20), the predominant attack on the cortical bone with respect to the bone especially at the proximal third of the radius, and to a lesser degree from the upper end of the femur. The lumbar spine is attained more rarely. Clinically, it may be asymptomatic or give localized or diffuse bone pain 62% (18, 19, 21, 22). Fibrocystic osteitis with clinical signs was a classical complication of primary hyperparathyroidism, nowadays it has become exceptional (3, 18, 20, 23, 24, 25). The occurrence of pathological fractures in known patients with hyperparathyroidism is found in 1.5% of patients (10, 26). Brown tumors are benign osteolytic lesions with giant cells related to the action of PTH on bone tissue (27). Maxillo-mandibular brown tumors are found only in 4.5% of cases, and can be responsible for facial deformities, falls or dental mobility (28). They preferentially touch the ribs, the clavicles, the pelvic girdle. These tumors can be isolated or multiple (27, 28). Chondrocalcinosis is a microcrystalline disease, secondary to the deposition of crystals of calcium pyrophosphates in the cartilages at the joints, resulting in calcifications (29,30). Parathyroid adenoma is the most common cause of chondrocalcinosis, and accounts for 5-6% (29). Other osteoarticular manifestations. enteropathies and tendinopathies, arthropathies (31). Among the digestive manifestations, peptic ulcer, pancreatitis, abdominal pain (9, 10,18). On the other hand, none of our patients reported any digestive symptoms. HTA is the major cardiovascular complication and is found in 50% of cases (9, 10, 18). In our series, hypertension was found in 50%, while palpitations were reported in 11, 54%. The diagnosis of primary hyperparathyroidism is biological. It is defined by the elevated hypercalcemia-PTH plasma association, or in discordance with serum calcium (9, 32, 39). The total calcemia may be normal in 5 to 22% according to the literature series. However, ionized calcium (Ca I) is practically constantly increased (98%) (11,19). In our series, all patients underwent an initial serum calcium dosage range of 94 to 176 mg / l with an average of 121.81 mg / l. 22 patients (84.62%) had hypercalcemia whereas 04 patients (15.38%) were normocalcemic. As a result, our data approximate those of the literature. Diagnosis is easy when hypercalcemia is associated with an elevated level of intact PTH. However, in 10 to 20% depending on the series, the intact PTH level is within the norm. In our series, the PTH assay was performed for all of our patients, and they all showed hyperparathormaemia with an average of 1115.06 pg / ml and extremes ranging from 92 to 2897 pg / ml, closer to the literature. Hypophosphatemia is present in 30% to 40% of patients with decreased tubular resorption (18). In our series, 11 patients received a phosphate dosage. It was found to be low in 09 patients, whereas it was normal in 02 patients. Urinary excretion of calcium is elevated in 30-44% of patients, especially in lithiasis (18). In our series, none of our patients received a calciuria assay. The imaging before the surgical gesture aims at the preoperative localization of a parathyroid adenoma, to perform a targeted surgery and to reduce the operative time. It also allows the identification of ectopic adenomas and preoperative detection of other cervical pathologies (33). In addition to the well known advantages of low cost and safety, ultrasound remains the first-line examination, with a sensitivity of 65% to 80% according to the authors and a specificity of 90 to 95%. The proportion of single-glandular involvement is 93.2%, while multi-glandular involvement is 6.8% (8, 33). In our series, all patients underwent a cervical ultrasound which showed a single parathyroid image in 46.15%, a double parathyroid image in 38.46%, a triple parathyroid image in 3.84% it was inconclusive in 15.38%. This means that there is a significant disparity compared to the data in the literature. In addition, thyroid nodules were objectified in 26.92% of the cases. 99mTc-sestamibi scintigraphy has been established as the preferred method of imaging, especially since it gives superior results to other techniques such as ultrasound, CT, MRI, angiography (8, 9, 11, 32, 33, 37, 38). Comparisons of the different methods, double-phase and subtraction, with the various acquisitions show that, whatever the type of acquisition, planar scintigraphy, TEMP and TEMP / TDM, the subtraction method is significantly superior to the image in dual phase and the sensitivity is greater in double isotope TEMP / TDM than in simple isotope (8, 33, 40). In our series, three patients

underwent a technical subtraction scintigraphy using 2 isotopes (99mTc-sestamibi and 123I), the results of which were in favor of a single parathyroid adenoma in two cases and double adenoma in one case. The combination of ultrasound and scintigraphy makes it possible to answer in many cases the preoperative localization of parathyroid adenomas with a positive predictive value close to 100% when the results of both techniques are concordant. These are therefore the examinations of choice in this indication (32,34). In our series, this was the case for three patients (11.54%). The cytopunction may also be of therapeutic interest, as is the case with the cytotoxic escapement of the parathyroid cyst. Nevertheless, few cases described in the literature. In our series, 04 patients (15.38%) benefited from an ultrasound-guided parathyroid cytopunction that returned benign in 03 cases, while it was inconclusive in 01 patients. The indication of CT remains essentially in the case of a discrepancy between the cervical ultrasonography and the sestamibi scintigraphy (8, 33, 35). CT may also be useful for the detection of complications of parathyroid adenomas such as brown tumors and renal lithiasis calcium. In our series, four of our patients (15.38%) benefited from a CT that objectified the parathyroid adenoma in all the cases. MRI is the classically indicated morphological imagery for ectopic parathyroid adenomas that escape cervical ultrasound. It remains superior to the scanner, which is relatively inefficient because of the artifacts, due in particular to the shoulders (36). The typical parathyroid adenoma is in hyposignal T1, hypersignal T2 and frank hypersignal after injection of gadolinium chelates. However, atypical adenomas have been described due to haemorrhagic or fibrous rearrangements (8, 33). The sensitivity of MRI is 4-88%, which increases when combined with sestamibi scintigraphy (8, 33). Basic treatment according to the recommendations of the NIH and the SFE, in case of surgical abstention certain principles must be respected (42, 43):

- 1. Drinks must be plentiful.
- 2. The use of medicinal products liable to cause hypercalcemia (thiazide diuretics, supra-physiological doses of vitamin D, lithium) should be avoided.
- 3. Avoid immobilization, and monitoring of serum calcium in case of prolonged immobilisation is necessary.
- 4. Dietary calcium intake should be normal (1000 mg / day on average).
- 5. In the case of vitamin D deficiency: Supplementation with low doses of vitamin D2 or D3 ergo or cholecalciferol is recommended (400 IU / d).
- 6. In case of bone damage, if surgery is not possible, medical treatment should be considered (17, 18, 41, 42, 43, 44).

Rehydration is carried out by isotonic saline serum, the flow rate of which is adapted to hemodynamic conditions. It compensates for extracellular dehydration which in itself aggravates hypercalcemia (32). In our series, 34.61% of patients have benefited from rehydration to correct pre-operative hypercalcemia. Alendronate was tested against placebo in 44 patients in a randomized, 2-year study with cross-over at 1 year for placebo-treated patients. It showed efficacy on bone mineral density at the lumbar and femoral levels, but it was ineffective at the radial level. A metaanalysis of 40 studies showed a similar effect of bisphosphonates and surgery on BMD (9, 12, 18, 32, 44). In our series, no patient was treated with biphosphonates. Diuretics of the loop are classically recommended but are controversial. According to the literature, they may normalize serum calcium in 35.89% but are not innocuous (Some cases of hyposphatemic hypernatremic comas as well as hypomagnesemias with alertness and tetany have been reported) (9.12.44). In our series, 15.38% of our patients were treated with diuretics without any complications. Hemodialysis with a calcium deficient bath is very effective, but the rise in serum calcium is very rapid at the end of the session. It is used in extreme cases such as oligo-anuric kidney failure or even advanced heart failure (12). In our series, hemodialysis was performed in a single patient (3.84%). This led to a decrease in serum calcium of 38.4%. The recommendations are in favor of correcting vitamin D deficiency in patients with parathyroid adenoma, but there are no studies with a high level of evidence to support this attitude (12). In our series, five of our patients (19.23%) received vitamin D treatment. Surgery remains the treatment of choice; it is always indicated in case of symptomatic parathyroid adenoma and in the absence of contraindication to surgery. The injection of ethanol into a tumor causes its necrosis. Alcohol control of parathyroid adenoma under ultrasound control in patients at high surgical risk or with a contraindication to surgical treatment (44, 45, 46). The endovascular ablation of a parathyroid adenoma hardly accessible to surgery was described in the years 1970-1980, especially by French and especially American teams with satisfactory results in the long term. Currently, the development of catheterization equipment, image acquisition, and embolization equipment make it easier and more reliable, with less risk. The arteriography thus makes it possible to demonstrate the nutritional pedicles of the adenoma, not always visible on the scanner and to perform the embolization (47). The risks are those of an arterial puncture, and the embolic risks during catheterization and during the embolization, which are however exceptional. Radiological efficacy control is immediate, and clinico-biological is very early (47). In our series, none of our patients received treatment with parathyroid adenoma by alcoholization or by embolization of the adenoma. Histologically, the differential diagnosis

is with hyperplasia (8). The main cell parathyroid adenoma is the predominant cell type. At the time of extemporaneous examination, the differential diagnosis occurs with hyperplasia (8). On the macroscopic level, the four glands are diffuse in volume, in the majority of the hyperplasia, whereas the adenoma appears as a tumor formation only one gland. In practice, borders are not always as clear (8). Microscopically, the persistence of a thin crown of parathyroid tissue, the absence of adipose tissue and the possible presence of anisocytosis, anysocaryosis, mitosis and atypia, sign the adenoma. However, these diagnostic arguments may be lacking when the extemporaneous examination is not on the entire gland but on a fragment; the normal parenchyma may then be missed and the diagnosis of hyperplasia may be mistaken. In the extemporaneous examination, if we have only a biopsy of the gland, the histological discovery of a very limited nodule may impose it on an adenoma; it is the finding of hyperplasia within the other glands, systematically biopsied, that rectifies the diagnosis (8). The main cell adenoma is the most frequently found type. In 5 to 10% of cases, the adenoma is oncocytic, consisting exclusively of oxyphilic cells, whereas the adenomas with clear cells are exceptional (8). In our series, extemporaneous examination revealed an aspect of parathyroid adenoma in 17 patients (65.38%), and parathyroid hyperplasia in 9 patients (34.62%). Nevertheless, the anatomopathological study revealed an aspect of parathyroid adenoma in all of our patients, whose cell type was not specified on the anatomopathological report. Immediate postoperative monitoring is carried out with the concern to diagnose a possible hematoma of the thyroid chamber which can progress to a compressive hematoma and require an emergency evacuation. In our series, none of our patients presented a local complication. Pulse, blood pressure, respiratory status, and local condition (6) are therefore monitored. During the first 24 hours, serum calcium is measured at the 4th hour, then the dosages can be spaced according to the evolution. In our study, transient hypocalcemia was found in two patients (7.69%), which is close to international data. PTH is measured preoperatively at the time of ablation, followed by 30 min, 60 min and 90 min after removal of adenomatous structures. The prognosis depends essentially on the precocity of the diagnosis as well as the rapidity of therapy. The success of surgical treatment is closely linked to local radiological investigations (6).

Conclusion:-

Parathyroid adenomas are common lesions representing the main etiology of HPTP, an endocrine disease characterized by inappropriate PTH secretion, leading to disturbance of calcium homeostasis. Clinical manifestations are varied. Nevertheless, the discovery of this pathology is most often fortuitous. The biological diagnosis of HPTP is defined by the association of elevated hypercalcemia-PTH plasma, or in discordance with serum calcium. The ultrasound-scintigraphy coupling, aims at the preoperative localization of the parathyroid adenoma, in order to carry out a targeted surgery and decrease the operative time. Surgery remains the treatment of choice. At the histological level, the differential diagnosis occurs with hyperplasia. The main cell parathyroid adenoma is the predominant cell type. Local complications and postoperative hyperparathyroidism are the main complications of surgical treatment of parathyroid adenomas.

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