



Parathyroid Adenoma: Diverse Modalities of Clinical Presentation. Series of Cases and Literature Review. January 2010-October 2020

Francisco M^{1*}, Victor M², Allan T², Guillermo C³, Alejandro R⁴, Rger M⁵, Teresa C⁶, Victor ER⁶, Carmen Q⁷, Angela MM⁸ and Alexis N⁹

¹Head & Neck Surgeon, Oncologic program Salud Integral Hospital, Nicaragua

²Cardiovascular Surgeon, medical staff hospital, Nicaragua

³General Surgeon, medical staff hospital, Nicaragua

⁴Vascular Surgeon, medical staff hospital, Nicaragua

⁵Radiologist, medical staff hospital, Nicaragua

⁶Nuclear Medicine, medical staff hospital, Nicaragua

⁷Pathologist, medical staff hospital, Nicaragua

⁸Internal Medicine, medical staff hospital, Nicaragua

⁹Resident of General Surgery, medical staff hospital, Nicaragua

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*Corresponding author: Francisco Medrano, Head and Neck Surgeon, Oncologic program Salud Integral Hospital, Managua, Nicaragua, Email: fmedranos@Hotmail.com

Abstract

The surgical treatment of Parathyroid Disease (PD) has change in the past two decades. The Parathyroid Adenoma (PA) represents 80%, some with symptoms others asymptomatic. The technological development of imaging methods has allowed greater precision in planning the surgical approach. The goal of parathyroidectomy is to cure. There are several surgical approaches from open cervical to minimal endoscopic surgery.

Objective: The main of this study is to present the clinical characteristic, the diagnosis methods: biochemical and imaging, surgical approached and follow up.

Methods: Descriptive study, Cohort, Series of cases. We reviewed the record of 450 patients diagnosed with tumor in head and neck during the period January 2010 to October 2020. We selected the record of patients with diagnosed of PA and the clinical characteristics of the patients according demographic aspect, symptoms, biochemical and imaging methods, complementary diagnosis test, surgical approach, histological classification according WHO Tumor of Endocrine Organs 4th edition 2017. The frozen section during the surgery indicted with the freezing microtome and stained with hematoxylin and eosin. The univariable review realized with frequency and percentage using Excel 2016.

Results: We selected 6 (1.3%) patients, male 5(83%) female 1(17%). The age range was 28-72 years, the median ages 49.6 in the neck located 4(66%), 1(17%) in upper mediastinum and 1(17%) in cervical and thoracic location. patient with recurrence after of five years. 1 with three PA and 1 with two PA. The parathyroid gland affected was: lower right 3 cases, upper left 1, lower left 5 cases and one upper mediastinum. The symptoms were nephrocalcinosis and chronic kidney failure

(CKF) 4 patients, bone loss (spine/hip) 2, cardiovascular diseases 1, left neck swelling and dysphagia 1. Imaging methods used: ultrasonography and technetium-99 Sestamibi Scanning the 5 patients, Magnetic Resonance Imaging (MRI) 4 and CT Scann 1 The bone densitometry: 2 (33%) patients with severe osteoporosis, 2(33%) with moderate, 1(16%) normal and 1 unknown. The surgical approach was: bilateral cervical exploration 2 patients, unilateral cervical exploration 2, minimally invasive thoracoscopic 1 and double cervical and thoracic open 1. The biochemical control of parathyroid hormone (PTH) was: range prior surgery 384-3000 pg/ML the mean 1,730.2 pg/ML. The percentage of decrease post-surgery was 99 %-98% Calcium prior surgery was 9.2-14.09 mg/dl the mean 11.2 mg/dl the range post-surgery was: 7.9-9.9 mg/dl the mean 8.6 mg/dl. Pathology register reveled PA, 5(83%) and 1(17%) a giant nonfunctioning Parathyroid cyst. During the follow up, only 1 patient presented recurrence five years later and required reintervention. None with post-surgery complication.

Conclusions: The multidisciplinary approach permitted the success obtained and surgery planning for each patient with PA. The results show like other papers, which using the technological development of imaging studies, the support of the frozen biopsy for the lack of PTH fast, allowed to corroborate the surgical remotion of the diseases gland with high percentage of cure.

Keywords: Parathyroid Adenoma; Nephrocalcinosis; Parathyroid Diseases; Pituitary Adenoma

Abbreviations: PD: Parathyroid Disease; PA: Parathyroid Adenoma; WHO: World Health Organization; pHPT: Primary hyperparathyroidism; PTH: Parathyroid hormone.

Introduction

The surgical treatment of primary hyperparathyroidism (pHPT) changed in the past two decades [1-3]. The prevalence of this condition is very variable. The anatomic knowledge and imaging methods allow a surgical planning with success rates of minimally invasive parathyroidectomy similar to those established for bilateral neck explorations [4-6]. The choice of imaging modality should be a consideration for efficacy, expertise, and availability of such techniques in clinical practice [7,8]. The reported success rate of this traditional approach, for skilled surgeons, is 90% [9]. There is controversy in surgical criteria, extent of surgery and minimally invasive approach, etc. There is universal agreement to surgical treatment. However, some protocols in highly specialized centers are not possible to perform in ours center due to their high costs. The main of this study is to present the clinical characteristic, the diagnosis method

biochemical, imaging and surgical approached and follow up of patients with PA.

Methods: Descriptive study, Cohort, Series of cases. We reviewed the record of 450 patients diagnosed with a tumor in head and neck during the period January 2010 to October 2020. We selected the record of patients with diagnosed of PA. The clinical characteristics of the patients according demographic aspect, symptoms, biochemical and imaging methods, complementary diagnosis test, surgical approach, histological classification according WHO Tumor of Endocrine Organs 4th edition 2017 [10]. The frozen section during the surgery indicted with the freezing microtome and stained with hematoxylin and eosin. The univariable review realized with frequency and percentage using Excel 2016.

Results: We selected 6 (1.3%) patients with PA, male 5(83%) female 1(17%) The age range was 28-72 years old, the median 49.6 in the neck located 4(66%), 1(17%) in upper mediastinum and 1(17%) in cervical and thoracic location. 1 patient with recurrence after of five years. 1 patient with three PA and 1 with two. The parathyroid gland affected according to Table 1.

Parathyroid Adenoma Localization	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Upper right gland						
Lower right gland	(+)	(+)			(+)	
Upper left gland					(+)	
Lower left gland	(+)	Recurrence (+)	(+)		(+)	(+)
Ectopic (Upper Mediastinum)				(+)		

Table1: Anatomic Localization of PA.

Symptoms show in Table 2.

Symptoms	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Bone loss(Spine/Hip)	(-)	(+)	(-)	(-)	(+)	(-)
Renal function	chronic failure	chronic failure	chronic failure	(-)	Chronic failure	(-)
Cardiovascular diseases	(-)	(-)	(-)	Hypertension	(-)	(-)
Neck swelling	(-)	(-)	(-)	(-)	(-)	(+)
Disphagia	(-)	(-)	(-)	(-)	(-)	(+)

Table 2: Symptoms more frequent in patients with PA.

Imaging methods used to locate PA according show Table 3.

Imaging methods	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Ultrasonography	(+)	(+)	(+)	(+)	(+)	(+)
Technetium-99 Sestamibi Scanning	(+)	(+)	(+)	(+)	(+)	(-)
Magnetic Resonance Imagen	(-)	(+)	(+)	(+)	(+)	(-)
CT Scan	(-)	(-)	(-)	(-)	(-)	(+)

Table 3: Imaging methods to locate parathyroid tissue.

The effects of HPT on bone density are assessed by bone densitometry at the spine and hip: 2 (33%) patients with severe osteoporosis, 2(33%) with moderate, 1(16%) normal

and 1 unknown. The surgical approach with biochemical control of PTH and Calcium prior and post-surgery according to Table 4.

Surgical approaches		PTH pg/MI prior surgery	PTH pg/MI post-surgery 1	PTH pg/MI post-surgery 2	Calcium mg/dl prior surgery	Calcium mg/dl post-surgery 1	Calcium mg/dl post-surgery 2
Case 1	Bilateral cervical exploration	1806	934	6.5	10.1	9.5	8.5
Case 2	Cervical exploration	2142	1428	1059	11.53	9.8	8.9
Case 3	Cervical exploration	3000	1000	25	9.8	8.8	8.2
Case 4	Minimally invasive-Thorascopic	384	250	56.1	14.9	11.3	9.9
Case 5	Bilateral cervical exploration	1319	263	21.8	11.2	10.7	7.9
Case 6	Doble cervical and thoracic open	unknown			9.72	9.65	8.46

Table 4: Surgical approach and biochemical control PTH and Calcium prio and post-surgery.

Pathology register reveled PA, 5(83%), and 1(17%) a giant nonfunctioning Parathyroid cyst. During the follow only 1 patient presented recurrence five years later in the contralateral parathyroid gland and required reintervention. None with post-surgery complication.

Discussion

The behavior of the parathyroid disease is very variable, depend of the region where was realized the research. The prevalence of this condition in the United States between women vs. men is similar to the reported by Eufrasino with a

major incidence of menopause women [11,12]. The European studies reported relatively low incidence, however, Scotland reported higher incidence [13]. Our series diagnose a small group of patients with parathyroid diseases concomitant with CKF. This explains that our results are different from other studies. The majority of our patients were men, however, De Lucia reported the effect of gender and geographic location on the expression of pHPT [14]. Others, reported that PD depend of race and was highest among blacks, followed by whites, but hispanic and other races were lower than that for whites [15,16]. The age range and median age are similar to studied by Eufrasino. Other papers reported age ranged from 20 to 99 years, the incidence is higher, such that in groups 70-79 the risk is greater [17]. The majority of our patients presented adenoma in a normal arrangement of the parathyroid glands, this could be explained because location of the parathyroid glands are constant in 75% of the population. However, the presence of one in ectopic position (mediastinum) demonstrates the complex embryonic development of the inferior parathyroid [18,19]. One of our cases was a giant cystic adenoma, occupying the neck and the mediastinum. The review of 14 cases show that large cysts were nonfunctioning as our study [20]. Large cyst formation is always associated with an adenoma with hemorrhage. Physiological pressure changes over the thoracic inlet may well explain the upward movement of any mass into the neck on forced expiration [21]. A cyst mass on the left side of the neck with dysphagia is a rare clinical manifestation [22-24].

The majority of patients had a single PA, similar to the reported by Udelsman, et al. [25,26]. A Review of the pathological findings in 140 Cases of pHPT by Lewis, the single adenoma represented 80% and parathyroid cancer is uncommon with less than 1.5% [27] there was no patient with tumor in other endocrine organ. Cushing and Davidoff reported a case of gigantism with an eosinophilic pituitary adenoma, an adrenal adenoma, an adenomatous goiter and parathyroid hyperplasia [28]. Coincidental adenomas of the islet cells of the pancreas, parathyroid, and pituitary has been reported by Shelburne, et al. [29] the majority of the our patients had nephrolithiasis as described Rejnmark [30] other trial reported prevalence ranged from 7 to 20% [31]. Sorensen reported the lowest range 3% in adults [32]. Nephrocalcinosis or silent nephrolithiasis are indications for parathyroidectomy in patients with suspected pHPT [3]. The association between parathyroid hyperplasia and CKF has been known since early 1930 [33]. Many observations suggest that secondary hyperparathyroidism (HPT) is often an early event in renal disease and parathyroid tissue involvement generally increases proportionately with the increasing severity and duration of functional renal impairment.

These results suggested that in renal HPT, the parathyroid glands initially grow diffusely and polyclonally, and that

the cells in the nodules are later transformed to monoclonal neoplasia and proliferate aggressively [34]. A little more than a third of our patients with bone mineral density were below at the spine or hip with higher risk to fracture. Similar to the reported by Misiorowski suggested that the prevalence of HPT is higher among patients with low bone mineral density [35]. The risk of fracture is frequent in patients with HPT compared with persons who did not have the condition. This group of patients makes them a candidate for surgical treatment as our two cases [36,37]. The accurate preoperative localization has become more important to enable a successful surgical outcome. Parathyroid ultrasound requires skilled radiologist and interpreters with knowledge of parathyroid embryology and anatomy to access parathyroid glands in eutopic and ectopic positions [38]. The sensitivity and specificity of sonography for identifying enlarged parathyroid glands were 74% and 96%; similar reported by Siperstein and Solorzano. Sonography correctly predicted a solitary adenoma or multiglandular disease [39-41]. All patients used the ultrasound as diagnosis tool of low cost but of great utility in low income countries, according The American Association of Endocrine Surgeons Guidelines. The CT and MRI are complementary imaging studies [42-44]. Nuclear medicine today has a role in the detection of the number of sick glands or ectopic gland [3,45,46]. Singh reported 63 % of sensibility and predicted positive value of 90% but decreased between 53%-74% in localization in second surgery [47,48]. On the other hand, a metanalysis reported that the sensibility decreased according the number of gland disease [49]. ^{99m}Tc-MIBI y SPECT/CT have demonstrated greater precision in the preoperative localization, with great superiority than ultrasound, CT and MRI but it is a very expensive technique [50]. Our patients presented indication for parathyroidectomy, according to the guidelines of The American Association of Endocrine Surgeons [13,51-53]. The success rate for surgeons in centers with expertise is a cure rate of 95% [54]. A case presented as a recurrence in the contralateral gland five years after the first surgery, similar to the reported by Karakas and Weber [55,56]. One of our cases approached by Thorascopic, demonstrate the importance of surgical skills with minimal invasive techniques with similar percentage of cure [57-59]. We had a multiple parathyroid adenoma case, as reported for several series. This patient classified as group 2 according to criteria of Lewis and Reymond: multiple parathyroid adenoma, three parathyroid glands large and renal insufficiency present [60,61]. The majority of our patients presented with intraoperative specimen biopsy, with the advent of other complementary intraoperative techniques, some authors have argued for the superiority of intraoperative hormonal analyzes over frozen cutting. PTH fast is a fast and reliable test to ensure adequate resection of parathyroid tissue, however it is expensive for our country. Aygun concluded that the routine use of frozen section examination is not recommended [62-64]. While experts condemn the util-

ity of the frozen tissue examination of the surgical specimen in parathyroid disease, as it is deemed difficult and ineffective in the event of multiglandular disease [65]. Secondly, the frozen tissue examination diagnosis is thus feasible in a well-selected population. The pathologist's expertise is, therefore, the main factor determining the reliability of this examination [66,67].

Conclusions

The multidisciplinary approach permitted the success obtained and surgery planning for each patient with PA. The results show like other papers, that using the technological development of imaging studies, the support of the frozen biopsy for the lack of PTH fast, allowed to corroborate the surgical remotion of the diseases gland with high percentage of cure.

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