Original Article

Effect of the Size of Parathyroid Lesion, Calcium and Parathormone Levels on the Outcomes of Patients Undergoing Parathyroidectomy

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ABSTRACT

Background: Hyperparathyroidism is a common disorder associated with a defect in metabolism of calcium and phosphorus in the body. Of the serious complications of the disease are pathologic fractures and brown tumours.

Patients and Methods: We herein study retrospectively the patients with hyperparathyroidism who underwent surgical treatment at a tertiary hospital during a 12-year period.

Results: 36 patients were enrolled in this study. The majority of the patients were females, the mean age was 46 years old. Pathologic fractures and brown tumours were present in about 14% of the patients each, while postoperative hypocalcaemia occurred in about 11% of the patients. In addition, we detected that the higher the serum calcium level on presentation the higher the chance to develop pathologic fracture or brown tumour, while there was an increased chance of having a post-resection hypocalcaemia with higher levels of parathormone hormone.

Conclusion: Patients with high serum calcium level, especially shooting levels should be recommended a surgery as of fracture and brown tumour risk. Also, the higher the level of parathormone, the more need for rigorous monitoring of serum calcium after surgery.

Key Words: Brown tumour; hypercalcaemia; parathyroidectomy; parathyroid adenoma.

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BACKGROUND

Primary hyperparathyroidism is characterized by hypercalcaemia in association with elevated or inappropriately normal parathormone hormone level[1].

Minimally invasive parathyroidectomy or otherwise called focused surgery for the imaging localized diseased parathyroid gland and bilateral neck exploration of all glands are the two performed approach for parathyroidectomy[2]. In a metanalysis both were effective surgical techniques with a superior safety profile for the earlier in terms of lower rate of hypocalcaemia and recurrent laryngeal nerve injury[3].

Surgical parathyroidectomy should be considered, especially if concomitant disorders exist, such as persistent hypercalcaemia or hyperphosphataemia, tissue or vascular calcification including calciphylaxis, and/or worsening osteodystrophy[4].

PATIENTS AND METHODS

This is a retrospective study, where the institutional registry at our hospital was revised for patients with hyperparathyroidism that attended the hospital from January 2006 till April 2021.

Inclusion criteria

1. parathyroid gland disease.
2. Received surgical treatment.

Exclusion criteria

1. No definite pathologic diagnosis.
2. Inadequate registered data.

The outcomes were postoperative hypocalcaemia, development of brown tumour and pathologic fractures.

The data of these patients were analysed, and statistical values were obtained using SPSS version 22 (Inc, Chicago, IL). Continuous variables are presented as mean when symmetrical or median and range when asymmetrical. Categorical variables are presented as proportions. Univariate analysis was done using Chi-Square test, Fisher's exact test (if cell count less than 5), Mann-Whitney test, and Spearman's correlation. *P value* <0.05 was considered significant.

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RESULTS

Thirty-six patients were enrolled in this study. The majority were females 28 (77.8%). The mean age was 46.4 +/- 14 years-old. Most of the lesions were left sided (21 patients). All patients were primary hyperparathyroidism except one patient who suffered secondary hyperparathyroidism to renal failure. In most of the patients (31, 86.1%) only one gland was affected. The median longest diameter of the lesion was 2.5 cm ranging from 0.5 to 4.8. Sestamibi parathyroid scan was used in the assessment of 14 (38.9%) and computed tomography in 2 (5.5%) patients, while the rest were assessed by ultrasound only. The mean serum calcium level was 9.9 +/-1.9 mg/dl, while the median serum parathormone hormone level was 801 (126-2444) pg/ml. Brown tumour was found in only 5 (13.9%) cases with a mean size of 4.8 +/- 1 cm. Also, pathologic fracture occurred in 5 (13.9%) patients. In the majority (20 patients, 55.6%) the parathyroid surgery was done without concomitant thyroid resection, in the rest, 15 (41.7%) patients had hemithyroidectomy and one (2.8%) patient underwent total thyroidectomy. In those who underwent concomitant thyroid surgery, the majority (15 patient, 93.7%) for associated multinodular goitre, in contrast to 1 patient (6.3%) for micropapillary carcinoma. In more than two thirds (28 patients) a focused resection of the involved parathyroid gland was done. In only 3 (8.3%) of the patients a video endoscopic approach was used. Hypocalcaemia postoperative was uncommon, occurring in only 4 (11.1%) patients. Pathology revealed adenoma in 28 (77.8%) patients. None of the patients developed major adverse events postoperatively (haematoma or stridor) (Table 1).

There was no correlation between the size of the lesion (as measured by the longest diameter) and serum calcium (p=.204) nor serum parathormone (p=.94) level.

Serum calcium level preoperatively was the only factor that was significantly associated with development of brown tumour (p=.001). While the age of the patient and the serum calcium were associated with presentation with pathologic fracture (p=.01 and .001, respectively). However, the serum basal level of parathormone hormone was the only factor significantly associated with postsurgical hypocalcaemia (p-value=.019) (Table 2).

On the other side, the number of affected glands was the only factor significantly suggesting the pathology, where single glandular affection had been almost always adenoma, while affection of multiple glands was corresponding to hyperplasia (<.001) (Table 2).

Table 1: Basic epidemiologic and clinico-pathologic criteria of the study patients

Variable	Value
Age	46.4 +/- 14 years
Sex	
Male	8 (22.2%)
Female	28 (77.8%)
Symptoms	
Neck swelling	16 (44.4%)
Brawn tumour	5 (13.9%)
Renal symptoms	2 (5.6%)
Pathologic fracture	5 (13.9%)
Bone aches	4 (11.1%)
Asymptomatic	3 (8.3%)
Side	
Rt	13 (36.1%)
Left	21 (58.3%)
Both	1 (2.8%)
Number of glands affected	1 (1-4)
Largest diameter	2.5 (0.5-4.8) cm
Calcium level	9.9 +/- 1.9 mg/dl
Parathormone level	801.5 (126-2444) pg/ml
Brown tumour	
No	31 (86.1%)
Yes	5 (13.9%)
Largest diameter of brown tumour	4.8 +/- 1 cm
Site of brown tumour	
Maxilla	1 (20%)
Mandible	1 (20%)
Clavicle	1 (20%)
Acetabulum	1 (20%)
femur	1 (20%)
Pathologic fracture	
No	31 (86.1%)
Yes	5 (13.9%)
Treatment	
Without thyroidectomy	20 (55.6%)
With thyroidectomy	16 (44.4%)
Excision	28 (77.8%)
Subtotal parathyroidectomy	3 (8.3%)
Total parathyroidectomy	1 (2.8%)
Open	33 (91.7%)
Endoscopic	3 (8.3%)
Hypocalcaemia postop	
No	32 (88.9%)
Yes	4 (11.1%)
Adenoma	27 (75%)
Atypical adenoma	1 (2.8%)
Hyperplasia	6 (16.7%)
Adenoma with hyperplasia	2 (5.6%)

DISCUSSION

Primary hyperparathyroidism is caused by a solitary adenoma in 80%, whereas four glands hyperplasia accounts for 10–15%, multiple adenomas for 5% and parathyroid

Table 2: A comparison between age of the patient, size of parathyroid lesion, number of affected parathyroid glands, serum calcium and parathormone preoperatively and outcomes

	Age	*P-value*	Number of glands	*P-value*	Longest diameter	*P-value*	Calcium level	*P-value*	Parathormone level	*P-value*
Brawn tumour		.59		.66		.7		.001		.21
No	46.9 +/- 14.3		1 (1-4)		2.5 (0.5-4)		9.4 +/- 1.6		572 (126-2444)	
Yes	43.2 +/- 13.5		1		1.6 (1.3-4.8)		12.4 +/- 1.4		920 (742-1026)	
Associated fracture		.01		.66		.32		.001		.29
No	48.8 +/- 12		1 (1-4)		2.6 (0.5-4.8)		9.4 +/- 1.5		594 (126-1487)	
Yes	31.8 +/- 17.5		1		1.6 (1-4)		12.5 +/- 1.5		860 (742-2444)	
Postop hypocalcaemia		.44		.6		.82		.48		.019
No	47.1 +/- 13.8		1 (1-2)		2.5 (0.5-4.8)		10 +/-1.8		612 (126-1026)	
Yes	41.2 +/- 17.5		1 (1-4)		2.75 (1-3.5)		9.4 +/- 2.8		1965 (1487-2444	
Postop pathology		.71		<.001		.65		.17		.64
Adenoma	47 +/- 15.1		1		2.5 (1-4.8)		10 +/- 1.7		742 (126-2444)	
Atypical adenoma	31		1		1.6		14.7		860	
Hyperplasia	47.8 +/- 7.2		2 (1-4)		2 (0.5-3.5)		8.5 +/-1.1		NA	
Adenoma & hyperplasia	42.5 +/- 14.8		1		2.4 (1.5-3.4)		9.7 +/- 0.6		360	

cancer for <1% of the cases[5,6].

While age, sex, and vitamin D level provided very minimal information to quantify risks of postoperative hypocalcaemia. The percentage of decrease of the parathormone hormone level from the preoperative to the lowest level after the removal of the abnormal gland(s) is the most significant predicting factor for the severity of postoperative hypocalcaemia[7]. This coincides with our study findings, where the higher the level presurgical serum parathormone hormone, the higher the incidence of postoperative hypocalcaemia, being the only significant predictor.

Primary hyperparathyroidism is usually diagnosed because of chance findings of raised serum calcium or complications associated with hypercalcaemia as polyuria, polydipsia, muscle weakness, gastrointestinal upsets, and nephrolithiasis, however; bone disease is rarely overt. Radiographic manifestations are seen in less than 2% of patients and include subperiosteal erosions, diffuse osteoporosis, cystic lesions (brown tumours), pathological fractures, 'salt and pepper' mottling of the skull and loss of the lamina dura in the mandible[8]. Incidence of fractures in hyperparathyroidism is quite low (about 10%) in a previous series and apart from vertebral compression fractures, no characteristic fracture pattern has been described[9]. Also, there has been several reports of fracture as a presenting symptom[10,11]. In our series, 13.9% of patients had a pathologic fracture, and the incidence was higher in younger patients and those with higher basal serum calcium level.

On the other hand, brown tumour, which is one of the skeletal manifestations of hyperparathyroidism, is a reactive lesion and do not represent a true neoplasm. As such, it may be difficult to diagnose because it present clinically and radiologically as other diseases, including giant cell tumours, multiple bone metastases, or multiple myeloma[12,13]. This diagnostic confusion may unfortunately lead to a massive bony resection surgery that can be totally avoided. In this study, the incidence of brown tumour was 13.9% and the only independent factor that contributes to it was the higher blood calcium level.

In an interesting study designed to search the relation between primary hyperparathyroidism (PHPT) and papillary thyroid cancer (PTC), the group with PHPT + PTC had a significantly smaller tumour diameter than the PTC only group. While, their results may support the idea that PHPT leads to overdiagnosis of PTC, they observed high rates of tumour capsule invasion and multicentricity in the PHPT + PTC group that may highlight an associative aetiology[14]. In this study, there was only one patient with micropapillary carcinoma in association with parathyroid adenoma, which make it difficult to assume a correlative aetiology.

The limitation of this study is being retrospective, in a small cohort of patient from one institution. However, we tried to establish a relationship between the main disease factors (lesion size, calcium level and parathormone level) and outcomes (complications) of the disease itself and of the corrective surgery, a zone where there is a paucity of studies targeting previously.

CONCLUSION

The size of the parathyroid pathology does not have any implication on outcomes. On the other hand, patients with high serum calcium level, especially shooting levels should be recommended a surgery as of fracture and brown tumour risk. Also, the high parathormone level is the signpost of development of postoperative hypocalcaemia,

so the higher the level, the more need for rigorous monitoring of serum calcium after surgery.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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