STUDY OF CLINICAL FEATURES, SURGICAL MANAGEMENT AND OUTCOMES OF PARATHYROID ADENOMA

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ABSTRACT

Introduction

Parathyroid adenoma is a benign tumor of the parathyroid gland. It is the common cause of Primary hyperparathyroidism (pHPT). Parathyroidectomy is the curative treatment for Parathyroid adenoma.

Objectives:

The objective was to study the clinical features, surgical management and outcomes of parathyroid adenoma

Materials and Methods:

This was a retrospective study, included patients who underwent surgery for suspected parathyroid adenoma, carried out from April 2014 to April 2018 in the Department of ENT & Head and Neck Surgery, National Academy of Medical Sciences(NAMS). Details of clinical data, biochemical investigations and radiological findings were recorded from all the cases. Final diagnosis was based on histopathological confirmation.

Results:

Eleven patients underwent parathyroidectomy at our center in the last four years. Clinically three cases had history of recurrent renal stones, one had abdominal pain and two had pathological fracture and five cases were detected incidentally while doing routine biochemical investigations. All patients underwent minimal invasive parathyroidectomy. In all cases serum calcium and PTH level reduced except in one case that needed re - exploration and after revision surgery his serum calcium and PTH also decreased significantly. Histopathology of all cases reported as parathyroid adenoma including the case that underwent revision surgery. None of the case diagnosed as parathyroid hyperplasia and carcinoma in histopathology. Histopathology following second surgery in revision case reported as intrathyroidal parathyroid adenoma.

Conclusion:

Parathyroid adenoma commonly presents with renal features. Some patients may remain asymptomatic. In all cases serum calcium and PTH was high before surgery. Parathyroidectomy is the mode of treatment. Intraoperative parathyroid hormone (ioPTH) assay improves the success rate of minimal invasive parathyroidectomy.

Keywords: Hypercalcemia, Hyperthyroidism, Parathyroid adenoma, Primary hyperparathyroidism,

INTRODUCTION

Parathyroid adenoma is a benign tumor of the parathyroid gland. It generally causes the hyperparathyroidism. Hyperparathyroidism literally means excess secretion of parathyroid hormone (PTH).On the basis of etiology and approach to management, hyperparathyroidism is classified into primary, secondary and tertiary. Primary hyperparathyroidism (pHPT) is a common clinical problem.[1] Parathyroid adenoma is the common cause for pHPT. In India, the incidence of pHPT is 2.5 per 1000 individuals.[2] The overall incidence rate of pHPT was 21.6 per 100,000 indivisuals annually in Minnesota.[3] In Nepal there is no such data of incidence of pHPT.

Parathyroid hormone (PTH) is a peptide hormone that is the primary regulator of calcium concentrations in the bloodstream. Hyperparathyroidism is a common cause of hypercalcemia and the primary disorder is most commonly due to an autonomously functioning solitary adenoma (80-85%), gland hyperplasia (10-15%) or multiple adenomas (5%). Primary hyperparathyroidism occurs more commonly in women and the onset before 50 years of age is rare.[4] The majority of patients with pHPT are asymptomatic and recognized coincidentally on biochemical testing in patients evaluated for unrelated complaints. Some patients at early stage complain of non-specific symptoms like abdominal pain, weakness, easy fatigability, intellectual weariness, psychiatric symptoms and a sense of not feeling well making it very difficult to diagnose. The incidence of kidney stones in primary hyperparathyroidism is 15-20% which makes it the most frequent overt target organ complication of primary hyperparathyroidism. Fractures are rarely reported. Most cases are sporadic and caused by a single parathyroid adenoma (85–95%) or multigland disease (5–10%), with parathyroid carcinoma accounting for $<1\%$.[5,6]

The diagnostic assessment of patients with primary hyperparathyroidism is based on the clinical evaluation, laboratory and radiological findings. Parathyroidectomy is the only curative treatment for pHPT, with first-time cure rates exceeding 95% of cases.[7] Cure is usually defined when the patient remains eucalcemic for six months after surgery, while persistent disease is defined if hypercalcemia is encountered in the six months postoperatively. The objective was to study the clinical features, surgical management and outcomes of parathyroid adenoma.

MATERIALS AND METHODS:

A retrospective study was conducted from April 2014 to April 2018 in Department of ENT & Head and Neck surgery, NAMS. In this study we have analyzed the data of operated cases with provisional diagnosis of parathyroid adenoma. Data was collected from medical record section and reviewed for clinical presentations, diagnostic work-up, postoperative biochemical outcomes (serum calcium and PTH) during hospital stay. A drop in PTH of 50% or more from the baseline PTH level within 15 minutes after removal of the pathological parathyroid gland indicates successful removal of the abnormal secreting parathyroid tissue. Approval for the study was taken from ethical board.

RESULTS:

Total eleven cases with provisional diagnosis of parathyroid adenoma underwent minimal invasive surgery during four years period in Department of ENT & Head and Neck Surgery, National Academy of Medical Sciences (NAMS). Nine cases were referred from Endocrinology Department and two cases were referred from Orthopedics Department. Ten cases were less than 55 years of age and remaining was 63 years old male. In our study there were six males and five females.

Among those two patients presented in Orthopedic Department, first patient presented with pain and swelling over right hip and unable to bear his body weight for one month and diagnosed fracture neck of femur. Next patient presented with multiple joint pain for two years, swelling with pain in right hip for two weeks and unable to bear weight for two weeks. Ultrasonography (USG) of neck and Technetium-99m methoxyisobutylisonitrile (^{99m}Tc MIBI) scintigraphy was suggestive of parathyroid adenoma in both cases. In both cases abdominal and Pelvic USG finding showed nephrolithiasis in bilateral kidneys. They were managed conservatively in orthopedic ward prior to parathyroidectomy.

One case had history of recurrent abdominal pain for seven years and underwent pylolithotomy twice in the past. His abdominal and pelvic USG findings were suggestive of chronic pancreatitis and bilateral multiple nephrocalcinosis. Three patients were presented with recurrent renal stones. They had history of multiple surgeries for removal of renal stones. Abdominal and Pelvic USG findings were nephrolithiasis in both kidneys. USG neck and ^{99m}Tc MIBI scintigraphy was suggestive of parathyroid adenoma (Fig.I).

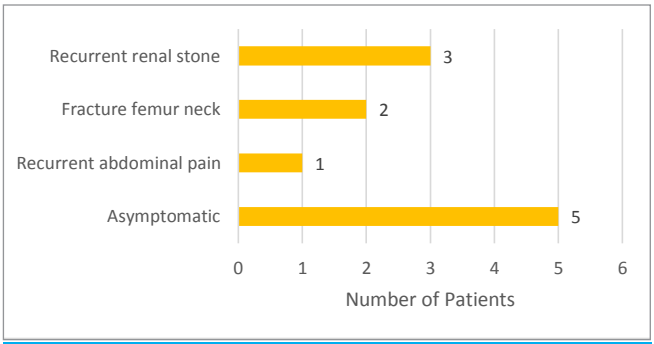

Fig I: Clinical presentation of the patients with parathyroid adenoma

Five cases had high serum calcium level on general health checkup and did further investigations like USG neck, ^{99m}Tc MIBI scintigraphy, parathyroid hormone level and diagnosed coincidentally.

USG neck showed the hypoechoic lesion at parathyroid region in nine cases. USG could not detect any lesion in two cases. Among those two cases one had history of recurrent renal stone and another did not have any symptom. ^{99m} Tc MIBIscintigraphy was suggestive of parathyroid adenoma in all eleven cases.

In this study inferior parathyroid gland was commonly involved than superior parathyroid gland (Fig.II). Single parathyroid gland involvement was in nine cases (in four cases left inferior, in four cases right inferior,one case left superior and in one case left superior and left inferior parathyroid gland).In one case bilateral inferior parathyroid glands were involved (Fig.III).

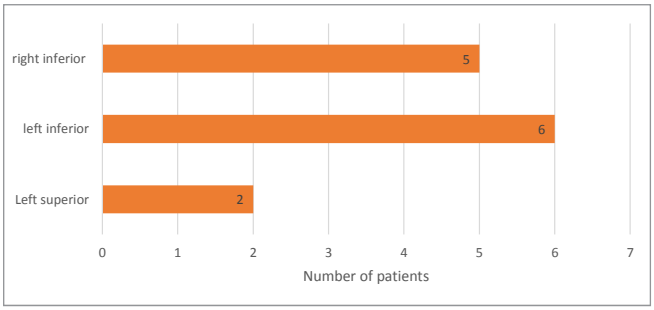

Fig II: The parathyroid gland involved by adenoma

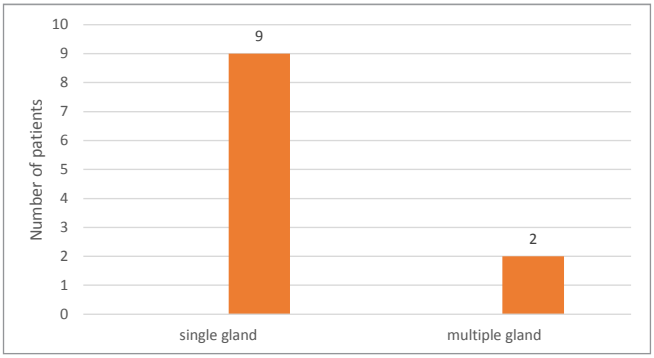

Fig III: Number of parathyroid gland involvement in each patient

In all cases biochemical finding revealed hypercalcemia and increased parathyroid hormones. Hypercalcemia was corrected by endocrinologists before parathyroidectomy. Then suspected parathyroid adenoma mass was removed with minimal invasive technique in all cases. In all cases ioPTH dropped by 50% of the preoperative level.

One patient with fracture neck of femur needed re-exploration as the serum calcium level did not fall down to normal level till one month following first surgery. Before revision surgery, we repeated the US neck which showed hypoechoic nodule and MIBI scan showed increased uptake at the upper aspect of left thyroid lobe. Left hemi thyroidectomy was done and postoperative histopathology reported as intrathyroid parathyroid adenoma. His serum calcium level dropped significantly in postoperative period and managed medically.

DISCUSSION

Hyperparathyroidism is the state of excess parathyroid hormone. Primary hyperparathyroidism is a common endocrine disorder manifested with elevated levels of parathyroid hormone (PTH) and serum calcium. Patients are generally asymptomatic. In the early stage symptoms are usually nonspecific like mild depression, weakness, anorexia, fatigue etc. In countries for which screening biochemistries are not routinely part of the health care system, symptomatic pHPT seems to predominate. In countries where screening biochemistries are routine, asymptomatic pHPT takes center stage. Although epidemiological studies on the

prevalence of pHPT have not been conducted in Asian countries, it seems that, in countries such as China and India, patients with pHPT still present with classic pHPT, namely, with organ manifestations and relatively high serum levels of calcium.[8]Nephrolithiasis is the most frequent presentation in patients with renal disorders (20%–30%), whereas severe bone disease has been identified in less than 3% of cases. In our study one case had history of recurrent abdominal pain, three cases had history of recurrent renal stone, two cases had pathological fracture and five patients were asymptomatic and diagnosed accidentally.

pHPT represents a common endocrine disease mostly in those countries in which screening is routinely done. In the western world also the disease tends to appear without any specific symptoms. In the early 70's widespread screening of serum calcium was introduced in western world. After the introduction of the routine screening for serum calcium, the diagnosis of pHPT has been increased.[9] In our country,screening of serum calcium was still not introduced. Diagnosis of pPTH is either accidentally or patients presented with complications of long-term hypercalcemia, such as bone deformities and nephrocalcinosis. It can be also sporadically diagnosed with disproportionately high or even normal PTH in combination with high or even normal calcium levels. Some clinicians believe asymptomatic patients with no complications and patients not fit for surgical procedure or refusing surgery can be managed medically, while others believe virtually all patients with biochemical evidence of pHPT, irrespective of how mild, should undergo parathyroidectomy as it converts to chronic mild pHPT.

Primary hyperparathyroidism generally occurs with higher rate in a population older than 55 years.[10] The onset before 50 years of age is rare.[4] In our study age group ranged from 30 years to 63 years. Ten cases were less than 55 years and one case was 63 years old male. pHPT occurs more commonly in women.[4] In our study there were six males and five females. As our cases were less in number gender difference was not significant. According to Lindner G et al, it occurs 2-3 times more frequently in women than in men and has a higher prevalence in postmenopausal women.[10] In our study, among five females three female patients were in postmenopausal.

In approximately 80% of cases, excessive production of PTH is due to a single parathyroid adenoma. Multiple glands involvement is less common. In this study also single gland involvement was in ninecases and in two cases multiple glands.

Imaging helps to localize the site of hyperfunctioning parathyroid tissue. Ultrasonography and Scintigraphy have long been the most commonly used localizing studies. In recent past most surgeons believed that localization techniques had to be reserved for patients undergoing re-exploration after a failed initial procedure.[9] In case of parathyroid adenomas the sensitivity of Sestamibi Scans is 80-90% in most series.[11] Combined Ultrasound (USG) and Sestamibi Scan have achieved an overall accuracy of 91% for preoperative localization of single gland disease in some reports.[12]In a recent series Sestamibi showed positive results in 100% of patients with pHPT presenting with severe bone disease, 84% in the group of patients with renal involvement but not bone involvement and 64% in patients with initial asymptomatic pHPT.[13]

Intraoperative parathyroid hormone monitoring has accuracy of up to 98.5%.[14] Monitoring ioPTH has improved the surgical success rates of pHPT from 90%-95% to 100% in some series.[16] In our study ioPTH assay was done in all cases and PTH dropped to 50% of the preoperative level was considered as the success of surgery. But in one case even with ioPTH dropped by 50% of preoperative level needed revision surgery. According to Wharry L ioPTH drop by 50% but not to normal level has been found to be associated with 19 times greater likelihood of surgical failure than a drop by 50% and to normal; that requires ioPTH to drop both by percent and to normal, has therefore been suggested.[19]

According to Sokoll LJ et al, sensitivity of US was higher than MIBI (78.2% vs 70%, but both were inferior to ioPTH (98.6%). USG and Sestamibi Scans were more sensitive at detecting single gland disease than multigland disease (85% vs 55% and 77.5% vs 45.5%, respectively), while

ioPTH was better in both situations (98.8% vs 96.7%).[17] So, ioPTH is better parameter for those especially undergoing minimal invasive parathyroidectomy (MIP). In our study MIBI scintigraphy was positive in all the cases, USG neck detected parathyroid mass in nine cases out of eleven cases.

Although classic bilateral neck exploration has been the standard care for decades, its indications have been progressively decreasing in the era of minimally invasive parathyroidectomy (MIP) as the later has many advantages like minimal incision, minimal dissections and short hospital stays.

Successful treatment can be achieved by a multidisciplinary team, where surgeon, endocrinologist, radiologist and nuclear medicine work combinely. Postoperative transient hypocalcemia may occur secondary to inhibition of the remaining parathyroid glands or devascularization due to surgery. True intrathyroid parathyroid adenoma account for less than 1% cases of hyperparathyroidism.[20]It is located completely within the thyroid gland, surrounded by thyroid parenchyma on all sides. There is no intervening thyroid capsule between the thyroid and parathyroid tissue. In our study one case was intrathyroid parathyroid adenoma.

The major limitation of this study was the small sample size,retrospective study and lack of long term follow-upcompared to other international studies.

CONCLUSION:

Parathyroid adenoma patients may present with different clinical features. The common clinical feature is nephrolithiasis and nephrocalcinosis. They may not have any symptom, so there should be the introduction of routine biochemical screening. Minimal invasive parathyroidectomy is the better option for treatment. Following surgery PTH and serum calcium level reduced significantly. Parathyroid adenoma is the common cause of primary hyperparathyroidism.

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