Turkish Journal of Endocrinology and Metabolism, (2000) 4 : 139-142 **ORIGINAL ARTICLE**

Evaluation of Sixteen Patients with Hyperparathyroidism

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Hyperparathyroidism is characterised by high serum calcium levels and inappropriately increased production of parathyroid hormone. In this study, we have evaluate d the clinical profile of 13 patients with primary hyperparathyroidism (two patients with non-medullary thyroid carcinoma) and 3 patients with secondary hyperparathyroidism. Although it has been suggested that the clinical profile of the hyperparathyroidism has changed over the past three decades, in our population 61.5% of the patients show nephrolithiasis and most of the patients show skeletal involvement with various severity including pathological fractures. These results indicate that hyperparathyroidism remains undetected and not diagnosed early enough in our population.

Key words: Hyperparathyroidism, Non-medullary thyroid carcinoma

Introduction

Hyperparathyroidism is an endocrine disorder characterised by excessive secretion of parathyroid hormone (PTH). In most of the patients a parathyroid adenoma is responsible from the clinical picture. Initially it was considered as a rare disease associated with life threatening skeletal complications, however, the development of biochemical autoanalyser and the routine measurement of serum calcium levels resulted in more common diagnosis of the disease (1). The annual incidence of hyperparathyroidism is 25-30 patients per 100.000 and although the disease can occur at any age, it is most common in the fifth and sixth decades of life (2). Primary hyperparathyroidism is the most common cause of hypercalcaemia in outpatient clinics but malignancy is the leading cause of hypercalcaemia in hospitalized patients (3). Previously, we have investigated the causes of hypercalcaemia in hospitalized patients and found that, primary hyperparathyroidism was present in 7% of the patients (4).

It is reported that a new clinical profile of hyperparathyroidism has emerged. That in this new clinical picture, nephrolithiasis or other complications are uncommon and the disease is often diagnosed after the discovery of hypercalcaemia with an elevated PTH concentration in a symptom-free patient (5). In this paper, we report the evaluation of 16 patients with hyperparathyroidism with various complications and striking features.

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Patients and Methods

In this retrospective study, we have evaluated 16 patients who were diagnosed and managed in the Endocrinology Clinic of Erciyes University Hospital between 1994-2000. The patients had been diagnosed as hyperparathyroidism in the presence of elevated blood calcium levels (>10.5 mg/dl), hypercalciuria (>250 mg/day for woman and >300 mg/day for man), hypophosphatemia (<2.5 mg/ml) and inappropriately high (>65 pg/ml) iPTH (intact Parathyroid hormone) levels determined by IRMA. Biochemical analyses were performed by an autoanalyzer (Koneldo 60i). All the patients were investigated for the presence of complications related to hyperparathyroidism and the presence of MEN Type 1 or 2A syndromes. Preoperative localization study was done with ultrasonography (USG) in all and technetium-sestamibi (MIBI) scanning in 7 patients. All the patients were treated surgically and the diagnosis was confirmed by histological examinations. The results are expressed as mean±SE.

Results

Ten (62.5%) women and 6 (37.5%) men were included in the study. Mean age was 43.5±2.7 (18-64) years. In patients with primary hyperparatyhroidism the most common symptoms were gastrointestinal disturbances such as nausea-vomiting and skeletal symptoms such as bone and joint pain. Among the patients with primary hyperparathyroidism 2 (15.3%) patients were diagnosed after a pathological fracture of femur neck and radiological investigations showed brown tumor in 5 (38.4%), pepper-pot skull in 9 (69.2%) and subperiostal resorption in 8 (61.5%) patients. In patients with primary hyperparathyroidism, abdominal USG showed nephrolithiasis in 8 (61.5%) patients, 2 (15.3%) patients have peptic ulcer operation and 2 (15.3%) additional patients had endoscopically proven peptic ulcer diseases.

Secondary hyperparatyhroidism was detected in 3 (18.7%) patients during the regular examinations of the patients with chronic renal failure (CRF). Four (25%) patients, including one with CRF, were normocalcaemic and all the patients were hypophosphatemic except one patient with CRF. Twenty-four hours urinary calcium output could not be obtained in patients with CRF and among the rest, only 2 (15.3%) patients showed normal urinary calcium levels. Some of the characteristics of the patients are shown in Table 1. The parathyroid adenoma was localised in 62.5% of the patients with USG and in all (seven) patients with MIBI scintigraphy. A demonstrative example of MIBI scintigraphy of a patient with primary hyperparathyroidism is shown in Figure 1.

Table 1. Biochemical indices in 16 patients with hyperparathyroidism.

	All Patients (n=16)	Patients with PHP• (n=13)	Normal Value
Serum			
Ca^{++} (mg/dl)	12.0±0.1	12.4±0.4	9-10.5
P (mg/dl)	2.7±0.2	2.0±0.3	2.5-4.5
ALP (IU/L)	921.2±216.9	789.0±170.0	100-280
Albumin (g/dl)	4.0±0.1	4.1±0.1	3.5-5
iPTH (pg/ml)	784.1±183.7	721.0±150.0	9-55
Urinary			
Ca^{++} (mg/day)	415.9±66.7	415.9±66.7	<250*- <300#

• PHP : Primary hyperparathyroidism, * For woman, # For man

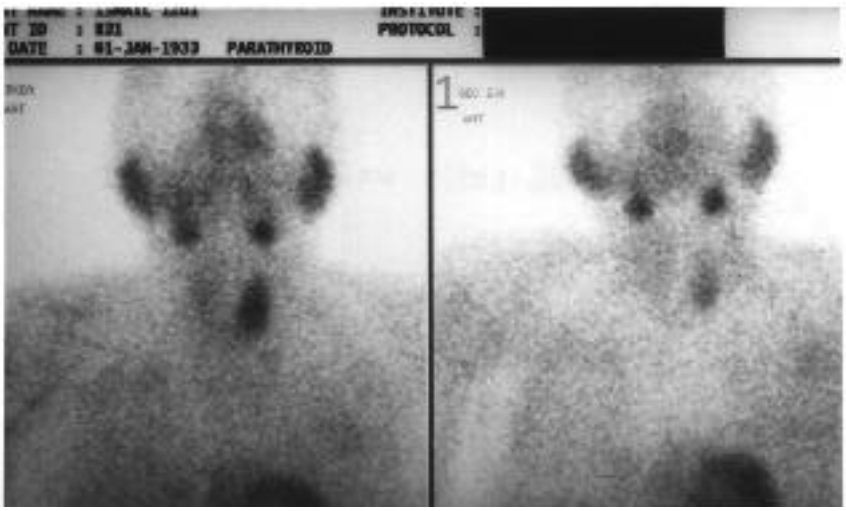

Figure 1. Technetium-99m sestamibi scan of a patient with primary hyperparatyhroidism. Prominent uptake of radiotracer in paratyhroid adenoma with disappearance of thyroid gland uptake in late image.

Multi-nodular goiter was present in 5 (38.4%) cases with primary hyperparathyroidism and subtotal thyroidectomy was performed to all of them. In 2 of these patients papillary microcarcinoma of the thyroid gland was diagnosed. Histopathological examinations showed a parathyroid adenoma in 14 (87.5%) patients and parathyroid adenomas associated with hyperplasia in 2 (12.5%) patients. Both of these patients were on hemodialysis program because of CRF. None of the patients have any component of MEN syndromes. All the patients were followed postoperatively with serum calcium, phosphorus and ALP levels to confirm the cure of the disease.

Discussion

The diagnosis of hyperparathyroidism is usually dependent on the initial recognition of hypercalcaemia. Before the introduction of the multichannel autoanalyser in the early 1970s, hyperparathyroidism was thought to be an uncommon disorder that was associated with serious skeletal complications and nephrolithiasis (2). Because of an increase in the prevalence of primary hyperparathyroidism and because a number of these patients have mild symptoms, different suggestions have arisen regarding whether parathyroidectomy is indicated for patients with asymptomatic hyperparathyroidism. In some reports hyperparathyroidism is described as a common disease, often with few symptoms which require no specific treatment in many cases (6) and conservative management is suggested particularly in asymptomatic elderly patients (7). We think that, untreated primary hyperparathyroidism, particularly in postmenapousal women may cause an increased loss of bone mass and increase the risk of fractures during the following years. On the other hand, it has been suggested that there are no methods of selecting those patients in whom symptoms or complications develop, so parathyroidectomy appears to be the treatment of choice for virtually all patients with hyperparathyroidism (8).

Definite indications for the surgical treatment of hyperparathyroidism are renal stones, parathyroid bone disease, young age and moderate to severe hypercalcaemia or significant hypercalciurua (1,5). Surgical therapy was performed in all of the our patients because they all have at least one indication according to these criteria. Although we could not able to evaluate bone mineral density in all patients, the existence of brown tumors in 38.4% and pathologic fractures in the 15.3% of the patients indicate that skeletal complications of hyperparathyroidism are still a serious problem in our population. It has been suggested that the occurence of nephrolithiasis in hyperparathyroidism has decreased to 10-15% (9,10). However, 61.5% of our patients have nephrolithiasis.

Twenty-five per cent of our patients (or 23% of patients with primary hyperparathyroidism) have normocalcaemic hyperparathyroidism. This may also be a conributing factor for the difficulty in the diagnosis of hyperparathyroidism. Vitamin D deficiency has been implicated in the pathogenesis of normocalcaemic hyperparathyroidism. It has also been suggested that vitamin D deficiency coupled with high PTH levels may lead to severe bone disease as a result of poor calcium reabsorbtion in renal tubules, poor calcium absorption from the gut and a consequent negative calcium balance (11). Although we could not measure 25 (OH) D3 levels in our patients, this may also be a contributing factor for severely affected bone disease in our population. Particularly, in terms of parathyroid bone disease and nephrolithiasis, these high rates of complications show that hyperparathyroidism could not be diagnosed early enough in this population. Similarly, patients with certain complications of hyperparathyroidism have been reported from different parts of Turkey (12).

It is interesting that two out of five patients with noduler goiter and hyperparathyroidism also have papillary microcarcinoma of the thyroid gland. One of these patients had been reported previously (13). Although the association between the thyroid disease and primary hyperparathyroidism has been previously described, the reason is not well known. Patients with hyperparathyroidism and a history of head and neck irradiation are thought to be at increased risk of thyroid carcinoma which are mostly occult tumors (14, 15). Neither of our patients had history of head and neck irradiation. We think that in patients with hyperparathyroidism and noduler goiter, the indications for subtotal thyroidectomy should not be too rigid and subtotal

thyroidectomy is a reasonable approach to the patients with noduler goiter and primary hyperparathyroidism.

A single parathyroid adenoma is the underlying cause in more than 80% of cases. Diffuse hyperplasia of all parathyroid glands occur in about 15-20% of patients (particularly in MEN 1 and 2A) and parathyroid carcinoma is very rare (<1%) (1). In our patients none of them have had MEN syndromes but two of the three patients with CRF showed parathyroid hyperplasia associated with tertiary parathyroid adenoma. In the absence of liver disease, the serum ALP levels often correlate with iPTH and may confirm the presence of uremic hyperparathyroidism. Despite the medical therapies such as dietary phophorus restriction, phosphate binders, calcium supplementation and vitamin D use, certain patients with CRF may require parathyroid surgery. But, when a parathyroid surgery is considered, differential diagnosis of osteomalasia should be clear because in the last condition parathyroidectomy will worsen the bone disease (16).

Preoperative localization methods such as USG, computed tomography and scintigraphy are not suggested for patients who have not parathyroid surgery previously. USG localised the adenoma in 62.5% of the patients and MIBI scintigraphy localised in all (seven) patients who were evaluated. Although our results show that MIBI scanning is a successful imaging technique, it is suggested that MIBI scintigraphy should not be used for diagnosing hyperparathyroidism and it should be reserved for localizing the abnormal parathyroid tissue in patients with hyperparathyroidism (17).

In conclusion, complicated hyperparathyroidism is an important health problem in our region and primary hyperparathyroidism should be kept in mind in all patients with bone and joint complaints. Also we think that, since the succesfull parathyroidectomy can be performed by experienced surgeons with minimal complications, it should be the treatment of choice.

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