Primary hyperparathyroidism – early diagnosis in patients referred for thyroid surgery

Robert A. Wahl
Franziska Hentschel
Christian Vorländer
Jochen Schabram

Abstract Background and aims: From 1986 to 1998, 190 patients presented for first-time operations for sporadic, non-malignant, non-multiple endocrine neoplasia primary hyperparathyroidism. Of these patients, 54% had been classified as “asymptomatic”, 41% as symptomatic and 5% as acute. One hundred and thirty-five patients (71%) were referred to us for parathyroid surgery. Fifty-five patients (29%) were referred for thyroid surgery with hitherto unknown hyperparathyroidism. This corresponds to a prevalence of primary hyperparathyroidism of 1% in patients referred for thyroid surgery (5450 patients during the same period of time). Patients/Methods: Patients referred for parathyroid surgery (group I, n=135) were compared with patients originally referred for thyroid surgery (group II, n=55). Group II was divided into group IIa: hyperparathyroidism preoperatively biochemically evident (n=26), and group IIb: borderline biochemistry, parathyroid enlargement evident at the operation (n=29). The groups were compared regarding clinical manifestations, serum calcium and parathyroid hormone, pathologic-anatomical substrates, operative complications and outcome. Results: Renal, osseous and gastrointestinal manifestations were more frequent in group I than in groups IIa and IIb (P<0.05). However, cardiovascular and neuromuscular symptoms were present in groups IIa and IIb in more than one-third of patients. Patients from group IIb were younger (49±12 years) than patients from groups IIa (60±13 years) and I (60±14 years). Adenomas were found in 85% of group I patients, in 45% of group IIa patients and in 21% of group IIb patients (P<0.01). In all other cases, hyperplasia was confirmed histologically. Serum calcium was higher in group I (3.0±0.42 mmol/l) than in groups IIa (2.63±0.16 mmol/l) and IIb (2.46±0.14 mmol/l) (P<0.01). Serum PTH was higher in group I (median 11.0 pmol/l) than in groups IIa and IIb (median 7.1 and 6.4 pmol/l, respectively) (P<0.05). Postoperatively, hypercalcemia persisted in two patients (1.1%) belonging to group I, with mediastinal adenomas. Serum calcium at discharge showed no differences between groups (group I: 2.22±0.16; group IIa: 2.22±0.15; group IIb: 2.20±0.11 mmol/l). Recurrent laryngeal nerve paralysis occurred early (4.2% of “nerves at risk”) and remained permanent (0.8% of “nerves at risk”) without significant differences between groups. Conclusion: Diagnostic efforts regarding parathyroid function should be mandatory before thyroid operations. “Asymptomatic” patients frequently (more than 30%) present with cardiovascular and neuromuscular, “unspecific” symptoms. Simultaneous parathyroid exploration is obvious in cases with biochemically evident primary hyperparathyroidism, but should also be performed in patients with borderline biochemistry.

Keywords Primary hyperparathyroidism · Calcium-screening · Parathyroid surgery · Thyroid surgery
Introduction

Surgery is the only curative treatment for primary hyperparathyroidism. While there is general agreement to operate on symptomatic patients with classical manifestations, there is often a considerable delay in diagnosis and treatment in so-called asymptomatic or mild hyperparathyroidism, which can be treated conservatively under certain conditions [1]. The aim of the present study was to compare patients referred to our surgical unit with the initial diagnosis of primary hyperparathyroidism with patients scheduled for thyroid surgery after being diagnosed as suffering from primary hyperparathyroidism subsequent to preoperative diagnostics. A comparison was also made with patients showing borderline or normal biochemistry preoperatively, but enlarged parathyroid glands intraoperatively (“incidentalomas”).

Patients and methods

From January 1986 to December 1998, 206 patients were operated on for primary hyperparathyroidism in our institution. Patients with multiple endocrine neoplasia (MEN)-I or II, parathyroid carcinoma and re-explorations were excluded. The remaining 190 patients who had a first-time operation for primary hyperparathyroidism were divided into: group I, patients referred for parathyroid surgery with primary hyperparathyroidism (n=135); and group II, patients referred to thyroid surgery, with previously unknown primary hyperparathyroidism (n=55). Group II was divided into two subgroups: group IIa, preoperatively evident primary hyperparathyroidism [serum calcium and parathyroid hormone (PTH) elevated; n=26] and group IIb, borderline serum calcium and/or PTH, parathyroid enlargement evident during the thyroid operation, no evidence of secondary hyperparathyroidism (n=29). In all these cases, classical bilateral parathyroid exploration was performed [2], primarily or in addition to the respective thyroid operation. In cases with single gland disease, the enlarged gland was removed. In multiple gland disease, the enlarged glands were removed; when all glands were enlarged, subtotal parathyrectomy was performed. Biopsies were used more deliberately in earlier years and have been restricted recently mainly due to situations when histologic confirmation of parathyroid tissue seemed to be necessary. The data were analyzed retrospectively regarding age, sex, clinical manifestations, pathologic-anatomical substrate, preand postoperative serum calcium and PTH, simultaneous thyroidectomy and complications (recurrent laryngeal nerve paralysis). Statistically, differences between the groups were tested with the chi-square test, Student’s t-test and the Wilcoxon/Mann-Whitney test: P<0.05 was regarded as adequately significant. Upon discharge from the hospital, follow-up was incomplete, with the exception of patients with persisting hypercalcemia or recurrent laryngeal nerve paralysis.

Results

Out of 190 patients, 55 (29%) were diagnosed by screening at thyroid surgery. Thus, with 5450 thyroid operations performed during this period of time, the incidence of primary hyperparathyroidism in this special population appropriates 1% (0.5% with clear cut diagnosis, which was missed before (group IIa), and another 0.5% in which hyperparathyroidism was borderline biochemically but definitely evident at the intraoperative situs, group IIb).

The differences between groups I, IIa and IIb are listed in Fig. 1 and Tables 1–3.

The mean age was 60 years in groups I and IIa and 10 years younger in group IIb. Thus, only group IIb had an earlier treatment in comparison with group I with respect to age (Table 1). The sex ratio of female/male was higher in groups IIa and IIb (2.7:1 and 3:1, respectively) as compared with group I (2.1:1) (Table 1).

Preoperatively, serum calcium levels were higher in group I than in group IIa and higher in group IIa than in group IIb. Also, serum PTH preoperatively was significantly higher in group I than in group II, with no difference between groups IIa and IIb. However, it has to be taken into account that PTH measurements were available in 7/29 patients of group IIb only. In the majority of this group, parathyroid exploration was based on borderline serum calcium and/or on the intraoperative situs only (“incidentalomas”). Postoperatively, serum calcium was in the mid-normal range in all groups at 2.2 mmol/l, and PTH was lower in group IIb, with no difference between groups I and IIa (Fig. 1).

Clinical manifestations

Almost all clinical manifestations were significantly more frequent in group I than in groups IIa and IIb (Table 1). This is not only true for the classic renal manifestations, with 30% vs 11% (15% in group IIa, 7% in group IIb) and osseous manifestations, with 53% vs 9% (15% in group IIa, 3.5% in group IIb). Gastrointestinal manifestations varied from 45% to 9% (8% and 10%), Ulcer disease as well as pancreatitis occurred in group I only (16% and 5%, respectively), whereas gastrointestinal symptoms in groups IIa and IIb were less specific. Cardiovascular symptoms, in particular hypertension, were the most frequent in all groups, with yet a significant difference between group I (59%) and groups IIa and IIb (42% and 38%, respectively). However, it has to be stressed that male patients of groups IIa and IIb, with 64% cardiovascular symptoms (54% hypertension), were as equally affected as in group I. Unspecific central nervous and neuromuscular symptoms showed no significant differences between the groups, but depression and fatigue where more frequent in group I (10% and 21%) than in groups IIa and IIb (5% and 7%), whereas minor vegetative symptoms were more frequent in groups IIa and IIb (18%) than in group I (10%). Acute hyperparathyroidism or crisis per definition occurred in group I only (7%). Altogether, 41% of the 190 patients from all groups had been classified as symptomatic (=specific symptomatic), 54% as “asymptomatic” and 5% as acute hyperparathyroidism.