

## AN UNEXPECTED HYPERPARATHYROIDISM AS A CONSEQUENCE OF RADICAL TREATMENT OF PRIMARY HYPERPARATHYROIDISM

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**AN UNEXPECTED HYPERPARATHYROIDISM AS A CONSEQUENCE OF RADICAL TREATMENT OF PRIMARY HYPERPARATHYROIDISM (Abstract):** The possibility of a rebound of the parathyroid hormone (PTH) plasma level after a temporary return to the physiological range following the ablation of a parathyroid adenoma is a well known phenomenon; on the opposite, the pathogenesis until now is not completely clear. This research includes 25 patients who underwent a parathyroidectomy for sporadic adenoma in the last 14 months. The aim of this communication is to identify the incidence and the duration of this phenomenon. In the 28% of the observations an unexpected increase of the PTH plasma level - with normal calcium serum levels and no clinical onset - has been detected after a temporary return to the physiological values in the immediate postoperative period. The normalization of the PTH was verified within 10-12 months in the three patients operated more than one year before, turning out to be a temporary phenomenon, as in the most part of the observations of the literature. The most decisive factors about the pathogenesis, after the confirmation of the absence of a mis-knowing parathyroid adenoma, seem to be the persistence of the “hungry bone syndrome”, the modification of the calcium sensibility of the parathyroid cells receptors and a microscopic hyperplasia of the residual parathyroid glands.

KEY WORDS: SECONDARY HYPERPARATHYROIDISM; PARATHYROIDECTOMY

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### INTRODUCTION

The possibility of a rebound of the parathyroid hormone (PTH) plasma level after a temporary return to the physiological range following the resection of a parathyroid adenoma was already evidenced in the '80s.

Anyway, for a long time a real attention hasn't been given to this phenomenon, probably because – the expected reduction of PTH in the hours and days immediately after the intervention when observed – the patient is considered definitely healed and any control is limited to the calcemia, also related to the elevated cost of the evaluation of PTH [1].

In those observations where the relapse of pathological plasmatic values of PTH is detected, we necessarily have the suspect (even though in most of the cases it will be not confirmed) of a misknowing of a second adenoma or a hyperplasia of the residual parathyroids.

The aim of this communication is to identify the incidence of this phenomenon and to make a hypothesis about the pathogenesis.

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## PERSONAL EXPERIENCE

The research includes 25 patients who underwent a parathyroidectomy (for hyperparathyroidism due to sporadic adenoma) in the last 14 months. There were 8 men and 17 women, aged between 34 and 84 years.

In seven of the twenty-five observations (28%) the increasing of the PTH plasma level (50-200% over the maximum normal value), with normal calcium serum levels, has been detected after a temporary return to the physiological values in the immediate postoperative period.

We are not able to precise the latency of the phenomenon from the intervention.

The first time the remark was occasional and it provoked strong concern related to the fear of a persistent hyperparathyroidism caused by a misknown lesion.

Ruled out this eventuality, mainly thanks to the verification of a normal calcemia, we have provided for an iterated check of PTH in the subsequent months, scheduling similar controls also for the following patients. In a recent case assiduous follow up was able to evaluate in the first postoperative day a calcemia under the threshold and a PTH plasma concentration significantly increased; in the fourth postoperative day after the intervention, the calcemia was normalized, whereas the plasma concentration of PTH remained elevated.

This way we had the opportunity to notice, first of all that the phenomenon is not at all exceptional: seven patients, the 28% of the ones taken in consideration, have shown this hormonal rebound post-parathyroidectomy. Secondly the normalization of PTH was verified within 10-12 months in the three patients operated more than one year before, as in the most part of the observations of the literature. In the other four patients, the parathyroidectomy is more recent and the hormonal rebound is still under way.

We also have to remark that no clinical onset has been associated with this unexpected and inappropriate sort of hyperparathyroidism.

## DISCUSSION AND CONCLUSIONS

The increasing of the PTH plasma levels – in presence of normocalcemia – after ablation of a parathyroid adenoma, doesn't represent an exceptional event and neither does it represent a negligible clinical condition.

From the literature data, the phenomenon was present in the 12-40% of the patients operated, commonly for a period of 3-12 months [2], sometimes persistent after one year or more [3] or even after fifteen years, as in the 11% of cases reported by Lundgren et al. [4].

Regardless of the frequency, the importance of this apparently unexplainable anomaly is due to the fact that – as well as for primary hyperparathyroidism – the involved patients have a significant increase of mortality for cardiovascular diseases.

In fact it seems demonstrated that the excess of PTH and calcium in the blood plays a hypertrophying effect on the myocardial musculature, effect that is reversible after the resolution of the hyperparathyroidism. It's not like this when the plasmatic increase of PTH persists – even without hypercalcemia – and in this situation the left ventricular hypertrophy remains, and with it the predisposition to hypertension and to myocardial ischemia [5].

There remains to clarify the numerous reasons of perplexity about the pathogenesis of this really peculiar sort of hyperparathyroidism post-parathyroidectomy.

The more plausible hypothesis is the one related to a process of adaptation to the bone demineralization that follows primary hyperparathyroidism [6].

The re-establishment after the removal of the cause needs an exceptional uptake of calcium and, therefore, a persisting solicitation of the residual parathyroids, even though the process shouldn't persist for a long time [7].

Likewise convincing – it's not excluded that the two events could be associated – is the possibility that the sensibility of the receptors of the residual parathyroid cells to the calcium would be modified, as they are accustomed to calcemic values higher than the physiological ones, re-established with the intervention.

Advanced age (>65 years old), and very high preoperative values of plasmatic PTH (>200 pg/mL) – with an accelerated bone turnover, as is evidenced by the increase of the alkaline phosphates and the decrease of the phosphoremy – very frequently are characteristic in these patients [8]. Maybe they are promoting factor, anyway they are elements that suggest an appropriate post-operative control.

Nevertheless it's necessary to underline the duty to probe the eventuality that the cause of the phenomenon could be a hypocalcemia due to a renal insufficiency, lack of vitamin D [9], bone tissue's diseases, intestinal malabsorption [10]

### CONCLUSIONS

The pathogenesis of hyperparathyroidism secondary to parathyroidectomy for adenoma keeps on being not completely clear. There is who has correlated it to a microscopic hyperplasia of the residual parathyroids after the adenoma exeresis. The most decisive factors seem to be the persistence offside of the usual time of the “hungry bone syndrome” and the modification of the calcium sensibility of the parathyroid cells receptors. An absolute or relative hypocalcemia could arise from the both and then the hyper-stimulation to the PTH release [2].

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