HIPERPARATIROIDISMO, CÁNCER

Título del artículo: Overproduction of an amino-terminal form of PTH distinct from human PTH(1-84) in a case of severe primary hyperparathyroidism: influence of medical treatment and surgery.
Revista: Clin Endocrinol (Oxf).. 2005; 62(6): 721-7
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Abstract original:

OBJECTIVE: Rare patients with severe primary hyperparathyroidism present with large parathyroid tumours, severe hypercalcaemia, very high PTH levels and osteitis fibrosa cystica. Some of these patients display a large amount of C-PTH fragments in circulation and present with a higher C-PTH/I-PTH ratio than seen in less severe cases of primary hyperparathyroidism. We wanted to determine how PTH levels and circulating PTH high-performance liquid chromatography (HPLC) profiles analysed with PTH assays having different epitopes could be affected by medical and surgical treatment in such patients.
DESIGN: A 55-year-old man with severe hypercalcaemia (Ca(2+): 2.01 mmol/l), very high PTH levels (CA-PTH 82.1 and T-PTH 72 pmol/l) caused by a large parathyroid tumour (7.35 g) and accompanied by significant bone involvement (alkaline phosphatase of 185 UI/l and subperiostal bone resorption of hands) was referred to us. Blood was obtained at various time points during his medical treatment, before and after surgery, to measure parameters of calcium and phosphorus metabolism, and of bone turnover. HPLC separations of circulating PTH molecular forms were performed and analysed with PTH assays having 1-4 (CA), 12-18 (T), 26-32 (E) and 65-84 (C) epitopes.
RESULTS: Before surgery, serum Ca2+ was nearly normalized with hydratation, intravenous (IV) pamidronate and oral vitamin D administration. Despite a decrease in Ca2+ to 1.31 mmol/l, CA-PTH and T-PTH levels decreased by half in relation to a threefold increase in basal 1,25-dihydroxyvitamin D [1,25(OH)2D] level (94 to 337 pmol/l). After this initial positive response, hypercalcaemia and elevated CA- and T-PTH levels recurred even if 1,25(OH)2D levels remained elevated. The tumour was removed surgically and proved to be poorly differentiated with nuclear atypia and mitosis. After surgery, the Ca2+ level and PTH secretion normalized. The higher CA-PTH level relative to the T-PTH level observed before surgery in this patient was related to the oversecretion of an amino-terminal (N) form of PTH recognized by PTH assays with (1-4) or (26-32) epitopes but not by the T-PTH assay with a (12-18) epitope. This molecular form represented 50% of CA-PTH measured in this patient, but only 7% in less severe cases of primary hyperparathyroidism. It was unaffected by medical therapy and disappeared after surgery.
CONCLUSION: The relationship between the overexpression of this N-PTH molecular form and severe primary hyperparathyroidism remains unclear. Further studies will be required in these rare patients to see whether N-PTH is a marker of less well differentiated parathyroid tumours and/or relates to the overproduction of C-PTH fragments in the presence of severe hypercalcaemia.