

Circulating forms of immunoreactive parathyroid hormone-related protein for identifying patients with humoral hypercalcemia of malignancy: A comparative study with C-terminal(109-141)- and N-terminal(1-86)-region-specific PTHrP radioassay

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We evaluated the circulating forms of immunoreactive PTHrP in 115 healthy subjects and 122 patients with malignant diseases by using radioassay systems (RAS) specific for the C-terminal (109-141) fragment of PTHrP (C-RAS) and for the N-terminal(1-86) (N-RAS). PTHrP levels in healthy controls ranged from 1.5 to 38.2 (mean: 24.5) pmol/L with the C-RAS and from 0.9 to 2.5 (mean: 1.7) pmol/L with the N-RAS. The ratio of circulating N-terminal fragment (N) to C-terminal fragment (C) of PTHrP was calculated to be about 1:14.4 in the healthy subjects. Of the 122 patients with malignant diseases, 40 (32.8%) had circulating PTHrP levels undetectable with the N-RAS, but only 11 (9.0%) patients had levels undetectable with the C-RAS. Of the former 122 patients, 41 (33.6%) had high PTHrP as determined with the C-RAS, and 10 (8.2%) had high PTHrP as determined with the N-RAS. The former of these included only 8 (19.5%) HHM patients, while the latter included 8 (80.0%) HHM patients. The circulating N to C ratio was about 1:70.7 in the HHM patients. The N and C obtained with the different RASs showed a close correlation ($r = 0.86$). The values also showed a close correlation with serum Ca; $r = 0.75$ for C-RAS and $r = 0.81$ for N-RAS. In addition, the correlations between the PTHrP reading obtained with the different RASs and serum Cr were: $r = 0.42$ with C-RAS and $r = 0.26$ with N-RAS. The circulating form of immunoreactive PTHrP fragments is therefore comprised mainly of PTHrP(109-141). In contrast, circulating concentrations of the PTHrP(1-86) fragment are very low, but detection of the PTHrP(1-86) fragment with the N-RAS is a more useful indicator of HHM with fewer false positive results and is less likely to be influenced by renal function than the detection of the PTHrP(109-141) fragment with C-RAS.

Key words: parathyroid hormone-related protein, humoral hypercalcemia of malignancy, radioassay, serum calcium