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Serum parathyroid hormone-related protein concentrations in patients with hematologic malignancies or solid tumors

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The clinical significance of parathyroid hormone-related protein in humoral hypercalcemia of malignancy was investigated by determining the serum parathyroid hormone-related protein concentrations in 167 normal subjects, 56 patients with hematologic malignancy and 144 patients with solid tumor. Serum parathyroid hormone-related protein was measured with a radioimmunoassay kit that recognizes the C-terminal portion of the molecule. The serum parathyroid hormone-related protein concentrations were 20.2–50.8 pmol/l (mean ± 2 SD) in normal subjects, and were elevated in 80% of the patients with malignancies with hypercalcemia, including squamous cell carcinoma and adult T cell leukemia. Moreover, two cases of B cell non-Hodgkin's lymphoma with hypercalcemia had high serum parathyroid hormone-related protein concentrations, which varied in parallel with the tumor size during the clinical course. Of 136 patients with solid tumors with normocalcemia, the serum parathyroid hormone-related protein concentration was slightly elevated in only 5.1%, all of whom were at an advanced stage. These data indicate that determination of the serum parathyroid hormone-related protein concentration is useful for differential diagnosis of humoral hypercalcemia of malignancy and prediction of its development.

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In 1987, four groups (1–4) purified parathyroid hormone-related protein (PTHrP) and Suva et al. (5) cloned and sequenced the gene of this protein. In addition, immunoreactive PTHrP was demonstrated in an extract of a humoral hypercalcemia of malignancy tumor (6, 7) by radioimmunoassay (RIA). In 1990, Burtis et al. (8) developed an immunoradiometric assay (IRMA) for PTHrP (1–74) and an RIA for PTHrP (109–138), and reported that both their assays were useful in the differential diagnosis of hypercalcemia. The value of determining urinary PTHrP (127–141) was also reported (9). However, the serum PTHrP levels in normal subjects are difficult to measure by these assays, and there have been few reports on the relationship between the clinical course and serum PTHrP level. Recently, Kasahara et al. (10) developed an RIA kit for PTHrP (109–141) with which we could measure the serum PTHrP concentrations in normal subjects and in patients with various diseases. Here we report data on the serum PTHrP concentrations in patients with hematologic malignancies or solid tumors who had normal serum creatinine levels, and the relationship between the clinical course and change in serum PTHrP.

Subjects and methods

Subjects

The subjects examined were 167 normal adults (92M, 75F) aged 20–60 years, 56 patients with hematologic malignancy and 144 patients with solid tumor.

Serum calcium was measured using the O-cresolphthalein complexing method after an overnight fast. The serum calcium concentration was corrected by the equation, "corrected calcium = measured calcium (mg/dl) + 4.0-albumin (g/dl)" and values in mg/dl were converted to mmol/l. Normal range of serum calcium was 2.25 ± 0.20 mmol/l (mean ± 2 SD). Hypercalcemia was defined as a serum calcium level of above 2.65 mmol/l (mean + 4 SD).

Serum creatinine was measured by Jaffé's test. No significant difference was observed between serum creatinine concentrations in normal subjects and tumor patients (mean ± 2 SD, 79.7 ± 26.6 vs 79.6 ± 17.7 μmol/l).