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Evaluation of serum concentration of parathyroid hormone-related protein and its implication in hypercalcemia in squamous cell carcinoma of the head and neck

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Abstract. Hypercalcemia is a common and serious complication associated with squamous cell carcinoma (SCC) and is considered to be caused by a tumor-derived factor, parathyroid hormone-related protein (PTHrP). However, the correlation between serum levels of calcium and PTHrP and the kinetics of PTHrP in SCC of the head and neck is unknown, because the behavior of the circulating form of PTHrP in patients has not been determined. In the present study, the PTHrP concentrations in serum samples from 54 patients (37 with SCC and 17 with benign tumors) were measured by a recently developed radioimmunoassay directed toward the C-terminal region of PTHrP, and the laboratory data including those calcium levels in corresponding samples were reviewed retrospectively. Results showed hypercalcemia in four patients with advanced cancer and in whom elevation of the serum PTHrP concentration was observed simultaneously. The regression analysis also revealed the linear relationship of the calcium level to the PTHrP concentration, but not to the concentration of phosphorus or creatinine, suggesting that monitoring of serum PTHrP level is useful for prediction of hypercalcemia associated with head and neck cancer.

Key words: hypercalcemia; PTHrP; serum PTHrP concentration; squamous cell carcinoma; head and neck cancer.

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Patients with neoplastic diseases including squamous cell carcinoma (SCC) of the head and neck often suffer from various complications, of which humoral hypercalcemia of malignancy (HHM) is a common and serious syndrome. Parathyroid hormone-related protein (PTHrP) has been isolated and cloned from hypercalcemic tumor cells[7,8,11,14] and is considered to be the predominant cause of HHM[9]. Recently, assay systems for detecting circulating PTHrP in patients have been developed and have assisted the diagnosis of hypercalcemia[2,13]. However, with these assays, it is difficult to determine the serum levels of PTHrP in normocalcemic patients or normal subjects. KASAHARA et al.[5] developed a novel radioimmunoassay directed toward a C-terminal region of PTHrP, consisting of the amino acid sequence 109 to 141, PTHrP (109–141), and reported measurement of the serum level of PTHrP as the concentration of PTHrP (109–141) in normal subjects. If hypercalcemia associated with head and neck cancer is actually caused by an increase of circulating PTHrP, its serum level should increase before the appearance of hypercalcemia or with progress of dis-