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Clinical Value of Calcitonin and Carcinoembryonic Antigen Doubling Times in Medullary Thyroid Carcinoma

Charles E. Jackson,* Robert A. Norum, Gary B. Talpos, Carolyn S. Feldkamp, and Armen H. Tashjian, Jr

Doubling times of basal and stimulated calcitonin (CT) levels and of random carcinoembryonic antigen (CEA) levels were compared over time in 11 patients with residual medullary thyroid carcinoma (MTC)—five with the sporadic MTC and six with the hereditary MTC. Four patients with an indolent form of the disease showed little change in CT levels over three to eight years and little change in CEA doubling times (42 to 70 months). Seven patients showing rapid progression of disease had CT doubling times of three to 11 months and CEA doubling times of two to 12 months (however, one patient showed no change in CEA). A twelfth patient had a marked increase in CT doubling during two separate periods of pregnancy and lactation. We conclude that both CT and CEA levels may be helpful prognostically in patients with residual MTC, and each should be determined at intervals. Doubling time calculations provide practical estimations whereby the effects of therapeutic approaches, pregnancy, and various environmental influences on the growth of MTC can be evaluated. (Henry Ford Hosp Med J1987;35:120-1)

Measurements of both calcitonin (CT) and carcinoembryonic antigen (CEA) in serum are of value in the clinical evaluation of patients with medullary thyroid carcinoma (MTC). Based on tumor size and age at surgery for MTC, we have calculated maximum volume doubling times to be 3.5 to 15 months in 20 patients (aged seven to 29 years) with multiple endocrine neoplasia type 2A (MEN-2A) and one to 2.5 months in five patients (aged two to five years) with MEN-2B (1). Miyauchi et al (2) and Saad et al (3) have reported the prognostic value of CT and CEA doubling times, respectively. We report here the CT (basal and stimulated) levels (normal < 0.35 ng/mL basal and < 0.55 ng/mL stimulated) and random CEA (normal < 2.5 ng/mL) levels measured over time in 11 patients with residual MTC (five with the sporadic form and six with the hereditary form of MTC).

Four patients were in an indolent stage of the disease in that they had no clinical evidence of rapid progression. Seven patients showed rapidly evolving disease, with four progressing to a fatal termination and three having rapid clinical progression as evidenced by palpation, thallium scintigraphy (4), or computed tomography.

The four patients in the indolent group showed little change in CT levels (basal and pentagastrin-stimulated levels) over three to eight years with little change in CEA during this period (doubling times 42 to 70 + months).

One patient, in the 15-month period before his death, had a basal CT doubling time of four months (32 to 460 ng/mL) and a CEA doubling time of eight months. One patient, in the 12-month period before her death, had a basal CT doubling time of three months (14 to 290 ng/mL) and a CEA doubling time of 12 months. Another patient, in the 37-month period before her death, had a basal CT doubling time of seven months and a CEA doubling time of 12 months. A fourth patient, in the 21-month period before his death, had a basal CT doubling time of 11 months and a CEA doubling time of 6.5 months.

One young patient with rapidly progressive tumor on palpation and thallium scan (4) had a basal CT doubling time of ten months and a stimulated CT doubling time of 11 months, with a CEA result persistently within normal limits. A second patient, in a 16-month period of increasing tumor burden, had a basal CT doubling time of nine months with a CEA doubling time of 14 months. A third patient, with rapidly advancing tumor burden on thallium scan and computed tomography, had a basal CT doubling time of seven months, decreasing later to two months, and a CEA doubling time of two months. This patient received radioactive iodine labeled anti-CEA (5) therapy (Dr. Stephen Stowe, Newark, NJ). Although his disease continued to progress clinically, this treatment was associated with a decrease in CEA levels, especially considering the rise expected on the basis of his CEA doubling time prior to treatment. It was noted that his CEA level increased at a more rapid rate than his CT level. Rougier et al (6) have discussed the occasional limitation of CT levels and the prognostic value of CEA determinations in the management of residual MTC, and Lippman et al (7) and Saad et al (3) have emphasized that virulent forms of MTC may show loss of immunoreactive CT. In MTC tissue culture studies, Tanaka et al (8) have associated this decrease in CT with the loss of chromosome 11 containing the gene which codes for CT.

A twelfth patient had stimulated CT doubling times averaging 46 months over 14 years and seven months during a 17-month period before his death, had a basal CT doubling time of 11 months and a CEA doubling time of 6.5 months.

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Figure—Serum calcitonin levels (basal • and stimulated ▲) and plasma CEA levels (△) in a 40-year-old woman with MEN-2A showing increases in calcitonin levels during two periods of pregnancy and lactation. The doubling time of calcitonin levels after stimulation averaged only 46 months during this 14-year period of observation during which the CEA levels remained low.

period encompassing one pregnancy and a marked increase in basal serum CT during a later pregnancy (Figure). Little is known about the effect of pregnancy and lactation on the progression of MTC. However, doubling time calculations may provide practical estimations by which the effects of pregnancy, calcium levels, and other environmental influences (9) on the growth of MTC can be evaluated.

We conclude that both CT levels and CEA levels may be helpful prognostically in patients with residual MTC and that each should be determined at intervals in attempts to ascertain the progression of the disease.

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