

## CALCITONIN AND MAMMARY CARCINOMA

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Ectopic production of hormones by neoplasms is a relatively unknown subject that may offer diagnostic possibilities. The calciotropic hormone calcitonin is known to be produced by the C-cells of the thyroid gland. The plasma calcitonin is usually increased in patients with medullary thyroid carcinoma (DEFTOS 1978). Increases in plasma calcitonin have also been found in patients with other endocrine malignancies, e.g. oat cell carcinoma of the lung and breast carcinoma (SILVIA et coll. 1974, COOMBES et coll. 1976). Especially when dealing with metastatic breast carcinoma, the plasma calcitonin level is reported to be increased in a majority of patients (COOMBES et coll. 1976, OLSEN et coll. 1978). An evaluation has been performed to elucidate whether determination of immunoreactive plasma calcitonin could be of any value in the preoperative examination of patients with breast carcinoma and whether calcitonin thus could be named a tumor marker. The results are now reported.

### Material and Methods

The material consisted of 33 women, mean age 56.8 years (range 36–88). Clinical examination, scintigraphy of the liver and skeleton, and microscopic examination of the breast specimen revealed no metastases in 13 patients.

Ten women had regional lymph node metastases and another 10 had known bone or other metastases.

Blood samples were obtained for determination of calcium, phosphorus, creatinine and calcitonin. Calcitonin was determined in serum by the radioimmunoassay method described by ALMQVIST et coll.

(1974). All determinations were made twice. The coefficients of variation were 18 per cent. The calcitonin levels were classified as normal or elevated.

### Results

All patients except 3 had normal plasma calcitonin levels (Table 1). Two of the 3 patients with elevated calcitonin had axillary lymph node metastases and bone metastases. Furthermore, one of these two women had large metastases in the liver and in both ovaries. Eight of the patients (24 per cent) had bone metastases but only 2 of these had elevated plasma calcitonin. Osteolytic bone metastases were found in 5 of these 8 women but only 2 of them had elevated plasma calcitonin. All 3 patients with elevated plasma calcitonin had normal serum calcium and phosphorus as well as creatinine.

### Discussion

Several authors (COOMBES et coll. 1975, OLSEN et coll., RASMUSSEN et coll. 1978) have found elevated plasma calcitonin in patients with breast carcinoma and particularly when distant metastases were present (Table 2). However, in the present series no correlation between plasma calcitonin level and women with breast carcinoma existed even in the presence of bone metastases.

The absence of correlation in the present series might be due to the fact that in the preparation of antibodies to human calcitonin, an extract from medullary carcinoma of the thyroid was used

(ALMQVIST et coll.). This may produce antibodies of another aminoacid composition than the corresponding calcitonin antibodies produced by breast carcinoma tissue. This suggestion is made as calcitonin from different species can differ in the aminoacid structure (DEFTOS). Such immunoheterogenicity has been further proved by ROOF et coll. (1979) in a series of patients with different types of malignant disease. However, high molecular weight immunoreactive calcitonin has been found in the plasma of patients with medullary carcinoma of the thyroid as well as in the medias in which breast carcinoma cells or cells from medullary carcinoma of the thyroid have been cultured (COOMBES et coll. 1976, DEFTOS, GOLTZMAN & TISCHLER 1978). This may indicate that the calcitonin antibodies should react towards calcitonin of both types of tissues.

The method used differs in one point from the method used by OLSEN et coll., who found a high correlation between calcitonin and breast carcinoma. They used synthetic calcitonin instead (DIETRICH et coll. 1975). However, this should not be responsible for the difference as mentioned.

Another reason for the poor correlation may be that calcitonin is not produced in the patients until bone metastases, and mainly osteolytic metastases, have appeared. OLSEN et coll. found that plasma calcitonin was frequently elevated in patients with osteolytic metastases. However, in the present material, 5 of 8 patients had metastases of this type but only 2 of them had elevated plasma calcitonin. The elevation of calcitonin in these patients could be a secondary effect and produced by the C-cells of the thyroid gland as a result of hypercalcemia due to osteolytic metastases. Recently, JØRGENSEN et coll. (1979) reported on 137 patients with breast tumours. They could not prove any increase in immunoreactive calcitonin in either benign or malignant tumors or the adjacent tissue. This is further emphasized in the present series, and a similar conclusion can be drawn from the results of RASMUSSEN et coll.

It may thus be concluded that the determination of plasma calcitonin is of no value in the evaluation of patients with breast carcinoma and it should not be referred to as a tumor marker of breast carcinoma.

### SUMMARY

Plasma calcitonin was determined in 33 patients with breast carcinoma. Eight patients had bone metastases as revealed at scintigraphy and radiography. Only 3 of the 33

**Table 1**

*Calcitonin in patients with breast carcinoma with or without visible metastases*

	Normal	Raised
No metastases	12	1
Regional lymph node metastases	10	0
Bone metastases (osteolytic bone metastases)	8 (5)	2 (2)
Total	30	3

**Table 2**

*Different series of plasma calcitonin in breast carcinoma*

	Number of patients with elevated plasma calcitonin	
	With or without regional metastases	With bone metastases
COOMBES et coll. (1975)	4/30	23/28
OLSEN et coll. (1978)	6/21	10/13
RASMUSSEN et coll. (1978)	0/8	1/26
Present series	1/23	2/10

patients had elevated plasma calcitonin, 2 had osteolytic bone metastases. It is concluded that the determination of plasma calcitonin is of no value in the evaluation of patients with breast malignancy and it should not be referred to as a tumor marker.

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