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SERUM CALCITONIN IN PATIENTS WITH OSTEOLYTIC AND OSTEOSCLEROTIC METASTASES FROM MAMMARY CARCINOMA

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Increased serum immunoreactive calcitonin (S-iCT) concentrations have been found in patients with mammary carcinoma (COOMBES et coll. 1976, MILHAUD et coll. 1977, OLSEN et coll. 1978). COOMBES et coll. found elevated S-iCT in 23 of 28 patients with breast carcinoma and metastatic disease, whereas only one of 13 with localized disease had increased levels, and OLSEN et coll. elevated S-iCT in patients with osteolytic bone metastases as compared with patients with local tumour. However, 2 patients with osteosclerotic metastases had very low S-iCT concentrations.

In contrast to these authors ROUSSEAU et coll. (1978) found marked hypercalcitonemia in a patient with osteosclerotic myeloma, and suggested that osteosclerotic bone lesions could be induced by ectopic secretion of calcitonin by tumour cells. Therefore, it was considered of interest to investigate whether S-iCT differed between patients with mammary carcinoma and osteolytic and osteosclerotic bone lesions, and furthermore to compare biochemical and clinical values in these two patient groups.

Material and Methods

The series consisted of 27 women with microscopically proven mammary carcinoma and with radiologically proven bone metastases; 19 had osteolytic and 8 osteosclerotic metastases. The mean age of the former group was 57.3 years (range 38–69), and of the latter 60.8 years (range 45–79). None of the patients received drug therapy or irradiation at the time of the present investigation. All patients had normal renal function evaluated by serum creatinine.

Serum concentrations of calcium, phosphorus, protein and calcitonin (S-iCT) were measured after fasting overnight. Serum calcium was corrected for individual variation in serum protein concentration (PEDERSEN 1973) and calculated as the calcium concentration corresponding to a protein level of 70 g/l (S-calcium corr.). S-iCT was measured by a radioimmunoassay as described previously (NIELSEN et coll. 1979, NIELSEN & OLSEN 1979) using a commercial antibody to synthetic human calcitonin (Calbiochem, USA) and synthetic human monomer calcitonin (Ciba, Switzerland) for standards and iodination. The detection limit was 20 pg/ml. Normal range was 0 to 120 pg/ml, and detectable values could be measured in 85 per cent of normal males and 59 per cent of normal females. The intraassay coefficient of variation was below 3 per cent at a serum concentration of 350 pg/ml and 14 per cent at a serum concentration of 30 pg/ml. The interassay variation coefficient was 14 per cent at a S-iCT concentration of 140 pg/ml.

A group of 13 normal women with a mean age of 47.4 years (range 37–57) was used as control group for the S-iCT values.

Statistical evaluation. Spearman's rank correla-

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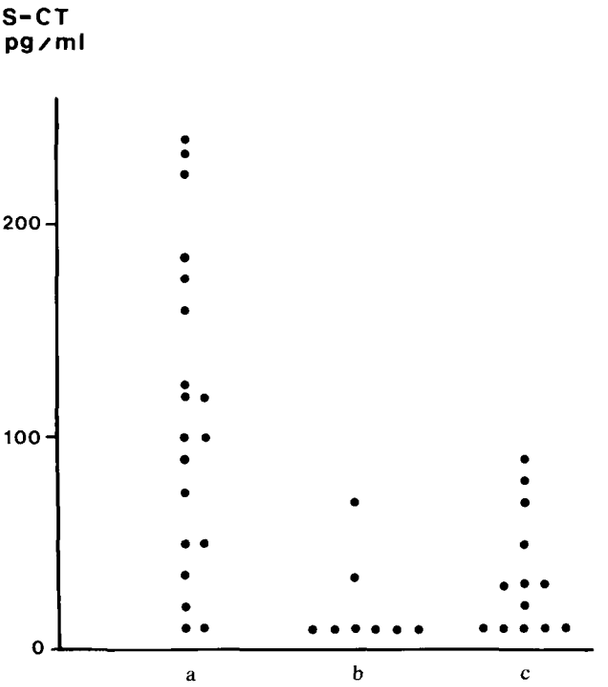
tion test was used for correlation analysis. The Mann-Whitney U-test was used for comparison of group means.

Results

A significantly higher S-iCT concentration was found in patients with osteolytic metastases as compared with patients with osteosclerotic ($p<0.01$; Figure) and with normal controls ($p<0.01$). No difference was found in S-iCT between patients with osteosclerotic metastases and normals. In the osteolytic group 11 of 19 patients appeared with S-iCT values higher than the maximum value in the control group, whereas in the osteosclerotic group all S-iCT values were normal.

One patient in the osteolytic group had hypercalcemia and 9 patients elevated S-alkaline phosphatase. None of the patients in the osteosclerotic group had hypercalcemia, whereas 6 had increased S-alkaline phosphatase. No significant difference was found in the values of S-calcium, S-phosphorus or S-alkaline phosphatase between the two groups (Table), nor any difference in the histologic classification of the tumour or in the localization of the bone metastases.



Serum calcitonin in patients with mammary carcinoma. a) Nineteen patients with osteolytic metastases, b) 8 with osteosclerotic metastases. c) Normal controls.

Discussion

Increased S-iCT was found in 11 of 19 patients with osteolytic bone metastases in contrast to normal S-iCT concentration in all 8 patients with osteosclerotic metastases. Previously, a high frequency of elevated S-iCT concentration was found in patients with metastatic disease from mammary carcinoma (COOMBES et coll. 1976, OLSEN et coll.).

RASMUSSON et coll. (1978) compared S-iCT in patients with osteolytic and osteosclerotic metastases. Normal or undetectable S-iCT was found in all but one of 26 patients, and no difference was demonstrated between patients with osteolytic and osteosclerotic metastases. The finding of normal or undetectable S-iCT values in most patients with osteolytic bone metastases is in contrast to most other reports on patients with breast carcinoma (COOMBES et coll. 1976, MILHAUD et coll. 1977, OLSEN et coll.). It might be due to that the patients in the series of these authors were treated with pred-

Table

Biochemical values (mean, range) in patients with mammary carcinoma and osteolytic and osteosclerotic metastases

Metastases	S-calcium corr. (mg/100 ml)	S-phosphorus (mg/100 ml)	S-alkaline phosphatase (units)	S-iCT (pg/ml)
Osteolytic (n=19)	9.74 (9.1–11.7)	3.6 (2.6–4.7)	426 (101–3 200)	112 (10-240)
Osteosclerotic (n=8)	9.75 (9.1–10.6)	3.4 (2.5–4.2)	283 (148–590)	21 (10–70)
p	NS	NS	NS	<0.01

nisone, anti-oestrogen and cytostatics during the analysis period.

Increased S-iCT in patients with malignant disease, other than medullary thyroid carcinoma, has been explained by an ectopic CT production from the tumour (COOMBES et coll. 1974, SILVA et coll. 1974) or by a physiologically increased CT secretion from the thyroid (SILVA et coll. 1975) to prevent osteolytic processes in the bones. In patients with pulmonary carcinoma both mechanisms have been demonstrated (SILVA et coll. 1974, 1975). In vitro experiments with lung and breast carcinoma tissue (COOMBES et coll. 1976) both types of tumour have been found to secrete CT. The present finding of increased S-iCT in patients with breast carcinoma with osteolytic, but not in those with osteosclerotic metastases, support the view that increased S-iCT may be due to a physiologically increased CT secretion to prevent osteolysis, rather than an ectopic production of CT.

SUMMARY

Serum concentrations of calcitonin, calcium, phosphorus and alkaline phosphatase were measured in 19 patients with osteolytic metastases and in 8 patients with osteosclerotic metastases from mammary carcinoma. A significantly higher mean S-iCT concentration was found in patients with osteolytic metastases as compared with those with osteosclerotic. No significant difference was found in S-calcium, S-phosphorus or S-alkaline phosphatase between the two groups.

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