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Hypercalcemia Associated with Transitional Cell Carcinoma without Bone Metastases: Description of Two Cases

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Key Words

Hypercalcemia
Transitional cell carcinoma
Bone scan

Abstract

Two cases of hypercalcemia associated with transitional cell carcinoma and negative bone scan are described. In both cases hypercalcemia appeared while there was evidence of tumor spread. Although hypercalcemia was controlled, both patients died shortly thereafter. Hypercalcemia rarely occurs in transitional cell carcinoma and its appearance may suggest spreading of the tumor and poor prognosis.

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Hypercalcemia is frequently associated with meta-static bone disease, it is less common in solid tumors without bone metastases, with only a few reports associating it with transitional cell carcinoma. Herein we present two cases of transitional cell carcinoma, one of the renal pelvis and the other of the bladder, with hypercalcemia and negative skeletal scan.

Case Reports

Case 1

L.L., a 48-year-old man, was admitted in January 1983 because of pain in the right loin and accelerated hypertension, with episodes of blood pressure value of 290/130. Physical examination on admission revealed moderate hypertension with Keith Wagener grade-I hypertensive retinopathy. Laboratory examinations were normal except for microscopic hematuria. Evaluation included a renal scan that demonstrated decreased perfusion of the upper pole of the right kidney and intravenous urography showed perfusion decreased secretion from the same region. Retrograde pyelography demonstrated a space-occupying lesion of the right renal pelvis which on angiography appeared to be avascular. Chest X-ray, liver and bone scan were negative. The patient was operated on and a tumorous mass was found in the renal pelvis, invading the perirenal fat tissue and blood vessels. Right nephrectomy was performed with incomplete resection of the tumor. The histology was of grade III transitional cell carcinoma with invasion of the renal parenchyma, the blood vessels and the right adrenal. The patient was readmitted in April 1983 because of polyuria and polydypsia accompanying a confusional state. On examination he was found to be cachectic and

dehydrated. Laboratory examination revealed: creatinine, 1.5 mg/dl; calcium, 15.3mg/dl, and phosphorus, 3.4 mg/dl. Skeletal scan revealed no bone metastases; protein electrophoresis was normal. The patient was treated with prednisone, saline infusion and furosemide and the calcium level decreased to 11.0 mg/dl. Albeit serum calcium decreased and the patient's condition deteriorated. He developed sepsis and died 4 weeks after admission.

Case 2

Z.A., a 67-year-old man, was admitted in April 1983 because of loin pain, anorexia and weight loss of 3 kg in the last month. He also complained of polyuria and constipation. In 1968 he underwent partial cystectomy because of transitional cell carcinoma of the bladder. Follow-up revealed recurrences that necessitated transurethral resection, the last was performed in April 1982. Physical examination revealed an enlarged irregular liver. Laboratory findings were: calcium, 13.9 mg/dl; phosphorus, 2.5 mg/dl, and creatinine, 1.7 mg/dl. The tubular resorption of phosphate was 46 %, protein electrophoresis was normal. Ultrasound examination of the kidney and the bladder showed right hydronephrosis, hydroureter and a tumorous mass occupying the posterior bladder wall. Skeletal scan revealed no bone metastases, liver scan and ultrasound were consistent with multimedullary liver. The patient was treated with saline infusions, furosemide and oral phosphate and the calcium level decreased to 11.6 mg/dl. However, kidney function deteriorated rapidly. The patient developed arrhythmia and cardiac arrest and died shortly thereafter.

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Discussion

Hypercalcemia is commonly associated with bone metastases, most frequently with carcinoma of the breast, lung and multiple myeloma. It is less common in solid neoplasms without bone metastases, but this association has received much attention since it is possible that these tumors release a factor which stimulates bone resorption such as: polypeptide with parathormone-like activity [1], prostaglandins of the E series [2] and vitamin D-like steroids [3]. Tumors of the uroepithelium are common. An incidence close to 20 per 100,000 in a population over the age of 40 was described by Gittes [4], but the association of these tumors with hypercalcemia in the absence of bone metastases is rare.

We describe here two patients with transitional cell carcinoma who developed hypercalcemia. In both of them hypercalcemia appeared with advanced disease and they died shortly thereafter. The association of hypercalcemia and large tumors of the uroepithelium was previously described by Eddeland and Hedelin [5]. We have been able to find 13 cases of hypercalcemia associated with uroepithelial tumors with documented histology in the literature. Of these tumors 4 were epidermoid carcinoma [5–9], 3 were squamous cell carcinoma [5, 10, 11], and 6 were transitional cell carcinoma [12–15]. Squamous cell carcinoma accounts for about 15% of all bladder tumors with about 76% of transitional cell carcinoma [16]. It is possible that squamous cell carcinomas are more commonly involved in releasing hypercalcemic factor similar to the finding by Bender and Hansen [17] in bronchogenic carcinoma. Evidence was found for two possible mechanisms that caused hypercalcemia in these tumors. Mandell et al. [13] and Beca-Giraudon et al. [8] described increased levels of parathormone in 3 cases. In 2 other cases McKay et al. [14] and Eddeland and Hedelin [5] found increased excretion of prostaglandin in the urine in the presence of a normal parathormone level.

These studies were not available in our cases. Hypercalcemia is rarely associated with transitional cell carcinoma and its appearance may suggest spreading of the tumor and poor prognosis.

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