Elevated parathyroid hormone-related peptide in a patient with an extragonadal germ-cell tumour and hypercalcemia

Steven Sorscher, MD

Hypercalcemia has been described as a paraneoplastic syndrome associated with most malignant lesions but is very rarely reported in association with germ cell tumours. Paraneoplastic hypercalcemia is typically related to the production of parathyroid hormone–related peptide (PTHrP).[1] I describe here what I believe to be the first case of germ cell tumour with hypercalcemia and confirmed PTHrP elevation.

Case report

A 49-year-old man arrived with abdominal pain, an elevated serum calcium level of 2.8 mmol/L (normal 2.1–2.6 mmol/L) and a history of bilateral undescended testicles, followed by left orchiopexy at 13 years of age and right inguinal exploration orchiectomy at 22 years. Computed tomography revealed a right retroperitoneal mass, 15 × 13 cm in dimension. A biopsy specimen showed nonseminomatous germ-cell tumour (seminoma and yolk sac elements). Bone scanning and ultrasonography of the left testicle showed nothing abnormal. Results of laboratory tests included serum albumin 25 g/L (normal 32–57 g/L), α-fetoprotein (AFP) 2766 μg/L (normal 0.2–10 μg/L), parathyroid hormone (PTH) 5.8 ng/L (normal 7–53 ng/L) and PTHrP 2.0 pmol/L (normal 0–1.5 pmol/L). Chemotherapy with bleomycin, etoposide and cisplatin had a marked response on CT and in laboratory values (including calcium, AFP, PTH and PTHrP), which returned to normal.

Discussion

Germ cell tumours may be testicular or extragonadal and seminomatous or nonseminomatous. In 1978, 2 cases of testicular germ-cell tumour with hypercalcemia were described, but the causative mechanism was not confirmed.[2] In 1992, da Silva and associates[3] reviewed all cases of extragonadal germ-cell tumour with hypercalcemia reported in the English literature to that time (3 cases) and presented 4 new cases of seminoma. None of the patients had bone metastases. No PTHrP levels were measured. In their opinion the hypercalcemia was not caused by PTHrP elevation. They noted that PTHrP had been associated with enhanced urinary excretion of adenosine monophosphate (AMP), which was not found in any of their 4 patients with seminoma. Further support for a non-PTHrP mechanism was seen in 1 of the 3 previously reported cases.[4] Grote and Hainsworth[4] had described an extragonadal seminoma with increased calcitriol level and concluded that this increased level caused the hypercalcemia, since PTHrP reportedly does not raise calcitriol levels.[4]

Finally, in 1995 MacDiarmid and Norman[1] reported the first case of extragonadal nonseminomatous germ-cell tumour associated with hypercalcemia. Because bone scans were equivocally abnormal, they suggested a humoral mechanism for the hypercalcemia without obtaining a PTHrP measurement.

In the case of extragonadal nonseminomatous germ-cell tumour reported here, PTHrP was found to be elevated and PTH suppressed, as would be expected when PTHrP is the cause of hypercalcemia. Abnormal laboratory findings normalized, and the tumour responded to chemotherapy.

After a careful review of the literature, I conclude that this represents the first case of biochemically confirmed PTHrP-induced hypercalcemia in a germ cell tumour and the second case of an extragonadal nonseminomatous germ-cell tumour associated with hypercalcemia. Although PTHrP production is the commonest mechanism for paraneoplastic hypercalcemia of a malignant tumour, there are other previously described possibilities.

Competing interests: None declared.

References

1. MacDiarmid SA, Norman RW. Extragonadal nonseminomatous germ cell tumour with hypercalcemia, masquerading as renal cell carcinoma: a case report. *Can J Surg* 1995;38:80-2.

2. Metcalfe JB, Carey TC, Barry JM. Genitourinary malignancy and pseudohyperparathyroidism. *J Urol* 1978;119:702-4.

3. da Silva MA, Edmondson JW, Eby C, Loeher PJ. Humoral hypercalcemia in seminomas. *Med Pediatr Oncol* 1992;20:38-41.

4. Grote TH, Hainsworth JD. Hypercalcemia and elevated serum calcitriol in a patient with seminoma. *Arch Intern Med* 1987;147:2212-3.

From the Department of Hematology and Oncology, Marshfield Clinic, Wausau, Wisc.

Correspondence to: *Dr. Steven Sorscher, Marshfield Clinic—Wausau Center, Oncology Clinic W2G, Wausau WI 54401; fax 715 847-3147; sorscher.steven@marshfieldclinic.org*