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Title

Case report: Penile squamous cell carcinoma associated with severe hypercalcemia and high levels of Parathyroid Hormone related Peptide (PTHrP) expressed in metastatic skin tissue.

Ricardo E. Barcia ^{(a)*}, María Julia Martín ^{(c)*}, Alejo Pérez de la Hoz ^(a), María de los Angeles Juárez ^(b), Claudia Gentili ^{(c)**}

(a) VI Cátedra de Medicina Interna, Hospital de Clínicas José de San Martín, Facultad de Medicina. Universidad de Buenos Aires. Buenos Aires. Argentina.

(b) Departamento de Patología. Hospital de Clínicas José de San Martín. Buenos Aires. Argentina.

(c) Instituto de Ciencias Biológicas y Biomédicas del Sur (INBIOSUR), Dept. Biología Bioquímica y Farmacia, Universidad Nacional del Sur-CONICET, Bahía Blanca, Argentina.

*Ricardo E. Barcia and María Julia Martín contributed equally to this work.

**Adress for Correspondence:

Dr. Claudia Gentili

Dept. Biología, Bioquímica y Farmacia-INBIOSUR

Universidad Nacional del Sur

San Juan 670

(8000) Bahía Blanca- Argentina

Tel.: 54-291-4595100, ext. 2430

Fax: 54-291-4595130

E-mail: cgentili@criba.edu.ar

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Abstract

It is known that high levels of parathyroid hormone-related protein (PTHrP) correlate with a bad prognosis in malignancies. Here we present a patient with advanced penile cancer (PC) without antecedents of HPV infections and bone metastases but with severe hypercalcemia. By qPCR we observed high levels of PTHrP mRNA in metastatic cutaneous tissue. This is the first reported case in Argentina of hypercalcemia induced by PTHrP in human PC. Furthermore, the association of PTHrP and this disease through qPCR allows us to consider this molecular technique as a novel tool for diagnosis in patients with PC.

Here we present a 49-year-old man with penile squamous cell carcinoma and severe hypercalcemia, without bone metastases and with normal and low levels of PTH and calcitriol (40 pg/mL and 13 ng/mL, respectively). He had no antecedents of HPV infections or phimosis.

During his hospitalization, the metastatic lesions on the skin rapidly increased (**Figures 1A and 1B**). A tumor tissue biopsy was obtained and revealed invasive squamous cell carcinoma, poorly differentiated (**Figures 2A and 2B**). qPCR revealed that PTHrP mRNA levels of tumor tissue were significantly higher than those observed in healthy skin (>40000 fold), indicating that the patient had humoral hypercalcemia of malignancy (HHM) secondary to secretion of PTHrP by PC.

Malignancy is the most common cause of hypercalcemia in hospitalized patients and HHM is secondary to the secretion of PTHrP¹⁻³. PC is a rare diagnosis in developed nations⁴. In Argentina, the cases of PC reported are associated with HPV and phimosis^{5,6} and until now there are no reports of PC associated with other causes.

Potential prognostic biomarkers in PC were identified by qPCR⁷. Herein, qPCR is employed for the first time as an innovative molecular technique for diagnostic applications in patients with PC.

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Figure legends



Figure 1. A. Invasive squamous cell cancer of the penis, one year after penectomy and chemotherapy, with metastatic lesions in the skin. **B.** During hospitalization, these lesions rapidly increased. This photo was obtained 5 days later with respect to the one shown in A.

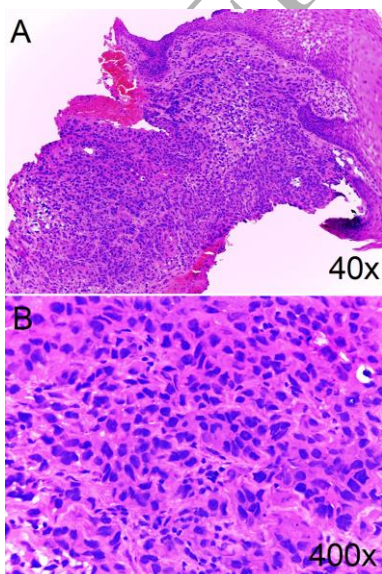


Figure 2. Squamous cell carcinoma, poorly differentiated. Atypical cells extend into the deep dermis. **A.** hematoxylin and eosin x 40. **B.** hematoxylin and eosin x 400.

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