Papillary urothelial bladder carcinoma associated with osteoclast-like giant cells

Stefan Krüger1, Reiner Johannisson1, Ingo Kausch2 & Alfred C. Feller1

1Institute of Pathology and 2Department of Urology, University of Schleswig-Holstein, Lübeck, Germany

Abstract. We report the case of a papillary urothelial carcinoma associated with osteoclast-like giant cells. A 60-year old woman presented with hematuria. A papillary neoplasm was detected by cystoscopy and removed transurethrally. Histological examination revealed a papillary urothelial carcinoma (grade I) associated with multiple stromal giant cells, which displayed morphological, ultrastructural and immunohistochemical characteristics of osteoclast-like giant cells. The formation of osteoclast-like giant cells in association with urothelial bladder carcinoma is a rare event, of which only six cases have been reported in the Anglo-American literature. It may cause diagnostic problems because primary giant cell tumor, giant cell carcinoma and foreign body stromal reaction have to be considered. Immunohistochemistry and electron microscopy may help to rule out these differential diagnoses.

Key words: Bladder, Osteoclast-like giant cells, Urothelial carcinoma

Introduction

The association of osteoclast-like giant cells with urothelial bladder cancer is a very rare event, of which only six cases have been described in the Anglo-American literature [1–4]. In three of these cases, this phenomenon was regarded as an unusual stromal reaction pattern secondary to urothelial carcinoma [2, 4], while a collision tumor of urothelial bladder carcinoma and primary osteoclastoma was assumed in the other three patients [1, 3]. The occurrence of abundant osteoclast-like giant cells may cause diagnostic problems, because other differential diagnoses like primary giant cell tumor, giant cell carcinoma or foreign body stromal reaction have to be considered. Here, we describe the seventh case of urothelial bladder carcinoma associated with osteoclast-like giant cells, and the first including ultrastructural findings.

Case report

A 60-year-old, previously healthy woman presented at the Department of Urology with a 2-week history of hematuria. Ultrasonographically, the urinary tract was un conspicuous except for a slight thickening of the right bladder wall. No intravesical tumor mass was detectable. Cytologic urine sample examination revealed signs of inflammation and hematuria as well as some urothelial cells with slight nuclear atypia, whose dignity remained obscure. No giant cells were detected cytologically. By cystoscopy, a papillary tumor measuring 1 cm in diameter was detected at the right bladder wall. The total tumor was resected in fragments which were immediately fixed in formalin for histopathological examination.

Histology revealed a non-invasive (stage pTa) papillary urothelial carcinoma (grade I according to the World Health Organization [5]; Figure 1). Moreover, a highly cellular subepithelial stroma containing abundant histiocytes and giant cells was evident. The morphology of the giant cells, which contained at least 8–10 haphazardly scattered nuclei each, was highly reminiscent of osteoclast-like giant cells (Figure 2). Immunohistochemically, these cells displayed significant reactivity for tartrate-resistant acid phosphatase...
(Figure 3) and CD68. No epithelial giant cells were detectable by immunohistochemistry using three epithelial markers (antibodies against pan-cytokeratin (KL1), human epithelial antigen (BE-REP4), and epithelial membrane antigen (EMA)). Ultrastructurally, the cytoplasm of the giant cells was filled with numerous mitochondriae (Figure 4).

Following transurethral tumor resection, the patient was released from our Hospital. Cytological controls of urine samples after 3, 6 and 12 months were without pathologic finding. The patient felt well and did not report any further hematuria.

Discussion

Urothelial bladder carcinomas may occasionally induce unusual stromal reaction patterns, like pseudosarcomatous stroma, osseous or cartilaginous metaplasia, or the formation of osteoclast-like giant cells. The diversity of stromal appearances of bladder cancer has important implications in differential diagnosis [6]. Concerning osteoclast-like giant cells, other differential diagnoses like primary osteoclastoma, giant cell carcinoma or foreign body stromal reaction have to be considered. The distinction of a giant cell tumor (osteoclastoma) from an osteoclast-like giant cell reaction may be difficult [1, 2]. Cellular atypia, mitotic activity of mononuclear stromal cells and blood vessel permeation of the giant cells may warrant the diagnosis of a primary giant cell tumor, while lack of these features and association with coexisting bladder

![Figure 1. Histology of a non-invasive papillary urothelial carcinoma, grade I (×100; H & E). An inflammatory tumor stroma is evident (no giant cells detectable in this area).](image)

![Figure 2. Higher magnification of the submucosal stroma. Numerous giant cells reminiscent of osteoclast-like giant cells are present (×600; H & E).](image)

![Figure 3. The giant cells display significant tartrate-resistant acid phosphatase reactivity (×600; immunohistochemistry).](image)

![Figure 4. Electron micrograph showing a part of a giant cell with two nuclei (N) and abundant mitochondriae, which are exemplarily marked by black arrows; the cell membrane is marked by an empty arrow (×10,000; epon embedding).](image)