Concurrent Malakoplakia and Papillary Urothelial Carcinoma of the Urinary Bladder

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Abstract. A case of malakoplakia and papillary urothelial carcinoma of the urinary bladder is reported. In this case, malakoplakia was an incidental finding in a biopsy of the urinary bladder of a 74-yr old female, who presented with hematuria. The biopsy showed a low-grade papillary urothelial carcinoma in close association with malakoplakia. This is a rare association of these lesions. (received 6 November 2000, accepted 30 November 2000)

Key words: malakoplakia; Michaelis-Gutmann bodies; papillary urothelial carcinoma

Introduction

It has been nearly a century since malakoplakia was first described by Michaelis and Gutmann [1]. By far, the most common location of this inflammatory lesion is the genitourinary tract, predominantly the urinary bladder [2-5]. Although it is known to occur subsequent to infections, malakoplakia has also been described in association with a variety of tumors, with or without a history of infection [2,4]. Two cases of malakoplakia of the bladder preceded by urothelial carcinoma have been recorded, but none has been seen concurrently with malakoplakia in the same specimen [4,5]. We report a case of malakoplakia and low-grade papillary urothelial carcinoma of the urinary bladder seen in the same biopsy.

Case Presentation

A 74-yr old female presented with hematuria. Her family history included breast cancer in her mother, leukemia in a sister, and myocardial infarction in a brother. Her father died of unknown cause. Urinalysis was significant only for the presence of numerous red blood cells. Bladder biopsy revealed a low-grade papillary urothelial carcinoma in close association with malakoplakia. Histologically, the neoplastic cells were characterized by papillary fronds and nests of urothelial cells. Intracytoplasmic inclusion bodies were present, consistent with malakoplakia. These findings are consistent with the histological features described in the literature. The patient underwent transurethral resection of the bladder tumor and is currently under observation.

Fig. 1. Photomicrograph of an H&E-stained bladder biopsy showing low-grade papillary urothelial carcinoma, associated with an aggregate of histiocytes in the lamina propria, containing intracytoplasmic inclusion bodies (x 100).
blood cells. No pyuria or bacteriuria was noted. Urine
cultures failed to show bacterial growth. After
preliminary examinations, cystoscopy showed a 5-cm
tumor in the lateral wall of the urinary bladder. Biopsy
was performed.

Materials and Methods

Paraffin-embedded sections of formalin-fixed tissue
were studied by routine histology using hematoxylin
and eosin (H & E), von Kossa’s, Giemsa’s, and Periodic
Acid-Schiff (PAS) stains. Immunohistochemistry was
performed on an automated immunostainer (Ventana
Corp, Tucson, AZ) by the avidin-biotin complex
technique, using monoclonal antibodies to CD68
(KP1, Ventana Corp.). Electron microscopic
examination was performed on formalin-fixed tissue
by standard methods.

Results

The bladder mucosa showed a papillary neoplasm
composed of disordered epithelial hyperplasia, mild
cellular pleomorphism, and occasional mitoses. These
findings were diagnostic of a low-grade papillary
urothelial carcinoma. The tumor was confined to the
lamina propria with no evidence of muscle invasion
or necrosis (Fig. 1). In the lamina propria and in close
proximity to the neoplasm, there were numerous
aggregates of CD68-positive cells with abundant
eosinophilic and granular cytoplasm surrounded by
various numbers of plasma cells and lymphocytes. The
PAS, toluidine blue, and von Kossa’s stains revealed
targetoid cytoplasmic inclusions in histiocytes (Fig. 2).
Occasional extracellular bodies of identical morphology
were also noted. Giemsa’s stain did not reveal any
organisms. Electron microscopy showed membrane-

Fig. 2. Light photomicrograph of a toluidine blue-stained 1-micron plastic section from the tumor,
showing a group of histiocytes containing many dense phagolysosomes as well as occasional “classic”
Michaelis-Gutmann bodies (arrow). Several small lymphocytes and plasma cells are also present.
The aggregate of reactive cells is flanked by urothelial carcinoma (magnification x 600).
bound bodies of varying size as well as characteristic laminated and calcified Michaelis-Gutmann inclusions (Fig. 3).

The patient was managed conservatively with no further medical or surgical intervention. She was well with no evidence of recurrence on last follow-up.

**Discussion**

Malakoplakia is an inflammatory process composed of loose infiltrate of foamy macrophages. The significance of bacterial infection as an etiologic factor cannot be overemphasized. Malakoplakia is related to chronic gram-negative bacterial infection, frequently *E. coli* and occasionally *Proteus* species. Malakoplakia is also seen with increasing frequency in immunosuppressed patients, particularly in transplant recipients. Abnormality of the phagosomes points to a defect in phagocytic function of macrophages [7]. Upon ultrastructural examination, the histiocytes contain intracytoplasmic, and occasionally extracellular, bodies of varying size and shape, which are believed to be bacteria in various stages of degradation [7,8]. The characteristic Michaelis-Gutmann bodies are considered the end-stage of this phagolysosomal degradation process [7]. However, cases of malakoplakia without clinical or laboratory evidence of infection have been reported. Some of these cases, including ours, were associated with neoplasms [2,6,9,10]. In these cases, malakoplakia was identified prior to, concurrent with, or subsequent to the diagnosis of malignancy [4,5,9,11]. Their morphology was identical to their counterparts in non-neoplastic settings.

Four cases of malakoplakia and malignancies of the urinary bladder have been reported [4,5,11,12]. One was a primary squamous carcinoma, one was a primary lymphoma of the urinary bladder, and the other two were urothelial carcinomas. History of urinary tract infection was elicited in each of these cases.

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**Fig. 3.** Electron micrograph of portions of the cytoplasm of two histiocytes, containing many residual body phagolysosomes. A large Michaelis-Gutmann body is on the right side of the figure. A histiocyte nucleus is labeled “N” (x 18,500).
In the two cases associated with urothelial carcinoma, malakoplakia was diagnosed after treatment of the carcinomas. To our knowledge, the present case is the first report of malakoplakia observed concurrently with papillary urothelial carcinoma of the bladder. The case differs from the previously reported cases in the absence of any history of urinary tract infection. This case report documents a rare association of two characteristic lesions of the urinary bladder.

References