Human Pathology (2006) 37, 1577–1582

Human PATHOLOGY
www.elsevier.com/locate/humpath

Inverted urothelial papillomas with foamy or vacuolated cytoplasm

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Received 3 March 2006; revised 19 May 2006; accepted 31 May 2006

Keywords:
Inverted papilloma;
Urothelial;
Xanthomatous;
Vacuolated;
Foamy

Summary Inverted papillomas of the bladder are uncommon benign neoplasms characterized by endophytic growth of urothelial cells as anastomosing cords, displaying minimal cytologic atypia. Reports of inverted papilloma associated with urothelial carcinoma or urothelial carcinoma arising within inverted papilloma highlight the difficulties in evaluating urothelial lesions with inverted growth patterns. Within the spectrum of findings in inverted papilloma, vacuolization and foamy (xanthomatous-appearing) cytoplasmic changes have not been previously reported. In the current study, we present 5 novel cases of inverted papilloma involving 2 men and 3 women ranging in age from 48 to 88 years, who presented with microhematuria (n = 3) or irritative symptoms (n = 2). Cystoscopically, the lesions were polypoid (n = 3), pedunculated (n = 1), or solid (n = 1), measured between 0.7 and 2.5 cm, and were all located at the trigone or bladder neck. Morphologically, all cases had some component of usual inverted papilloma along with areas displaying foamy or vacuolated cytoplasm encompassing 30% to 90% of the lesion. These "clear cells" were seen both in distinct regions within the biopsy and, more frequently, intermingled with usual inverted papilloma cells. In 3 of 5 cases, these findings were sufficiently unusual to cause confusion with urothelial carcinoma. The diagnostic dilemma encountered in these cases of inverted papilloma with foamy or vacuolated cytoplasm warrants their distinction from other benign and malignant urothelial lesions with inverted growth and/or clear cell features.

1. Introduction

Initially recognized by Paschkis in 1927 [1] and named by Potts and Hirst in 1963 [2], inverted papillomas are rare but distinctive urothelial lesions that account for between 1% and 2.2% of bladder neoplasms [3-5]. They predominantly occur in males [6-9], present clinically with hematuria or dysuria, and have a smooth polypoid appearance on gross or cystoscopic examination [8]. Although the classic morphologic criteria for inverted papilloma have long been defined [10], reported cases with aberrant cytologic features have caused significant confusion regarding the biologic potential of inverted papilloma [3,4,9,11]. The current study

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doi:10.1016/j.humpath.2006.05.014

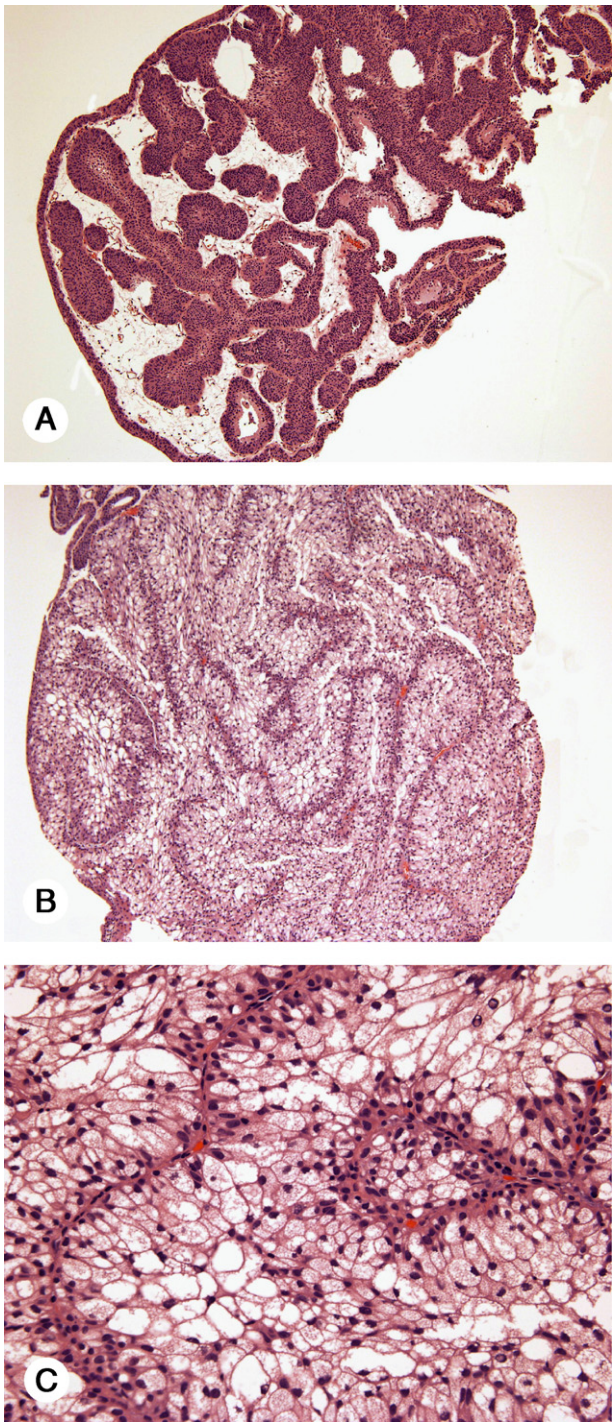

Fig. 1 Case 1. Fragment of usual-appearing inverted papilloma (A). Separate fragments demonstrating anastomosing cords thickened by cells with abundant cytoplasm (B). High-power view of foamy (xanthoma-like) cells seen in the broad anastomosing nests (C).

describes a series of inverted papilloma with foamy (xanthomatous-appearing) or vacuolated cytoplasm, findings that may cause sufficient cytologic and architectural distortion to suggest a diagnosis of urothelial carcinoma.

2. Materials and methods

We identified 5 cases of inverted urothelial papilloma with either foamy or vacuolated cytoplasm from consultative files and collected and re-reviewed all original slides. Each case was evaluated histologically for the presence of usual inverted papilloma architecture, percentage of lesion demonstrating foamy or vacuolated cytoplasm, nature of the stroma, and the presence of nuclear atypia. We also noted whether regions demonstrating foamy or vacuolated features were intermingled with areas of usual inverted papilloma in the same fragment or present in distinct fragments. Paraffin blocks were obtained for each case and unstained sections were stained with periodic acid-Schiff (PAS), PAS with diastase (PAS-D), and mucicarmine stains to determine whether unusual cytoplasmic features were the result of glycogen or mucin accumulation. Additional unstained paraffin sections from each case were immunohistochemically labeled for vimentin and cytokeratin 7 (CK7) by using standard three-step biotin-strepavidin protocols. Finally, the provisional diagnoses of the submitting institutions were reviewed, and demographic, cystoscopic, and clinical presentation data were obtained from the patients' urologists.

3. Results

Of the 5 patients studied, 2 were male and 3 were female with a mean age of 67.6 years (range, 48-88 years). Three of 5 patients presented with microscopic hematuria and 2 with irritative symptoms of urgency, frequency, and/or incontinence. Cystoscopically, the lesions were polypoid (n = 3), pedunculated (n = 1), or solid (n = 1) and were located at or adjacent to the trigone or bladder neck. Three cases were submitted with a differential diagnosis of either invasive urothelial carcinoma (n = 1) or inverted growth pattern of low-grade urothelial carcinoma (n = 2). The remaining

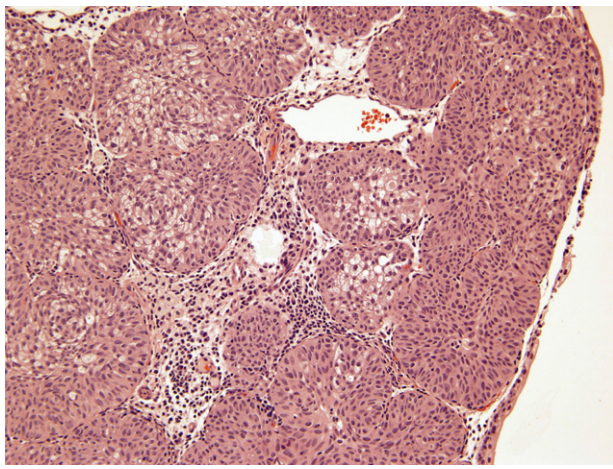

Fig. 2 Case 2. Admixture of foamy cells with more typical-appearing cords of inverted papilloma.