Urothelial melanosis of the bladder

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Urothelial melanosis is a rare finding characterized by abnormal pigmentation noted on cystoscopic evaluation and histologically defined by melanin deposition in the urothelium. Although generally considered benign, few cases of urothelial melanosis have been reported in the literature and the risk of recurrence or progression remains largely unknown. Four cases associated with urothelial cell carcinoma have been previously described. Here, we report a case of urothelial melanosis and review previously published cases in the literature.

Key Words: melanosis, melanin, bladder, urothelium

Introduction

Melanosis is a histologic term describing benign tissue deposits of melanin pigment with documented cases occurring in the skin, oral mucosa, colon, and, rarely, in the bladder.[1] No pathophysiologic mechanism explaining the abnormal melanin deposition in such cases has been reported. Due to its rarity and especially those found in the bladder, the natural history of such lesions is largely unknown. The medical literature contains only 12 reported cases of urothelial melanosis.[1-7]

Symptoms of individual urothelial melanosis cases are variable ranging from minimal to more profound urinary complaints. Cystoscopically, the lesions are grossly evident and have been described as diffuse black or brown discoloration of the urothelium. The differential diagnosis for such lesions include reactive urothelium, carcinoma in situ, urothelial carcinoma, adenocarcinoma, and benign etiologies such as vascular or pigmentation abnormalities. Due to this diagnostic uncertainty, urothelial biopsy is needed to rule out malignancy.

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Further treatment and surveillance of urothelial melanosis after biopsy is unclear, with variable suggestions reported in previous cases. Additionally, the risk of melanosis or melanoma in other organ systems is largely unknown. We report a new case of urothelial melanosis and discuss the clinical implications of this diagnosis based upon the current literature.

Case report

A 65-year-old Caucasian male non-smoker with a history of hypertension presented for evaluation of gross hematuria and clot retention. He reported a several year history of lower urinary tract symptoms including nocturia, urinary frequency, and weak stream. Due to the severity of the hematuria, a Foley catheter was placed for bladder irrigation to remove suspected intravesical clots. Five days later, he returned for cystoscopy revealing moderate bladder trabeculations with a large area of brownish discoloration at the bladder dome and patchy areas of similar brown discoloration along the anterolateral bladder wall. Urine cytology collected at the time of cystoscopy was interpreted as "atypical urothelial cells of uncertain significance." A CT urogram completed as part of standard gross hematuria upper tract evaluation was unremarkable. The patient was subsequently taken to the operating room with cystourethroscopy again revealing patchy brown discoloration over much

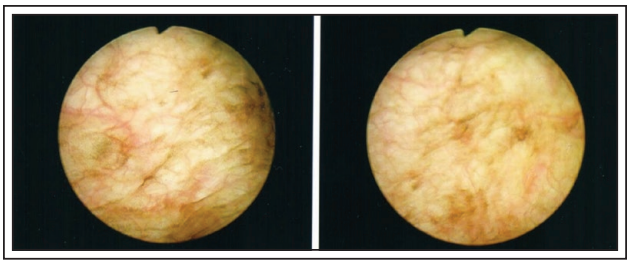

Figure 1. Cystoscopic images show patchy brown discoloration of the bladder urothelium.

of the bladder wall, Figure 1. Multiple biopsies were obtained of the suspicious lesions. To ensure further resection was not required, an intraoperative frozen section analysis of one biopsy was performed revealing benign tissue, favoring urothelial melanosis.

Permanent histology demonstrated benign urothelial mucosa with chronic inflammation and pigmented urothelial cells, Figure 2. The pigmented cells were found to stain avidly with Fontana-Masson stain, which is specific for melanin deposits, Figure 3. The specimen did not reveal any evidence of atypia or dysplasia.

Due to the finding of simultaneous and delayed urothelial carcinoma in other published cases, the patient has subsequently been evaluated every three months with history and physical examination and repeat urine cytology. He was also referred to a dermatologist for a full skin evaluation, which was negative. His gross hematuria resolved and his urinary symptoms were much improved after initiation of an alpha-blocker. Urine cytologies remain negative and the patient is scheduled to return for surveillance cystoscopy at 1 year.

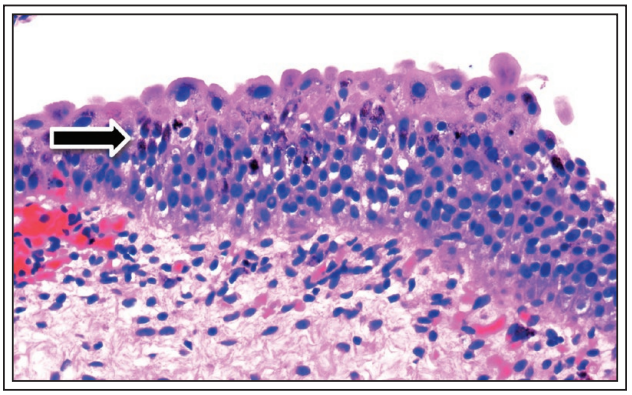

Figure 2. H&E stained histologic section of biopsy specimen shows urothelial cells with dark intracystoplasmic pigment (arrow).

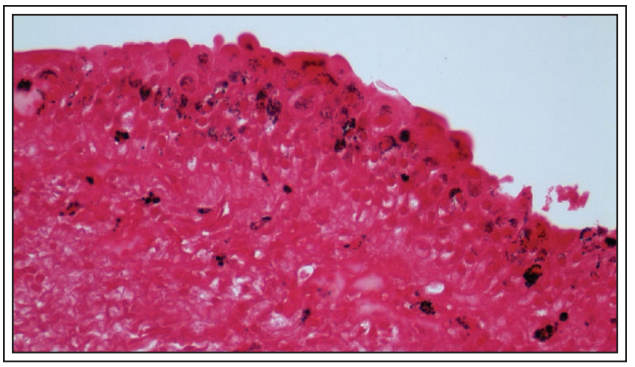

Figure 3. Fontana-Masson stain of biopsy specimen reveals melanin deposition.

Discussion

A review of 12 urothelial melanosis cases in the current literature corroborates the benign features described by pathology in the case above. In other published cases, patient age has ranged from 43 to 86 years old with no obvious gender predilection.[2] Similarly, reported cases have demonstrated no ethnic predilection, occurring in both African-Americans and Caucasians, though many of the documented cases do not indicate the patient's race. Presenting symptoms varied significantly and included various combinations of urinary frequency, urgency, hematuria, dysuria, and incontinence. Despite unpredictable presentations, all reports detail similar cystoscopic and histologic findings. Reports describe diffuse black or brown areas of discoloration across the urothelium noted on cystoscopic evaluation.[1,3,7]

Diagnoses were confirmed histologically with findings of dark pigmented granules within the urothelium and positive Fontana-Masson staining, which is specific for melanin. Confirmation can be further accomplished by applying bleach and noting clearing of this staining.[7] Immunostains for HMB-45 (common melanoma marker) and S-100 (marker of neural tissue/melanoma) are classically negative.[6]

Although melanosis is a benign entity, isolated case reports have described both subsequent development and concomitant high grade urothelial cell carcinoma (UCC) in patients initially presenting with simple melanosis.[2,4,6] Sanborn et al reported a case of urothelial melanosis in a 63-year-old woman referred for evaluation of multiple urinary tract infections. She developed hematuria 1 year after her initial melanosis diagnosis and was found to have high grade UCC.[6] Harikrishnan et al reported a case of melanosis of the bladder in a 50-year-old man who presented

with hematuria and was found to have concurrent high grade UCC of the distal ureter and renal pelvis as well as urothelial melanosis.[2] Additionally, two patients reported by Patel et al were found to have concurrent melanosis and urothelial dysplasia and invasive urothelial carcinoma.[4] Based on the limited information regarding the natural history of urothelial melanosis, it is difficult to predict its evolution over a patient's lifetime. Melanosis of the bladder may be an incidental and otherwise clinically insignificant finding or it could be a possible precursor for malignancy. While there remains no consensus on follow up in the literature, most authors recommend that continued surveillance at least be considered.

In addition, though exceedingly rare, there have been reported cases of melanoma of the bladder.[8] It would seem logical that malignant transformation of urothelial melanosis could possibly lead to the development of melanoma. None of the urothelial cases in the literature, however, have been associated with a melanosis diagnosis, suggesting that it is not a risk factor for development of melanoma.[3] An argument can still be made for a thorough dermatologic evaluation to rule out any suspicious cutaneous pigmented lesions.

In conclusion, we present a case of benign urothelial melanosis diagnosed during the evaluation of gross hematuria. While the diagnosis is rare, it should be considered when classic brown or black pigmented lesions are seen on cystoscopic evaluation. Careful inspection should be performed and the diagnosis confirmed with a biopsy as other published cases have demonstrated concomitant UCC. Endoscopic surveillance should be considered given rare reports of delayed development of dysplastic changes. □

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