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Melanosis of the Bladder: A Case Report and Review of the Literature

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Abstract

Melanosis of the bladder is a pathology defined as intracytoplasmic brown-black pigment deposit in urothelial cells without cytological atypia. A 69-year-old man case showed melanic pigment in the bladder wall through specific immunochemistry. Melanosis of the bladder's real prevalence and malignant potential are hard to define, due to its prevalence among asymptomatic adults hasn't been described by this moment, and follow-up though periodic Urethrocystoscopy would be necessary in order to clarify its malignant potential.

Keywords: Bladder; Melanin; Malignant; Bladder pigmentation

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Introduction

Melanosis of the bladder is defined as a rare benign lesion caused by melanin deposits in bladder tissue. It can be seen in any organ but more frequently in the skin and oral mucosa [1-3]. It is required for its diagnosis to prove melanin pigment. We present a typical case of melanosis of the bladder with immunohistochemical characterization and we make a review of the English literature thus far. We highlight its benign aetiopathogenesis [1-16].

Case Report

A 69-year-old man presented with a history of urinary obstruction with urgency to void. He had hypertension without other personal antecedents. Urine cytological exam and all complementary analysis were negative. Cystoscopy revealed trabecular wall of the bladder and diffuse black discoloration of the bladder mucosa **(Figure 1).** No focal lesions were identified. Several biopsies were realized. Biopsy specimens were processed and stained with Haematoxylin Eosine (H and E), which revealed abundant intracytoplasmic brown-black pigment granules deposit in urothelial cells and lamina propria **(Figure 2).** There was no inflammatory or cytological atypia.

Histochemical stain for iron reaction (Perls´ Prussian blue stain) and Periodic Acid Schiff (PAS) ruled out hemosiderin and lipofuscin deposits, respectively. Neither, melanocytes were detected by immunohistochemical with Melan-A **(Figure 3).** Brown pigment deposit was positive for Fontana-Masson stain, which was hand tested in our laboratory **(Figure 4).** Our diagnosis was of melanosis of the bladder. Nowadays, the patient successfully follows periodic reviews by urologist through cystourethroscopy.

Discussion

Brown-black granules in the bladder can be the result of three different pigments: hemosiderin, lipofuscin, and melanin. Hemosiderin is an iron-containing intermediate product of hemoglobin degradation, and it is distinguished by its positive reaction with Perls´ stains. Lipofuscin is a degradation membrane product that is accumulated on lysosomes and positive for PAS stain. Bladder urothelial cells have telolysosomes, which are rich in lipids, and have lipofuscin-like morphology and are positive with PAS stain [1-16]. Furthermore, Lipofuscin deposits have been reported in patients with phenacetin abuse [17,18] and ciprofloxacin treatment by interstitial cystitis [7]. However, the aetiology of melanosis is unclear. Some hypotheses talk about an aberrant migration from the neural crest cells during embryological development or transdifferentiating of urothelial stem cells. None of the hypotheses about deposit origin to date have been conclusive. Symptoms are nonspecific, such as haematuria, dysuria, difficulty voiding, cystitis or urinary incontinence. Therefore, its diagnosis is based on suggestive

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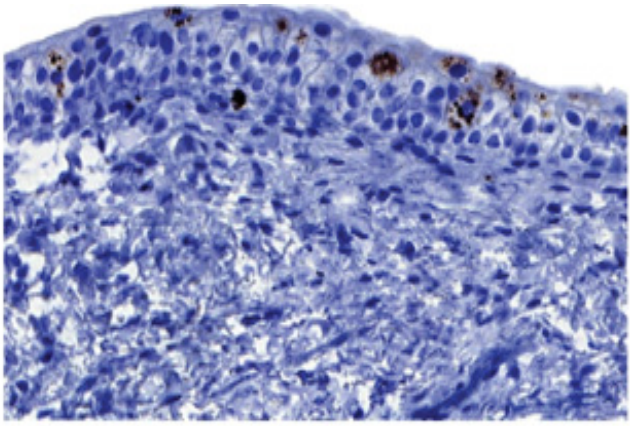

Figure 1 Cystoscopy revealed trabecular wall of the bladder and diffuse black discoloration of the bladder mucosa.

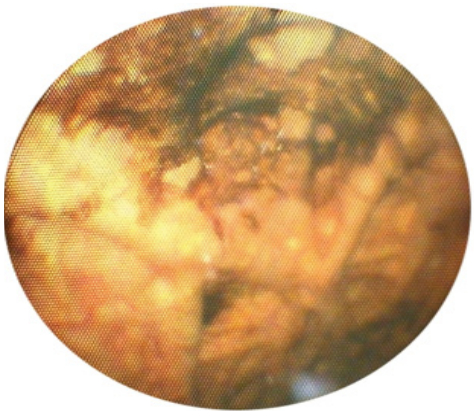

Figure 3 Melanocytes were detected by immunohistochemical with Melan-A.

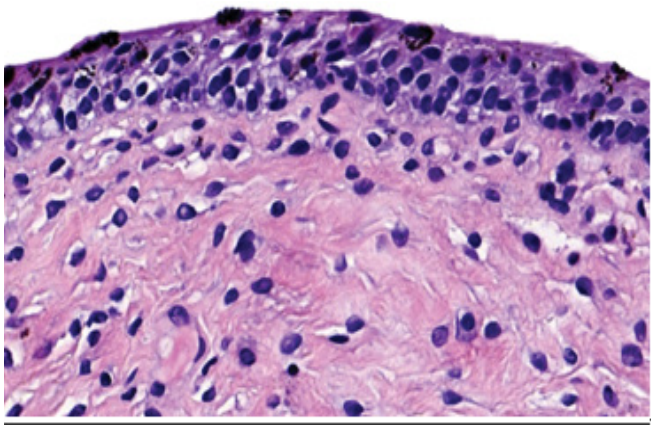

Figure 2 Intracytoplasmic brown-black pigment granules deposit in urothelial cells and lamina propria.

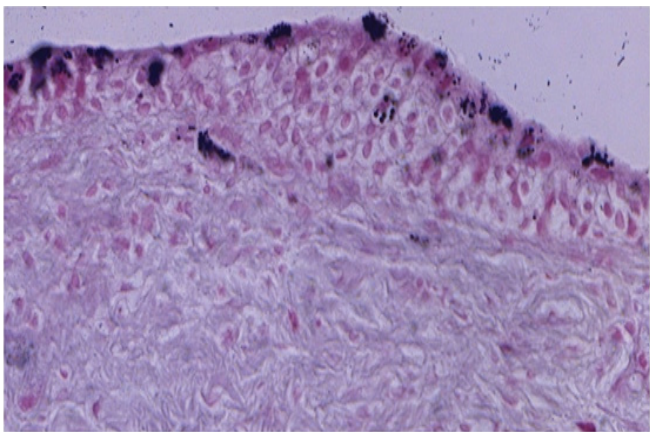

Figure 4 Brown pigment deposit was positive for Fontana-Masson stain.

Table 1 List of cases of urinary melanosis of the bladder, reported in the English literature.

#Case/ Author	Publication Year	Age (years)	Sex (Male/ Female)	Urinary symptoms	Others personal Antecedents	Treatment	Follow-up / Interesting dates
#1 Alroy, J., et al. [1]	1986	71	M	Asymptomatic bloody urethral	Systemic hypertension	Methyldopa, triamterene and hydrochlorothiazide	-
		72	M	Urinary obstruction	-	-	-
#2 Chong, F.K., et al. [4]	1999	86	F	Urinary incontinence and dysuria	-	-	-
#3 Wieringa M.D. et al. [5]	2005	52	M	Macroscopic haematuria	-	-	-
#4 Di Fiore F et al. [6]	2006	72	M	Dysuria and smelly urine	-	Several antibiotics, nonspecific.	-
#5 Jin B, Zaidi SY, Hollowell M, et al. [7]	2009	77	F	Urinary incontinence and severe urgency	-	Tolterodine tartrate	-

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#Case/ Author	Publication Year	Age (years)	Sex (Male/ Female)	Urinary symptoms	Others personal Antecedents	Treatment	Follow-up / Interesting dates
#6 Sanborn L, MacLennan G et al. [2]	2009	63	F	Recurrent cystitis	-	-	1 year later: high-grade invasive papillary transitional carcinoma was diagnosed
#7 Talmon G.A., et al. [8]	2010	56	F	Overactive bladder symptoms	-	-	6 months: asymptomatic
#8 Willys C.B., et al. [9]	2011	71	F	Chronic incontinence and intermittent voiding dysfunction	Subarachnoid haemorrhage, hypothyroidism and epilepsy.	Phenytoin, thyroxine, isosorbide mononitrate, telmisartan, atorvastatin, ezetimibe, aspirin and nitrolingual spray	-
#9 Stuhldreher, P.P., et al. [10]	2011	elderly	F	Hematuria	-	-	-
#11 Lightowlers S., et al. [14]	2011	58	M	Urinary tract infections	Ex-smoker	-	6 months later: the lesions had resolved completely on cystoscopy.
#10 Harikrishnan JA., et al. [11]	2012	50	M	Haematuria, loin pain	Hypertension	On treatment	Transitional cell carcinoma in the right renal pelvis and distal right ureter was diagnosed together melanosis vesica.
#12 Pandian SS., et al. [12]	2016	75	M	Painless, frank haematuria	Hypertensive, and middle cerebral artery aneurysm. Non-smoker.	On treatment	
#18 Godinho R., et al. [15]	2016	64	M	Macroscopic hematuria and lower urinary tract symptoms	Smoker and transurethral resection of prostate		Two years of follow up
#13 Susanna E. Yau., et al. [13]	2017	50	F	Hematuria and urinary obstruction and flank pain, fever and chills previously	Hypertensive. Smoker	On treatment	The patient was diagnosed with urothelial carcinoma and melanosis of the bladder synchronously.
#14 Mera Z., et al. [16]	2018	66	M	Urinary retention and lower urinary tract symptoms	-	-	8 years later: complete resolution of melanosis.

brown-like cystoscopy images from the bladder wall and thorough histopathological analysis. Atypia cytological should be ruled out for its diagnosis. And granules must be positive with melanic stain and negative with Perls´ and PAS stains.

We have made a review of the English literature about bladder melanosis **(Table 1).** We have found fifteen cases in all. The age of the patients ranges from 50 to 86 years. There were nine men and seven women. Twelve of them were individual cases of unspecific clinic and diagnostic of urinary bladder melanosis. Three reports (#6#10 and #13)2,5,16 was associated with tumoral pathology. In the 6th and 10th case, the diagnosis was made during follow up contacts. And in the 13th case, both detections were made simultaneously. Also, in two reports (#11 and #14), the lesions had completely resolved in six months and eight years after the diagnosis, respectively [16-19].

The connection between bladder melanosis and malignancy is unknown, currently. Some authors believe melanosis is a premalignant lesion [2-20] and other ones believe both entities are a continuum. Despite this, we suggest that there is no existing relationship between both entities. Being that: (1) the real incidence of only melanosis vesical is not known because it is a diagnosis by chance, on patients with unspecific urinary symptoms, (2) as a rule, bladder biopsy lacks melanocytes and (3) not all cases with melanosis and bladder tumour might have been published.

Conclusion

Melanosis of the bladder has an unknown incidence for this reason should be known considered by urologists and pathologists to avoid a potential malignant misdiagnosis. Demonstrating the melanin pigment in the absence of atypia cytological is the diagnostic key. The scientific community believes melanosis is a benign entity, what we support. However, melanocytes within the urothelial mucosa could have malignant potential. For this reason, its presence should be reported by the pathologist. Demonstrating the melanic pigment in the absence of atypia cytological is the diagnostic key. In short, the published cases are few and lack follows up, what explains the lack of management guidelines for this disease, beyond routine urethrocystoscopy although it may not be able to be considered to large-scale health program.

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