

CASE REPORTS

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Urinary bladder melanosis with complete resolution case report

Daniela I. Mateescu¹ , Hamdi Dahir¹, Amit Goel², Eleanor Ray¹ and Sanjeev Madaan^{1*}

Abstract

Background Melanosis of the bladder is a rare condition characterized by multifocal, diffuse melanin pigmentation of the urothelial mucosa or lamina propria without any proliferation of melanocytes. Less than 25 cases have been reported so far of which only four patients had concurrent urothelial carcinoma.

Case presentation We are reporting a case of melanosis of the bladder in a 58-year-old female associated with pTaG1 transitional urothelial cell carcinoma (TCC) of the bladder who presented with symptoms of recurrent urinary tract infection (UTI). Cystoscopy and biopsy results confirmed benign melanosis.

Conclusion Our case is unique because bladder melanosis associated low grade TCC with complete resolution of both conditions within one year.

Keywords Bladder melanosis, Recurrent urinary tract infections, Transitional cell carcinoma, Case report

1 Background

Melanosis refers to abnormal deposits of melanin in the cells [1]. This condition can be seen in any organ but more frequently occurs in the skin and oral mucosa. Melanosis of the urinary bladder is a rare benign condition and less than 25 cases have been reported so far, usually detected incidentally via cystoscopy investigating lower urinary tract symptoms (LUTS) [1]. Melanosis of bladder with concurrent urothelial carcinoma is even rarer with only four reported cases. We report a case of benign melanosis concurrent with TCC.

2 Case presentation

A 58-year-old female with a history of hypertension, high cholesterol, and osteoarthritis of the left hip joint was referred to our clinic for recurrent urinary tract

infections. Her symptoms were foul-smelling urine and dribbling. Her post void residue (PVR) was 216 ml and her urine was positive for nitrites, although all urine cultures previously done in General Practitioner setting were negative. The patient was a non-smoker and drank around 40 units of alcohol per week. She was started on prophylactic Trimethoprim and was planned for flexible cystoscopy. Flexible cystoscopy revealed black discoloration of the bladder walls with no obvious growths or lesions. A rigid cystoscopy was done which revealed a reticular black discoloration area on the right side, anterior wall, and dome of the bladder (Fig. 1). Two biopsies were taken and sent for histopathology examination. The specimen was reported as melanosis and pTa G1 TCC of the bladder. There was the presence of brown tissue pigment in the urothelium (Fig. 2), which was confirmed to be melanin with positive Mason Fontana (Fig. 3). The other causes of pigmentation are excluded by negative Perl's stain (Fig. 4) for hemosiderin and negative PAS for lipofuscin. Check rigid cystoscopy was done after 5 months and not at 3 months due to delay caused by the COVID-19 pandemic effect on the waiting list. The procedure showed the melanosis present at previous sites and four white patches.

*Correspondence:

Sanjeev Madaan
Sanjeev.Madaan@nhs.net

¹ Department of Urology and Nephrology, Darent Valley Hospital, Dartford, Kent DA2 8DA, UK

² Cellular Pathology Department, Maidstone Hospital, Hermitage Lane, Maidstone ME16 9QQ, UK

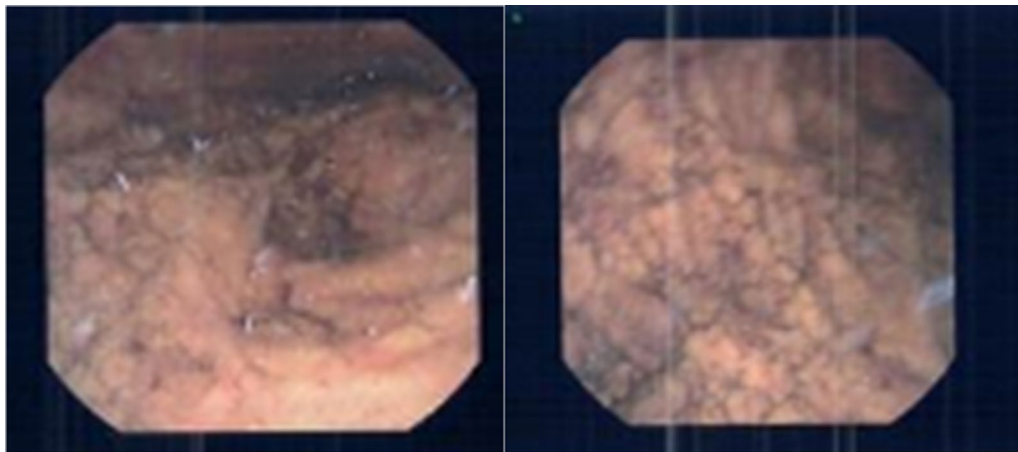


Fig. 1 Initial flexible cystoscopy February 2020

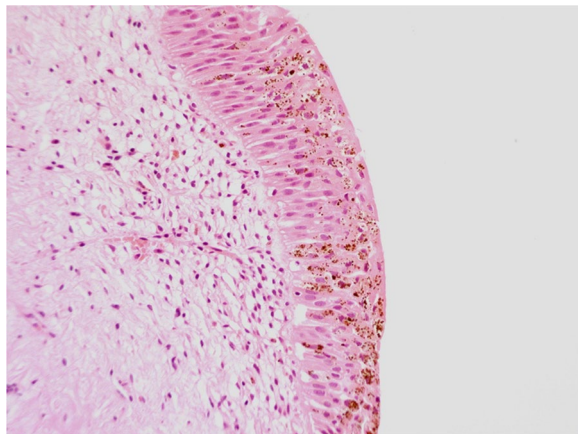


Fig. 2 Bladder urothelium with pigment in keeping with melanosis. H&E 20x



Fig. 4 Negative Perl's stain in bladder urothelium. Perl's stain 20x (If iron it would show blue granules with Perl's stain)

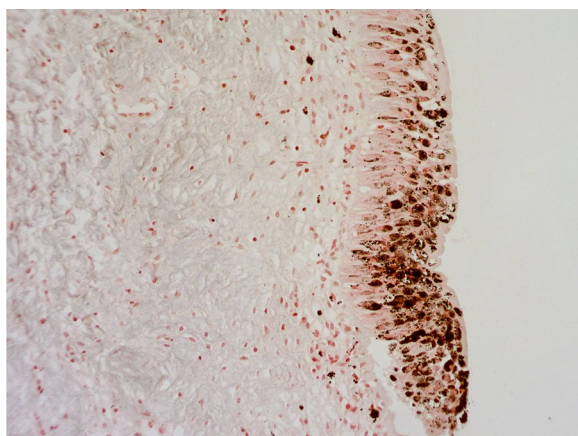


Fig. 3 Positive Fontana stain (black granules), confirming melanosis of bladder. Masson-Fontana 20x

Biopsies sent showed extensive keratinizing squamous metaplasia with mild chronic inflammation (Fig. 5).

The patient was put in a low risk category for bladder cancer surveillance as per the European Association of Urology guidelines for non-muscle invasive bladder cancer and therefore did not receive any adjuvant treatment. Moreover, she was advised to continue trimethoprim 100 mg for UTI and have intravesical glycosaminoglycans replacement therapy (iAluRil) intravesical instillation. Her LUTS settled and a cystoscopy done after further 6 months showed complete resolution of melanosis. She has been advised of yearly check cystoscopy and patient remains recurrence free clear after 2 years follow-up (Fig. 6).

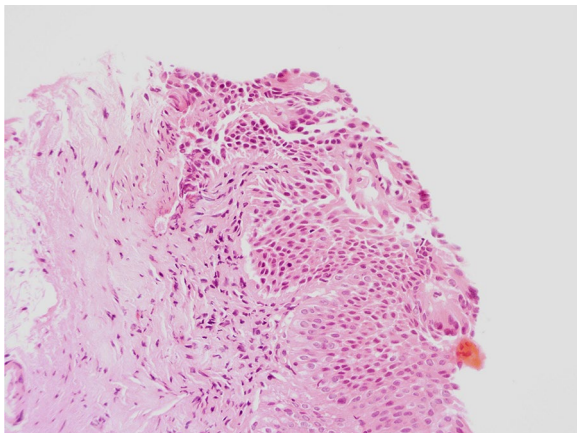


Fig. 5 G1pTa Urothelial carcinoma of bladder (Arrow). H&E 20x

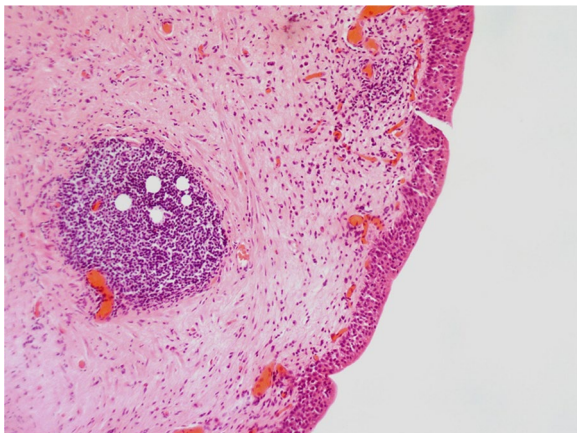


Fig. 6 Bladder biopsy after 1 year. No melanosis. H&E 10x

3 Discussion

Bladder melanosis is a rare condition that has been incidentally reported in a limited number of cases during cystoscopies performed for the investigation of LUTS [2]. Moreover, bladder melanosis associated with transitional cell carcinoma has been reported in less than 5 cases worldwide. Our case is unique because bladder melanosis was associated with low-grade TCC and had complete resolution within one year.

There have been four reported cases in the literature of patients diagnosed with bladder melanosis and urothelial carcinoma (Table 1). In three out of four reported cases, patients presented initially with haematuria [3–5]. In one case, the patient originally presented with recurrent UTIs, and was found to have bladder melanosis. She represented one year later with haematuria and was then found to have TCC [6].

All patients had cystoscopy, which in all the cases demonstrated dark pigmentation. Four out of five cases, including our case, underwent a TURBT [3, 5, 6]. One

patient underwent a laparoscopic nephroureterectomy as they were found to have a ureteric tumour [4]. Regarding follow-up, three out of five cases, including our case, had regular surveillance cystoscopy [4, 6].

To date, the clinical presentation of bladder melanosis has been non-specific, with symptoms varying from recurrent cystitis and dysuria, to more concerning symptoms like gross haematuria, acute renal failure, and palpable mass [5]. Due to the rarity of the condition, it is yet unknown whether any of these symptoms are caused by bladder melanosis or whether, in itself, bladder melanosis is asymptomatic and only incidentally reported in cystoscopies [7].

Bladder melanosis is reported during cystoscopies as a velvety appearance of the urothelium with brown-black deposits which can be found in any area of the bladder. Moreover, the lesions can be flat or can have a small punctate appearance [6]. It is paramount for biopsies of the lesions to be taken to rule out any other aetiologies for dark pigmentation. To date, bladder melanosis is considered to be a benign condition. However, as mentioned above, its presence has been reported in conjunction with malignant proliferation, either as a predecessor or simultaneous. Further research is needed to better understand bladder melanosis's true significance.

The presence of bladder melanosis is proven histopathologically with Fontana-Masson staining. The melanin granules have the capacity to reduce the ammoniacal silver nitrate, resulting in black appearance. Furthermore, adding strong oxidizing agents bleaches the specimen, confirming the presence of melanin [6].

The differential diagnosis includes malignant melanoma, which is distinguished by proliferation of melanocytes, which are positive for S-100 and HMB-45 (which would be negative in melanosis). As there is no proliferation of melanocytes, there is nothing to suggest that surveillance with cystoscopy follow-up would be of much benefit for melanosis. In our case, there was no evidence of melanin pigment in the bladder biopsy taken after one year.

Few theories have been proposed with regards to bladder melanosis formation, but the pathophysiological mechanism of the condition is still obscure. The bladder urothelium does not normally contain melanocytes. The question of how does the urothelium gain melanocytic cells has been raised. Most of the published reports assume that: 1. During embryological development, the melanocytes have an aberrant migration; 2. Local trans-differentiating of urothelial stem cells [8]. None of the above theories has a solid research background, making the validity of the proposals questionable. Furthermore, it has been proposed that bladder melanosis is the result of an abnormal reaction of the mucosal nerve plexus or

Table 1 A table demonstrating the key features of patients who have been found to have concurrent melanosis and urothelial carcinoma

Paper	Age	Gender	Symptoms	Diagnostic features	Treatment	Follow up
Bladder melanosis with concurrent urothelial carcinoma [2]	50	Female	Haematuria and urinary obstruction	Pigmented bladder and fungating mass from right VUJ Histology-muscle invasive urothelial carcinoma with squamous features	TURBT A right nephrostomy tube was placed. The patient began neoadjuvant chemotherapy	Planned cystectomy and urinary diversion
Urinary tract transitional cell carcinoma and melanosis of the bladder: a case report and review of the literature [3]	50	Male	Loin pain and haematuria	Diffusely pigmented bladder as well as a right ureteric TCC Histology- grade 3 invasive TCC	Right laparoscopic nephroureterectomy with an open lower end	Regular cystoscopic and radiological surveillance
Urinary Bladder Melanosis Associated with Urothelial Dysplasia and Invasive Urothelial Carcinoma [4]	69	Female	Haematuria	Black-colored tumor involving trigone, obscuring both ureteric orifices Histology- High-grade urothelial carcinoma invading into muscularis propria	TURBT and insertion of JJ stents	Not a candidate for radical surgery The patient passed away after 2 months
High grade transitional cell carcinoma [5]	63	Female	Recurrent UTI One year later developed haematuria	Originally, cystoscopy showed pigmented areas Histology was benign One year later, cystoscopy revealed a mucosal tumor Histology- G1pT1 N0M0 TCC of bladder	TURBT and intravesical bacillus Calmette-Guérin therapy	Surveillance cystoscopy every 3 months, and imaging of upper tracts
Our case	61	Female	Recurrent UTI	A black pigmented lesion in the bladder. Suspicious urothelium in the dome of the bladder Histology- G1 pT1a urothelial tumor of the bladder, keratinizing squamous metaplasia	TURBT	Routine surveillance

resulted secondary to the plasticity of the urothelium [8]. Only one case reported the presence of melanosis after bladder Botox therapy but it is yet unknown whether the innervation of the bladder was the culprit [8].

4 Conclusion

We report an unusual case of bladder melanosis associated with non-muscle invasive bladder cancer showing complete resolution after one year.

4.1 Learning points

1. Bladder melanosis is considered to be benign in nature and no specific symptoms have yet been reported
2. Biopsies of suspected areas are the gold standard for correct diagnosis
3. Bladder melanosis may be associated with concurrent urothelial carcinoma.

Abbreviations

TCC	Transitional urothelial cell carcinoma
UTI	Urinary tract infection
LUTS	Lower urinary tract symptoms
PVR	Post void residue
PAS	Periodic acid-Schiff
iAluRil	Intravesical glycosaminoglycans replacement therapy
TURBT	Transurethral resection of bladder tumor

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Author contributions

DM main author, analysed and interpreted patient data and compared with current data available. HD designed table comparing patients with same diagnosis. ER supervised, corrected and read final manuscript. AG provided histopathology images and interpretation. SM corresponding author supervised and corrected manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent for publication of the patient's clinical details and clinical images was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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