**CASE REPORTS**

**Acquired childhood bladder melanosis**

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**Abstract**

**Background:** Bladder melanosis is rare. It has previously been described only in the fifth decade of life or beyond; it has not been described in childhood. Previous descriptions have generally been case reports, and so the natural history is poorly understood. Urinary symptoms present at the time of cystoscopy have frequently been attributed to bladder melanosis. A possible suggested aetiology is aberrant migration of melanocyte migration during embryogenesis.

**Case presentation:** We present the first case of bladder melanosis in a child. He had been under our care since the age of 5 years with urinary incontinence and at that time, had undergone cystoscopy demonstrating normal bladder mucosa. A diagnosis of idiopathic detrusor overactivity with underactive voiding had been made. After other unsuccessful treatments, intravesical botulinum toxin was proposed. At the age of 13, repeat cystoscopy prior to botulinum toxin, demonstrated widespread pigmented areas in the bladder mucosa. Histology showed bladder melanosis. Our finding is important for several reasons. This is the first reported case of bladder melanosis to affect a child. The previous normal cystoscopy in our patient would refute the explanation that bladder melanosis is a congenital condition. Furthermore, the development of melanosis on the background of stable symptoms raises the possibility that the condition may be asymptomatic.

**Conclusions:** This unique finding of bladder melanosis in a child has provided further insight into this rare and poorly understood condition.

**Keywords:** Childhood, Bladder, Melanosis

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**Background**

Bladder melanosis is a rare condition, first described in 1986 [1]. To date, the condition has been described only in adults over the age of 40 years. We describe the first case of melanosis in a child.

**Case presentation**

Our patient presented in 2011 at the age of 5 years with symptoms of day- and night-time urinary incontinence. He had a single episode of frank haematuria. Ultrasound demonstrated a solitary right kidney. In the absence of other explanations for his haematuria, he underwent cystoscopy. This confirmed a single right ureteric orifice but otherwise normal urethra and bladder.

His urinary incontinence was challenging to manage. He underwent protracted treatment and investigation. Of note, he was found to have an abnormal bladder residual due to underactive voiding, but otherwise, videourodynamic were unremarkable. He did not respond to urotherapy, desmopressin, antimuscarinics (tolteridine, solifenacin), beta 3 agonists (mirabegron), or transcutaneous electric nerve stimulation (TENS). He even learnt clean intermittent catheterisation (CIC). CIC had been recommended five times a day, but in practice was performed twice a day. By the time of his cystoscopy in 2019, he had been performing CIC for 34 months. Ultimately, ambulatory urodynamics demonstrated detrusor overactivity. He and his family agreed to intra-vesical botulinum toxin treatment. During this, he started treatment with fluoxetine for severe anxiety and reached a BMI of 43.8.
In 2019, at the age of 13 years, he was taken to theatre for his first intra-vesical botulinum toxin treatment under general anaesthesia. At cystoscopy, we were surprised to find that the bladder had extensive patches of pigmented mucosa interspersed amongst the normal mucosa (Fig. 1). This pigmentation did not extend into the urethra. Cold-cup biopsies were taken, and a decision was made not to proceed with botulinum toxin treatment.

Biopsy of the bladder tissue showed dark pigment within epithelial cells as well as fibroblasts and macrophages in the lamina propria (Fig. 2). The epithelium was otherwise normal with no dysplasia. Melanocytes were not seen. There was no evidence of fungal infection or melanoma. The specimens were negative for S100 and HMB45 immunostaining. The pigment stained black with Masson-Fontana (Fig. 3), in keeping with melanin.

Bladder melanosis was present and unchanged on subsequent cystoscopies, performed to administer botulinum toxin, up to 29 months later.

**Discussion**

Bladder melanosis was first described less than 40 years ago [1]. Since then, there have been only case report descriptions. A review article in 2014 described only 16 cases in the literature up until that time [1]. To our knowledge, there have been only another six cases reported subsequently [2–6].

The diagnosis of melanosis is based on histology findings. The finding of golden brown or dark granules has a differential that includes melanin, lipofuschin, and haemosiderin. Lipofuschin is most commonly found in lysosomes as a product of membrane degradation and is rich in lipids. Lipofuschin is stained by periodic acid-Schiff stain and Zeihl-Neelson staining and has been documented in patients on long-term ciprofloxacin. Haemosiderin is derived from the breakdown of haemoglobin and is stained by Perl’s Prussian blue stain. Melanin is seen as golden yellow-brown pigment intracellularly and extracellularly on light microscopy. Melanin is bleached by acid and reduces the ammonia silver nitrate solution in Fontana-Masson stain, to give a black colour.

The origin of melanin in the bladder in this condition is difficult to explain. Normal bladder urothelium does not contain melanocytes or melanosomes. It is suggested that the melanin granules are produced by melanocytic cells that either underwent aberrant migration from the neural crest during embryogenesis or were derived through aberrant differentiation of urothelial stem cells [7]. Melanocytes can be detected using melanocytic markers such as MelanA, S-100, and HMB45 which are antigens on the melanocyte. MelanA is detected by antibodies such...
as A103 and M2-7C1; Pmel 17 antigen is detected with HMB-45 monoclonal antibody. S-100 is another immuno-

histochemical protein found in melanomas [8]. All melano-\n
mas may not show all the markers, but this does not affect their clinical course or prognosis. These markers

have not been detected on biopsy specimens [2, 9]; hence,

melanocytes are not found in cases of bladder melanosis.

The clinical significance of bladder melanosis is also

uncertain. Of those described in the literature, 6 were

associated with haematuria, 5 with symptoms of LUTS,

7 with UTI or cystitis, 5 with incontinence, 2 with void-
ing difficulties, 1 with renal calculi, and 2 with abdomi-
nal pain. Some patients had a combination of the above

symptoms. Three of the patients with haematuria were

associated with bladder malignancy.

There have been 4 patients reported to have malig-
nancy associated with the finding of bladder melanosis.

In 2 of these patients, melanosis was found with concur-

rent urinary tract malignancy with bladder transitional
cell carcinoma (TCC) in one and ureteric and renal TCC

in the other [3, 10]. Both of these patients presented with

haematuria. Another patient was found to have bladder

TCC 1 year after the original discovery of bladder mela-
nosis [11]. She presented originally with recurrent UTI,

at which time the biopsy demonstrated melanosis. A year

later, she developed haematuria, and repeat cystoscopy
disclosed high-grade superficial TCC. The final docu-

tented case of malignancy with bladder melanosis was

in a woman who had extensive melanosis of the vulva,
vagina, and bladder in association with melanoma of the

vulva [12]; she was subsequently found to have mela-
noma within the bladder and vagina.

The clinical course of the above patients is not men-
inated in the case reports. Most of the patients in the

papers are in their eight decades of life. Three patients

who had TCC have been under surveillance and were

well. In only one case where a man in his 50s presented

with obstructive symptoms due to urethral stricture, a

resolution of melanosis was seen once the stricture was

treated. Some authors have attributed the symptoms and
even predisposition of malignancy to melanosis. How-
never, the case reports tended to be descriptions of point
incidence, rather than serial bladder examinations, and

so the natural history of the condition has only been

speculated on. All patients who have been found to have

bladder melanosis will by definition have had symptoms;

whilst the prevalence of bladder melanosis in the wider

asymptomatic population is unknown, it is therefore pos-

tible that bladder melanosis is an incidental finding at

cystoscopy performed to investigate other problems.

There is limited information on the natural history of

melanosis. There is a single previous case report of a

patient who developed melanosis after a previous normal

cystoscopy [2]. This is particularly interesting as the

authors report there was a subsequent spontaneous reso-

lution of the bladder melanosis. In another patient where

the melanosis was resected, there was no subsequent

recurrence [13].

Our patient is important in several respects. This is the

first description of bladder melanosis in a child; all other
descriptions of bladder melanosis have been in adults

over the age of 40 (range 43–86 years) [9]. Furthermore,

this is the only second case of acquired bladder melano-
nosis. This would suggest it is unlikely that melanosis
arises from neural crest migration during embryogen-
esis. Another important consideration is that melanosis

occurred during the presence of symptoms that he has

had at the time of his first initial and negative cystoscopy;

this would suggest that the melanosis has not contribut-
to symptoms but have developed after the symptoms

were present. This would support the view that blad-

der melanosis may be an asymptomatic and incidental

finding.

It may be asked whether melanosis developed in this

patient as a result of his treatment. None of the medica-
tions he has taken has been associated with pigment de-
oposition. It is difficult to imagine that the extremely low

current that is used with TENS therapy can trigger mel-
nin deposition. Intermittent catheterisation is very unlikely
to have been a trigger; the distribution of melanosis in the

bladder was widespread and not favoured to areas of the

bladder mucosa that a catheter may have damaged. Interm-

ittent catheterisation is widely performed by many of

our patients undergoing cystoscopy, and we have not seen

even a mild variant of melanosis in them.

Our view is that melanosis has not contributed to

symptoms in our patient. We would favour an interpreta-
tion that melanosis may be asymptomatic and that it is

possibly discovered incidentally during the investigation

of coexisting symptoms.

A final consideration is the reaction of the patient

and parents to the cystoscopy findings. The patient and

parents were distressed at the report of the cystoscopy

appearance. The novelty of the finding and the wait for

the histology results were difficult; it exacerbated the

child’s pre-existing anxiety. We hope that by provid-
ing this report, we may allow surgeons encountering a

similar situation to provide a better reassurance to their

patients whilst histology is awaited.

**Conclusion**

This is the first description of bladder melanosis in a

child. This is only the second case demonstrating that

melanosis is acquired. The development of melanosis on
the background of unchanged urinary symptoms suggests that the condition may be asymptomatic.

**Abbreviations**

TCC: Transitional cell carcinoma; TENS: Transcutaneous electric nerve stimulation.

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**Authors’ contributions**

RV is the corresponding author and involved directly in the management of the case and collecting of the data with reviewing the literature and writing the case report. MA is the histopathology consultant who helped in understanding and presenting the histopathology findings. AT is the supervising consultant with a direct contribution to the writing of the paper. All authors have read and approved the manuscript.

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**Declarations**

**Ethics approval and consent to participate**

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**Consent for publication**

Written consent taken from the parents.

**Competing interests**

The authors declare that they have no competing interests.

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