Case Report

DOI: 10.7860/JCDR/2022/56806.16865

A Rare Case Report of Neurofibromatosis Type 1 with Bladder Ganglioneuroma in a Paediatric Patient

Surgery Section

ANKIT VYAS[1], MAYANK AGARWAL[2], ALHAD MULKALWAR[3], SUJATA PATWARDHAN[4]

ABSTRACT

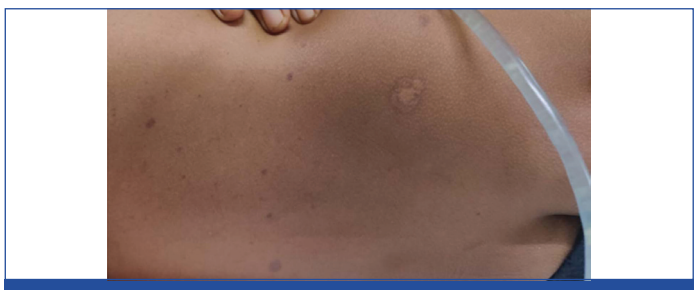
Neurofibromatosis type 1 (NF1) is a rare Autosomal Dominant (AD) disease manifesting in paediatric age group with an incidence of 1/3500 births. It has a varied clinical presentation most commonly involving skin followed by the skeletal and central nervous systems. Genitourinary involvement is very rare. Peripheral neuroblastic tumours are classified into Neuroblastomas (NB), Ganglioneuroblastomas (GNB) and Ganglioneuromas (GN). They are classified according to their stage of maturation in a spectrum, which starts from NB, the most primitive form, and extends to GN, the most mature form. The authors hereby present a rare case report of a paediatric patient presenting with NF1 features and a bladder ganglioneuroma. The 11-year-old male child presented with a history of haematuria since two weeks accompanied with increased micturation frequency and nocturia. Neurocutaneous markers suggestive of a diagnosis of Neurofibromatosis type 1 were observed during clinical examination. Computed Tomography Intravenous Urogram (CT-IVU) revealed a large irregular pelvic mass involving the wall of the urinary bladder. Enlarged mesenteric lymph nodes were observed during exploratory laparotomy, frozen section bipopsy of which was reported as ganglioneuroma. Partial cystectomy was performed along with complete excision of the mass. Histopathological examination confirmed the diagnosis of bladder ganglioneuroma.

Keywords: Neurogenic tumours, Pressure changes, Intravenous urogram

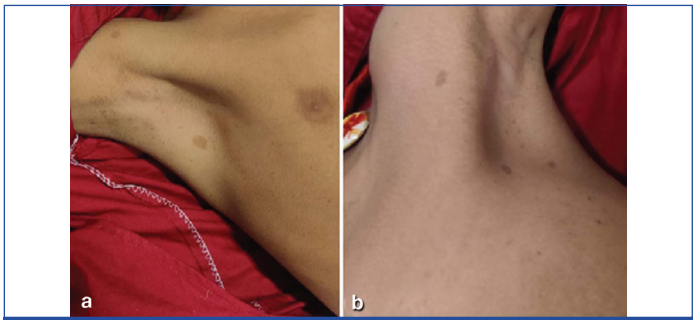
CASE REPORT

An 11-year-old male child presented to the Paediatric Outpatient Department with complaints of painless, gross, total haematuria, not associated with blood clots or tissue bits, with increased frequency and nocturia since two weeks. He had history of similar haematuria episodes two years ago, which subsided spontaneously. On examination, following findings were noticed- multiple hyperpigmented macules (>6 Café-au-lait spots) and patches (>5 mm) over trunk and thigh [Table/Fig-1], axillary freckling [Table/Fig-2], lisch nodules in both the eyes. A diagnosis of Neurofibromatosis type 1 (NF1) was made based on the Neurofibromatosis Conference Statement published by the National Institutes of Health Consensus Development Conference [1].

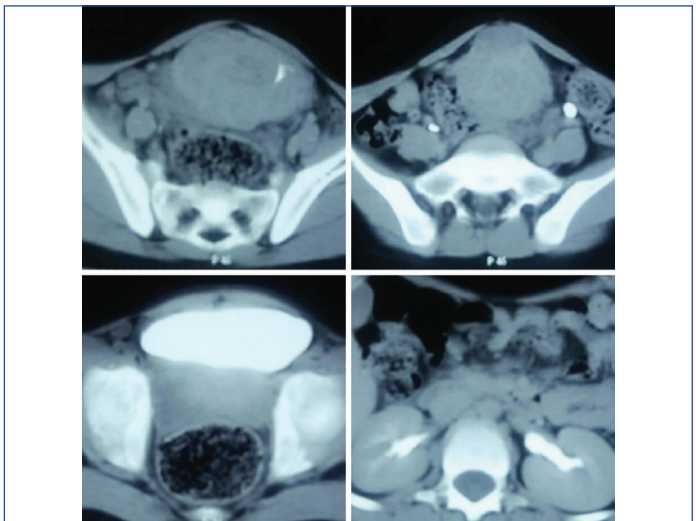
Computed Tomography Intravenous Urogram (CT-IVU) was suggestive of a 12×5 mm large irregular heterogenous hyperdense mass lesion in pelvis involving entire urinary bladder wall and bilateral Vesicoureteric Junction (VUJ) causing backpressure changes [Table/Fig-3]. Although rare, neurofibroma of the urinary bladder is the most common urinary tract manifestation of neurofibromatosis 1 and hence, a provisional diagnosis of the same was made based on the history and clinical examination of the patient [2]. On cystoscopy, no intraluminal growth was seen. He underwent exploratory laparotomy during which enlarged mesenteric lymph nodes were noticed. Frozen section biopsy was reported as a ganglioneuroma. Bowel was otherwise healthy without any lesion. There was a 10×5 cm tumour arising from anterior bladder wall and extending posteriorly [Table/Fig-4]. Bilateral ureteric orifices were not involved. Partial cystectomy was done with complete excision of mass. Recovery in postoperative period was uneventful. Histopathology



[Table/Fig-1]: Hyperpigmented macules (Café-au-lait spots) over the trunk of the child.

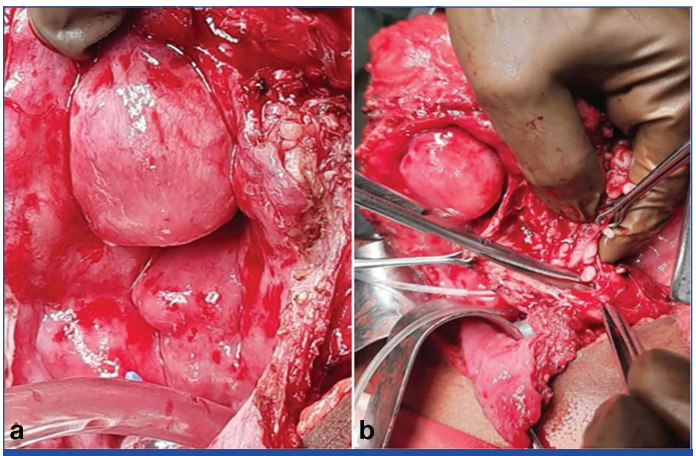


[Table/Fig-2]: Axillary freckling seen in the right; a) as well as the left; b) axilla.

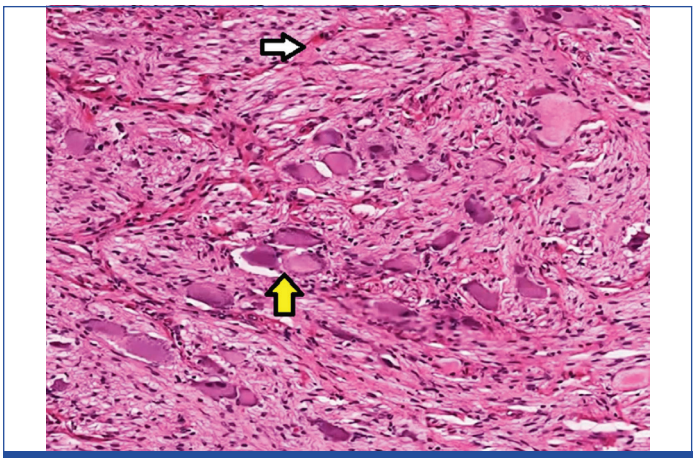


[Table/Fig-3]: Computed Tomography Intravenous Urogram was suggestive of a 12×5 mm large irregular heterogenous hyperdense mass lesion in pelvis involving entire urinary bladder wall and bilateral Vesicoureteric Junction (VUJ) causing back-pressure changes.

report confirmed the diagnosis of a bladder ganglioneuroma [Table/Fig-5]. On follow-up after a month, the presenting symptoms were reported to be completely resolved.



[Table/Fig-4]: a): A large tumour of size 10×5 cm arising from anterior bladder wall; b): extending posteriorly along with enlarged mesenchymal lymph nodes.



[Table/Fig-5]: Photomicrograph (H&E x100) of the excised specimen depicting bundles of Schwann cells (white arrow) in a myxoid stroma giving it a uniform appearance. Interspersed nests and clusters of mature ganglion cells (yellow arrow) can also be seen, thus, confirming the diagnosis of bladder ganglioneuroma.

DISCUSSION

Neurofibromatosis (type 1 and type 2) is an autosomal dominant neurocutaneous disorder which is characterised by tumours on the nervous system and skin [3]. NF1 rarely involves the genitor-urinary system, the urinary bladder being the most common organ involved in such cases [4]. Ganglioneuromas are neurogenic tumours that often arise from sympathetic ganglion cells and less frequently from adrenal medulla and peripheral nerves. They are slow-growing and have a more benign character compared to other cell types [5]. They most commonly present as an isolated finding, but rarely, they are also seen in association with neurofibromatosis type 1 (NF1) [6].

Almost 60% of cases are in patients under 20 years of age [7]. They are most commonly located in the retroperitoneum (52%) and mediastinum (39%) [8]. Ganglioneuromas are also uncommonly known to occur at sites such as bones and pelvis [9-11]. However, ganglioneuromas are very rarely seen in the urinary bladder. They account for less than 0.5% of all primary bladder tumours [12]. They have a benign course. They are not known to secrete hormones and cause symptoms only by means of pressure effect or bleeding from tumour [13]. Composite paraganlioneuroma-ganglioneuromas involving the bladder have been documented in five case reports so far [13-17]. However, a case of a ganglioneuroma with NF1 features has not yet been reported in literature and this is the first such case report. The clinical behaviour of these tumours is generally benign and thus treatment decisions should be based on the presence or absence of symptoms [14].

Asymptomatic patients can be managed by surveillance with Ultrasonography (USG) and cystoscopy as the risk of complications outweighs the benefits of surgical resection. Symptomatic patients can be treated by Transurethral Resection (TUR) or large masses can be managed by partial or total cystectomy depending upon degree of involvement [15]. No case of recurrence after complete resection or malignancy has been noted so far. Ener K et al., and Hartman C et al., described an isolated bladder ganglioneuroma completely treated by TUR [18,19]. Tubre RW et al., reported a similar case of isolated bladder ganglioneuromas arising from dome, treated by partial cystectomy [20]. There has not been any incidence of recurrence or malignant transformation in any of the published reports. Preoperative or postoperative chemotherapy or radiotherapy has no value in treatment, except when it is associated with ganglioneuroblastoma changes, in which case there might be some role for chemotherapy. Even with residual disease, cessation of all other treatments and close follow-up may be adequate [19].

CONCLUSION(S)

Ganglioneuromas are rare benign tumours of the autonomic nervous system that infrequently occur in the urinary system. They are non functional tumours causing symptoms mainly by local compression effect. TUR is a suitable option for small, localised growth. On the other hand, extraluminal masses can be treated by excision as done in the present case (partial cystectomy). Prognosis is good and no recurrence has been reported yet. Even residual masses can be observed closely if asymptomatic. Role of chemoradiotherapy is not yet established.

REFERENCES

[1] Neurofibromatosis conference statement. National Institutes of Health Consensus Development Conference. Arch Neurol. 1988;45(5):575-78.
[2] Hintsa A, Lindell O, Heikkilä P. Neurofibromatosis of the bladder. Scandinavian Journal of Urology and Nephrology. 1996;30(6):497-99.
[3] Le C, Bedocs PM. Neurofibromatosis. [Updated 2021 Oct 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459329.
[4] Bouty A, Dobremez E, Harper L, Harambat J, Bouteiller C, Zaghet B, et al. Bladder dysfunction in children with neurofibromatosis type I: Report of four cases and review of the literature. Urol Int. 2018;100(3):339-45.
[5] Bekelis K, Meiklejohn DA, Missios S, Harris B, Saunders JE, Erkmen K. Ganglioneuroma of the internal auditory canal presenting as a vestibular schwannoma. Skull Base Rep. 2011;1(2):89-94.
[6] Bacci C, Sestini R, Ammannati F, Bianchini E, Palladino T, Carella M, et al. Multiple spinal ganglioneuromas in a patient harboring a pathogenic NF1 mutation. Clin Genet. 2010;77(3):293-97.
[7] Smets A, Mortele K, Wever N De, BenoitY, Praet M, Kunnen M. Coexistence of an adrenocortical carcinoma with an abdominal ganglioneuroma in a child. Pediatr Radiol 1998;28(5): 329-31.
[8] Acín-Gándara D, Carabias A, Bertomeu A, Giménez-Alvira L, Colao L, Limones M. Giant retroperitoneal ganglioneuroma. Rev Esp Enferm Dig. 2010;102(3):205-07.
[9] Zugor V, Schott GE, Kühn R, Labanaris AP. Retroperitoneal ganglioneuroma in childhood-a presentation of two cases. Pediatr Neonatol. 2009;50(4):173-76.
[10] Hayes FA, Green AA, Rao BN. Clinical manifestations of ganglioneuroma. Cancer. 1989;63(6):1211-14.
[11] Cobellis L, Messalli EM, Rossiello R, Montone L, Cobellis G. Bilateral pelvic ganglioneuroma: clinicopathologic findings: A case report. Eur J Obstet Gynecol Reprod Biol. 2004;117(2):242-44.
[12] Chen CH, Boag AH, Beiko DT, Siemens DR, Froese A, Isotalo PA. Composite paraganglioma-ganglioneuroma of the urinary bladder: A rare neoplasm causing hemodynamic crisis at tumor resection. Can Urol Assoc J. 2009;3(5):45-48.
[13] Dundr P, Dudorkinova D, Povýsil C, Pesl M, Babjuk M, Dvorácek J, et al. Pigmented composite paraganglioma-ganglioneuroma of the urinary bladder. Pathol Res Pract. 2003;199(11):765-69.
[14] Usuda H, Emura I. Composite paraganglioma-ganglioneuroma of the urinary bladder. Pathol Int. 2005;55(9):596-601.
[15] Lam KY, Loong F, Shek TWH, Chu SM. Composite paraganglioma-ganglioneuroma of the urinary bladder: A clinicopathologic, immunohistochemical, and ultrastructural study of a case and review of the literature. Endocr Pathol. 1998:9(1):353-61.
[16] Hurwitz R, Fitzpatrick T. Clinicopathological conference: A neuro-ectodermal tumor in the bladder. J Urol. 1980;124:417-21.
[17] Leestma JE, Jr E BP. Paraganglioma of the urinary bladder. Cancer. 1971;28(4):1063-73.
[18] Ener K, Mustafa A, Emrah O, Aylin Y, Murat K, Fatih A, Muhammet O. Bladder Ganglioneuroma: A Rare Case Report. Uro Today Int J. 2013;6(3):38.

[19] Hartman C, Williamson AK, Friedman AA, Palmer LS, Fine RG. Bladder ganglioneuroma in a 5-year-old girl presenting with a urinary tract infection and hematuria: Case report and review of the literature. Urology. 2015;85(2):467-69.

[20] Tubre RW, Locke N, Kats A, Lee E, Murphy JP. Ganglioneuroma of the bladder: Case report and literature review. Ped Urol Case Rep. 2015;2(4):01-06.

PARTICULARS OF CONTRIBUTORS:
1. Resident, Department of Urology, Seth Gordhandas Sunderdas Medical College and the King Edward Memorial Hospital, Mumbai, Maharashtra, India.
2. Assistant Professor, Department of Urology, Seth Gordhandas Sunderdas Medical College and the King Edward Memorial Hospital, Mumbai, Maharashtra, India.
3. Intern, Seth Gordhandas Sunderdas Medical College and the King Edward Memorial Hospital, Mumbai, Maharashtra, India.
4. Professor and Head, Department of Urology, Seth Gordhandas Sunderdas Medical College and the King Edward Memorial Hospital, Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Alhad Mulkalwar,
Intern, Seth Gordhandas Sunderdas Medical College and the King Edward Memorial Hospital, Mumbai, Maharashtra, India.
E-mail: alhad.mulkalwar@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 02, 2022
- Manual Googling: Jul 21, 2022
- iThenticate Software: Sep 06, 2022 (19%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Apr 01, 2022**
Date of Peer Review: **Jun 28, 2022**
Date of Acceptance: **Jul 25, 2022**
Date of Publishing: **Oct 01, 2022**