Neurofibromatosis Masquerading as Disorder of Sex Development

Sir,

A six-year-old child reared as female presented for evaluation of genital ambiguity. There was no past history of salt wasting crisis or maternal exposure to androgenic drugs during pregnancy. There was history of neurofibromatosis 1 (NF 1) among her father, paternal uncle, and grandmother. Clinical evaluation showed height of 96 cm (<3rd percentile) and weight of 14 kg (<3rd percentile). Bone age was compatible with her chronologic age. Evaluation of genitalia revealed presence of an enlarged phallus like structure [Figure 1a]. No gonads were palpable in the labioscrotal fold or inguinal region. There was presence of a small vaginal opening with a distinct urethral meatus. There were multiple cafe-au-lait spots over the body with a giant macule of size around 17.5 cm × 8 cm around diaper region [Figure 1a]. Ophthalmological evaluation showed presence of multiple lisch nodules in bilateral iris. Magnetic resonance imaging (MRI) of abdomen and pelvis revealed normal Mullerian structures and clitoral enlargement [Figure 1b]. There was no bladder involvement. Hormonal evaluation revealed normal pre pubertal serum gonadotropins, 17 hydroxy progesterone (17-OHP), dehydroepiandrosterone sulfate (DHEAS), and testosterone levels as per age specific cut offs. The karyotype analysis revealed normal female 46 XX pattern. The patient underwent nerve sparing reduction clitoroplasty. Histopathology of excised tissue confirmed the presence of clitoral neurofibroma [Figure 2a and b]. The patient is under periodic follow up for documentation of any recurrence.

Involvement of the external genitalia is extremely unusual in neurofibromatosis.[1-3] It has also been suggested that any child with genital neurofibromatosis should be evaluated for bladder neurofibromas based on a few cases with involvement of both external genitalia and bladder.[2] In cases of neurofibromas involving the female external genitalia, examination generally reveals clitoral enlargement resembling a phallus, and some patients report pain if presenting after puberty.[3] Occasionally, this enlargement masquerades as an intersex disorder and is confused with virilizing congenital adrenal hyperplasia.[3] Overall, the incidence of malignant degeneration of neurofibromas ranges from 13% to 29%, which increases with age.[2] The management of clitoral neurofibroma include surgical excision with all attempts to preserve the clitoris and its adjacent neurovascular structures. It has also been suggested that regular postoperative surveillance has to be carried out to monitor for local recurrence.[3] The endocrine manifestations of NF 1 in children comprises of short stature, growth hormone deficiency, growth hormone hypersecretion, central precocious puberty, diencephalic syndrome, pheochromocytoma, and gynecomastia.[4] The above case describes another rare facet of NF1 which is of particular interest to the endocrinologist. The possibility of clitoral neurofibroma should always be kept in mind while evaluating cases with genital ambiguity and any stigmata of neurofibromatosis. Hence, it should be noted that NF1 can have interesting gamut of endocrine manifestations.

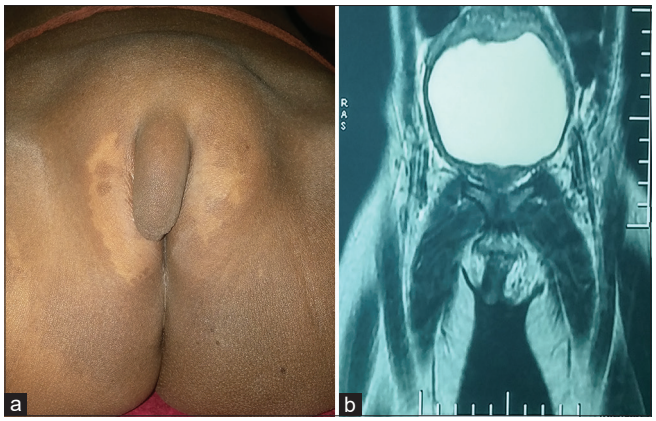

Figure 1: (a) A giant cafe-au-lait macule of size around 17.5 cm × 8 cm covering the entire diaper region. The hypopigmented areas seen in the vulval area represent the normal skin color. (b) MRI (T2 w image) showing clitoral enlargement without any bladder involvement

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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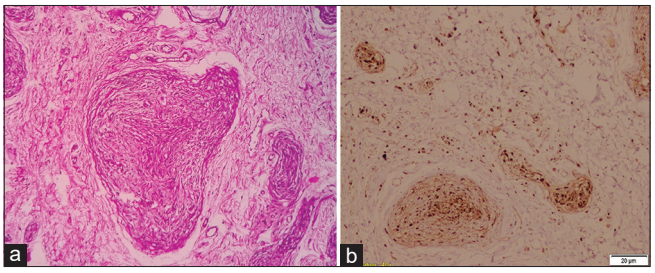

Figure 2: (a) Histopathology of excised tissue confirmed the presence of proliferating fascicle of spindle cells with wavy nuclei typical of neurofibroma. (b) The excised tissue stained positively with neural stain S 100

Conflicts of interest

There are no conflicts of interest.

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