Neurofibromatosis, Down's syndrome, and acquired abnormalities

Syed Yousuf Ali, Vimala Manne[1], Ranjit Manne[2], Chennamaneni Himani

Departments of Dermatology and STD, Shadan Institute of Medical Sciences, [1]Dr. VRK Women's Medical College, Teaching Hospital and Research Centre, [2]Department of Orthodontics, Panineeya Institute of Dental Sciences and Research Centre, Hyderabad, Telangana, India

Access this article online

Website: www.idoj.in

DOI: 10.4103/2229-5178.182362

Quick Response Code:

Address for correspondence:
Dr. Syed Yousuf Ali, House No. 9-4-77/A/79, Al Hasnath Colony, Toli Chowki, Hyderabad - 500 008, Andhra Pradesh, India.
E-mail: syedbidar@gmail.com

ABSTRACT

We report a patient with Down's syndrome and neurofibromatosis who presented with a keloid, sebaceous cyst and acanthosis nigricans, along with dental and ophthalmological defects. The coexistence of neurofibromatosis type 1 and Down's syndrome which are two unrelated genetic conditions is itself a rarity.

Key words: Acanthosis nigricans, Down's syndrome, keloid, myopia, neurofibromatosis, sebaceous cyst

INTRODUCTION

Neurofibromatosis affects 1:3,000 individuals, and characterized by largely benign but often debilitating tumors that grow in the nervous system.[1] It is caused by mutations in tumor-suppressor protein encoding genes. NF1 is typically diagnosed in childhood by appearance of café au lait spots. Its course is unpredictable: It can cause a variety of benign nerve tumors including plexiform, dermal, and optic glioma tumors; in some cases malignant peripheral nerve sheath tumors can develop in the plexiform tumours. Around two-thirds of individuals with NF1 develop learning disabilities.[1]

Down's syndrome is one of the most common and easily recognized genetic conditions in humans.[1,2] The estimated prevalence in the United States is approximately 15 per 10,000 live births (ie, 1 out of every 700).[1,3] The incidence increases with maternal age.[1] Most often, it is the result of nondisjunction on chromosome 21 during maternal meiotic division.[4]

CASE REPORT

We herein present the case of a 17-year-old boy with complaints of skin lesions over the back associated with mild itching since 3 months. He was a known case of Down's syndrome with a history of seizures in childhood [Figure 1]. The lesions gradually increased in size and number, and similar lesions started developing over his forehead since 2–3 weeks. On examination, multiple skin colored papules of varying size were present over the entire back and the forehead.

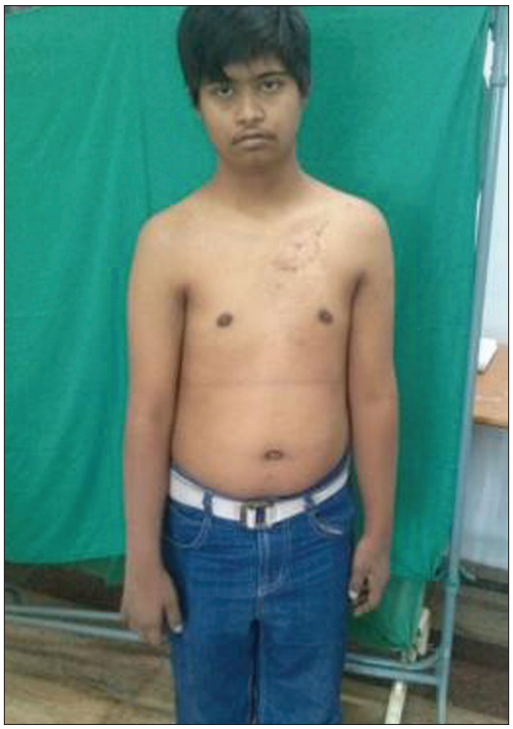

Figure 1: Physical appearance of Down's syndrome

Cite this article as: Ali SY, Manne V, Manne R, Himani C. Neurofibromatosis, Down's syndrome, and acquired abnormalities. Indian Dermatol Online J 2016;7:198-200.

A solitary sebaceous cyst was noted over the back. Bilateral axillary freckling was also noted. Velvety thickening of the skin and hyperpigmentation of the axillae suggestive of acanthosis nigricans was present. The characteristic features of Down's syndrome, including simian crease, mongoloid facies, and mental retardation were present. The patient had a history of delayed milestones. There was no history of consanguinity. Canities and a solitary keloid over the chest were also seen apart from the clinical features of Down's syndrome. On oral examination, scrotal tongue, abnormal dentition, and cusp abnormalities were noted [Figure 2]. Mental retardation present. Speech and hearing was normal. Ophthalmological examination revealed Lisch nodules and patient was found to have myopia. Thyroid profile revealed subclinical hyperthyroidism. Liver function tests and lipid profile were normal. Other investigations such as CT scan brain, 2D echo, and ECG were normal. Histopathology of the nodule from the back revealed focally thinned out epidermis with intact basal layer; the papillary dermis showed a mild perivascular infiltrate. Deeper dermis showed a benign spindle cell proliferation suggestive of neurofibromatosis [Figure 3].

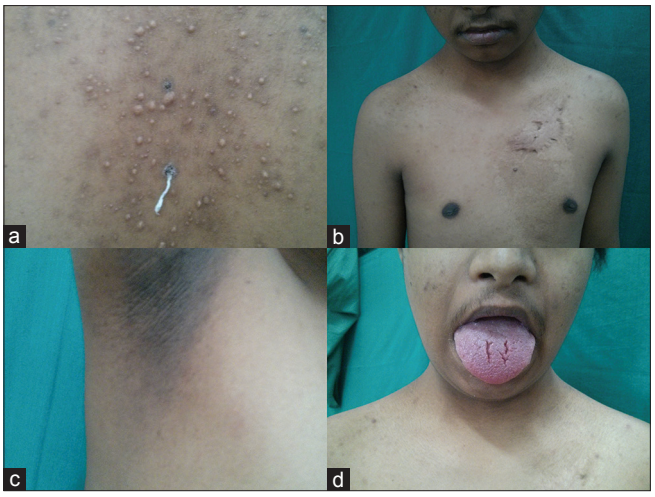

Figure 2: (a) Neurofibromas (b) sebaceous cyst (c) acanthosis nigricans, and axillary freckling (d) Scrotal tongue

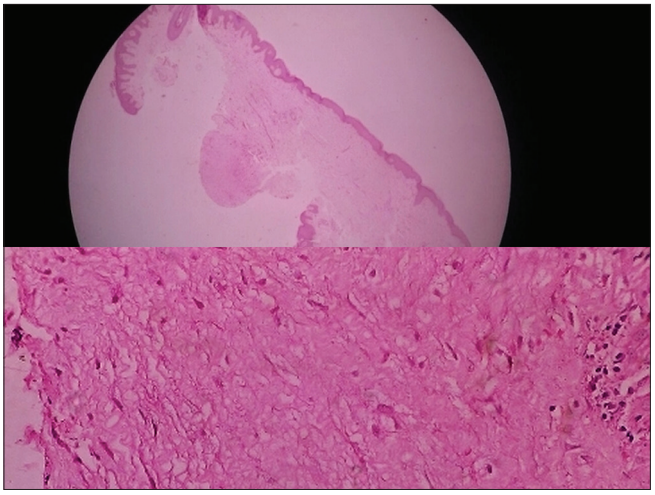

Figure 3: Focally thinned out epidermis with intact basal layer with the papillary dermis showing a mild perivascular infiltrate. Deeper dermis showed a benign spindle cell proliferation suggestive of neurofibromatosis. (H and E, ×40)

DISCUSSION

The presentation of a patient with two unrelated genetic disorders is uncommon, although not statistically impossible. A Medline search of the literature revealed only three such reports.[1,4,5] However, in two of these reports, a third medical condition was also present. In one report, breast cancer was reported. In the other, the patient had juvenile xanthogranuloma. Third report addressed dental care among patients with Downs syndrome.[6] Our patient had Down's syndrome, neurofibromatosis, dental anomalies, and ocular defects and keloids. In the large majority of cases, Trisomy 21 is due to a nondysjunctional event during maternal meiosis. NF-1 is caused by a mutation in the NF-1 gene on chromosome 17. There is no current evidence to support the idea that this is anything other than a chance occurrence. The two conditions are not related, and the likelihood of a person being born with these two conditions is approximately 1 in 2,700,000 births.[1] They however overlap in their manifestations. Both are associated with intellectual impairment to differing degrees. Macroglossia occurs in both conditions, as may facial, dental, and occlusal abnormalities. Hearing and speech are affected in both conditions, as may the ability to maintain an acceptable level of oral hygiene. The impairment observed with NF1 is thought to be mediated by neurofibromin dysregulation. Neurofibromin is the product of the NF1 gene. Mutations in the gene results in abnormal control of cell growth, differentiation, and aberrant myelination.[1,7] Our patient with of neurofibrmatosis type 1 with Down's syndrome is the first such to have a keloid and sebaceous cyst apart from myopia and dental anomalies. The unpredictable nature and course of the two genetic disorders along with multiple acquired conditions in this patient make it difficult for patients, teachers, care givers, and medical/dental providers to create and maintain long-term care plans.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Schaffer R, Goss L, Romer MM, Kalamchi S. Down syndrome and neurofibromatosis: A case report. Spec Care Dentist 2014;34:313-8.
2. Gorlin RJ, Cohen MM Jr, Hennekam RC. Syndromes of the Head and Neck. 4th ed. New York: Oxford University Press; 2001. 35.
3. Parker SE, Mai CT, Canfield MA, Rickard R, Wang Y, Meyer RE, *et al*.; National Birth Defects Prevention Network. Updated national birth prevalence estimates for selected birth defects in the United States, 2004-2006. Birth Defects Res A Clin Mol Teratol 2010;88:1008-16.
4. Satgé D, Sasco AJ, Goldgar D, Vekemans M, Réthoré MO. A 23-year-old woman with Down syndrome, type I neurofibromatosis, and breast carcinoma. Am J Med Genet 2003;125A:94-6.
5. van Leeuwen RL, Berretty PJ, Knots E, Tan-Go I. Triad of juvenile xanthogranuloma, von Recklinghausen's, neurofibromatosis and trisomy 21 in a young girl. Clin Exp Dermatol 1996;21:248-9.
6. Bull MJ. The Committee on Genetics. Health supervision for children with Down syndrome. Pediatrics 2011;128:393-406.
7. Gardiner K, Herault Y, Lott IT, Antonarakis SE, Reeves RH, Dierssen M. Down syndrome. From understanding the neurobiology to therapy. J Neurosci 2010;30:14943-5.