Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi

Case Report

Segmental neurofibromatosis with Lisch nodules

Gayathri A [a], Ramachandran R [b], Murali Narasimhan [c,*]

[a] Junior Resident (Dermatology), SRM Med College & Research Centre, SRM Nagar, TamilNadu, India
[b] Associate Professor (Dermatology), SRM Med College & Research Centre, SRM Nagar, TamilNadu, India
[c] Professor & Head (Dermatology), SRM Med College & Research Centre, SRM Nagar, TamilNadu, India

ARTICLE INFO

Article history:
Received 15 September 2020
Accepted 22 November 2020
Available online 8 March 2021

Keywords:
Segmental neurofibromatosis
Lisch nodules
Neurofibromatosis

ABSTRACT

Neurofibromatosis (NF) is an inherited neuroectodermal abnormality that primarily affects the growth of neural tissues, and Riccardi classified it into eight types. Segmental neurofibromatosis, which is a rare form of neurofibromatosis, is classified as type 5. We report a case for very unusual presentation of segmental NF with unilateral lisch nodules and uncommon sites involving the scalp. Moreover, we could find only one case report of segmental NF with lisch nodules in the literature and could not find any case report involving the scalp.

Introduction

Neurofibromatosis (NF) is a common genodermatosis presenting with a wide variety of clinical manifestations. Riccardi had classified NF into eight types. Although type 5 NF is frequently seen, Segmental NF (type 5) is quite rare.[1] Here, we report a middle-aged female presenting with segmental NF of unusual site involving the scalp and the presence of unilateral Lisch nodules.

Case report

A 37-year-old female patient, born of non-consanguineous marriage, presented with skin-coloured raised lesions over the scalp and forehead since 14 years of age. Although the lesions were asymptomatic, the patient sought consultation for gradual but steady increase in the size of the lesions for past 5 months. There was no history of visual or auditory disturbances, neurological symptoms, speech impairment and skeletal abnormalities. Patient's parents, siblings and children did not have any skin manifestations.

On examination, few skin-coloured, soft, non-tender papules and nodules of size ranging from 0.5 mm to 1 cm were seen in a linear configuration adjacent to midline over right frontal region of the scalp and forehead involving ophthalmic segment (V1) of the right trigeminal nerve (Fig. 1). Button hole sign was noted in the nodular lesions. Café au lait spots, axillary and palmar freckles were absent.

Ophthalmic examination revealed Lisch nodules over the iris of right eye (Fig. 2). The histopathological examination (H&Estain, 400X magnification) of single excised lesion showed ill-defined circumscribed dermal neoplasm composed of small spindle cells with eosinophilic cytoplasm and wavy nuclei in a collagenous stroma (Fig. 3). Computed tomography of the brain revealed no abnormalities.

* *Corresponding author.*
E-mail address: leecutis@gmail.com (M. Narasimhan).
https://doi.org/10.1016/j.mjafi.2020.11.021

According to the clinical and histopathological findings, a diagnosis of segmental NF was made. The patient has been followed up for 6 months, and no neurological complications or malignant lesions were noted. Patient consent for inclusion in study was also obtained.

Discussion

Riccardi classified NF into eight types, namely NF-1 (von Recklinghausen disease), NF-2 (acoustic form), NF-3 (mixed form), NF-4 (the variant with diffuse Café au lait macules and neurofibromas with or without CNS tumours), NF-5 (the segmental type with Café au lait macules or neurofibromas limited to a unilateral, segmental distribution), NF-6 (Café au lait spots without neurofibromas), NF-7 (the late-onset type) and NF-8 (the unspecified type).[1]

NF1 or von Recklinghausen disease is a neural crest–derived multisystem disorder. It occurs due to mutation in NF1 gene on chromosome 17q. It is inherited as an autosomal dominant disorder with complete penetrance and variable expressivity from very mild to very severe forms. The prevalence of NF1 ranges from 1 in 2500–3300 live births. The typical findings of NF1 include neurofibromas, café au lait macules, axillary freckling, optic glioma, Lisch nodules, bone abnormalities and a positive family history. Other less common features like macrocephaly, epilepsy, mental retardation, hypertension, various endocrine disorders, pheochromocytoma, rhabdomyosarcoma and malignant peripheral nerve sheath tumours may occur.[2]

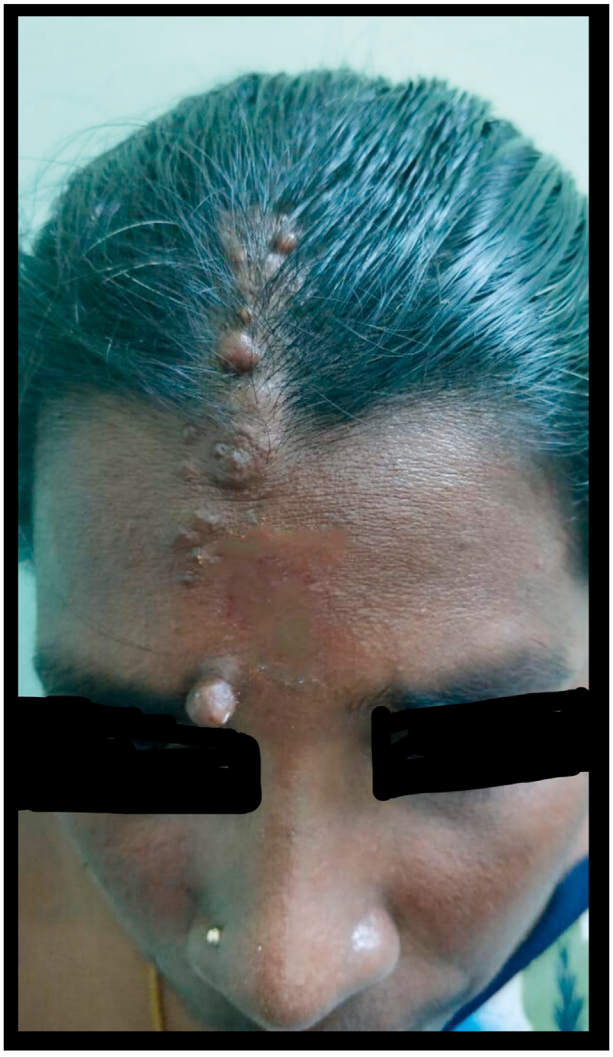

Fig. 1 – Clinical picture showing few skin-coloured, soft, non-tender papules and nodules in linear configuration noted over the right side of the scalp and forehead.

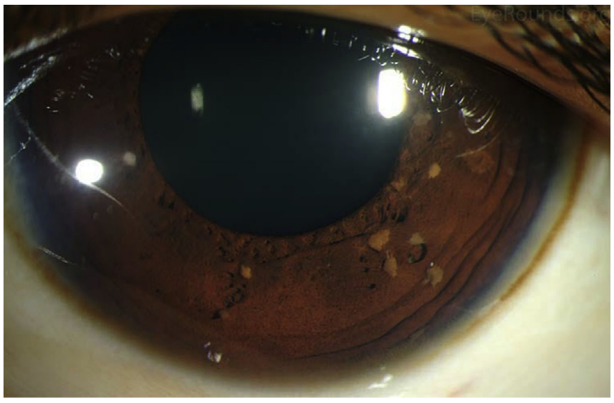

Fig. 2 – Slit lamp examination showing multiple Lisch nodules over the right iris.

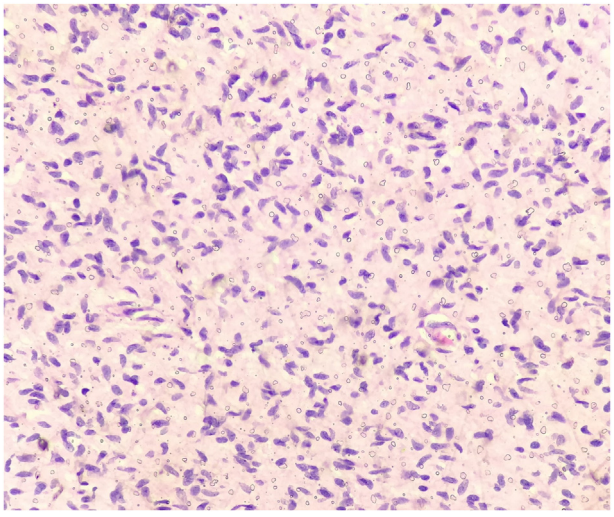

Fig. 3 – Histopathological picture showing ill-,defined circumscribed dermal neoplasm composed of small spindle cells with eosinophilic cytoplasm and wavy nuclei in a collagenous stroma. (H&E stain, 400× magnification).

Segmental NF or mosaic-localized NF1 is a rare variant, presenting as café au lait macules or neurofibromas, affecting limited body segments. The prevalence of segmental NF ranges from 0.0014% to 0.002%, that is, one in 36,000 to 40,000 populations. Unlike NF1, segmental NF occurs due to post-zygotic somatic mutation of NF1 gene. It occurs during late embryonic life and affects various cell lines. So the presentation of segmental NF varies from patient to patient, that is, the pigmentary changes occur earlier in childhood and neurofibromas occur in later age. The children with pigmentary changes may not develop neurofibromas in adulthood.

Table 1 – The difference between NF1 and NF5.

Features	Von Recklinghausen disease (NF1)	Segmental neurofibromatosis (NF5)
Inheritance	Autosomal dominant	Non inheritable. The disease occurs due to postzygotic somatic mutation.
Prevalence	1 in 2500–3300	1 in 36,000–40,000
Family history	Almost always present	Mostly absent
Transmission to offspring	Present, due to autosomal dominant inheritance with complete penetrance and variable expressivity	Extremely rare. In some, gonadal mosaicism may occur and transmit the disease.
Involvement	Generalized and bilateral	Localized and unilateral
Café au lait macules and axillary freckling	+	+\-
Cutaneous neurofibroma	+\-	+\-
Plexiform neurofibroma	+\-	+\-
Lisch nodules	+	–
Systemic involvement	+	–
Risk of associated malignancies	5–15%	5.3%

Because of the somatic mutation of terminally differentiated cells, it is considered as a non-inheritable disorder, and there is no evidence of genetic transmission. Some patients with segmental NF may have offspring with full-blown NF type 1. It indicates gonadal mosaicism in these patients who may transmit the disease.[3] The percentage of body involvement in segmental NF determines the risk of occurrence of generalised NF1 in offspring.[4]

Riccardi proposed criteria to diagnose segmental NF as neurofibromas or café au lait macules involving unilateral segment, absence of systemic involvement including Lisch nodules and internal neurofibromas, no midline crossing of the lesions and absence of family history.[5] In our case, all the above criteria were met, except for absence of Lisch nodules. The differences between NF1 and NF5 described in Table 1.

Roth et al[6] further classified the segmental NF into four types (to resolve the confusion in categorizing the patients), as true segmental (as per Riccardi's criteria), hereditary, localized with deep involvement and bilateral involvement.

Ruggieri et al.[3] clinically classified segmental NF into those with only pigmentary changes, with only neurofibromas, with isolated plexiform neurofibromas and with both pigmentary changes and neurofibromas. In their study, segmental NF presented commonly as pigmentary changes in the form of café au lait macules or axillary freckling with hyperpigmented background and with associated features like Lisch nodule (two cases), NF1 complications (learning difficulties, optic pathway gliomas and pseudarthrosis in less than 10% patients). Transmission to offspring was noted in small number (seven cases) of patients. The second most common form was with only neurofibromas, in which nodular cutaneous neurofibromas were seen, and no other associated features were seen, except transmission to offspring in one case. Third form with pigmentary changes and neurofibromas in which both café au lait macules and dermal neurofibromas were seen and no other associated features were noted. It must be differentiated from NF1, if more than one dermatome was affected. The least common form was painful solitary plexiform neurofibromas, affecting head or neck.

Segmental NF has mostly been reported in thoracic, cervical and lumbar segments. Only 10 cases have been reported to involve the face.[5] Scalp lesions have also not been reported, as was manifested in our patient. In 6% of cases, bilateral involvement has been reported, and 93% of patients do not have family history of NF.[7]

Reports of Lisch nodules are rare in segmental NF (only with neurofibroma type – single case report)[8] as they do not usually involve the head and neck area, unlike our case where multiple iris hamartomas were seen only on the involved side but not on the contralateral side. If Lisch nodules are absent, risk of transmission to offspring is reduced.[9]

Long-term follow-up is needed in these patients to assess the progression. These patients have 5.3% risk of developing malignancies, compared with 5–15% risk in NF1. Malignancies reported with segmental NF include peripheral nerve sheath tumours, malignant melanoma, solid organ cancers like carcinoma of breast, colon cancer, lung carcinoma, gastric carcinoma and Hodgkin lymphoma. The most frequently associated malignancies are peripheral nerve sheath tumour and malignant melanoma.[10]

Conclusion

Segmental NF is a rare form of NF. Here, we report this case for very unusual presentation of segmental NF with unilateral Lisch nodules and uncommon site involving the scalp. Although the risk of transmission to offspring is less, the potential for rare systemic involvement and malignant transformation does exist. So we must have multidisciplinary follow-up for these patients at regular intervals to screen for complications.

Disclosure of competing interest

The authors have none to declare.

REFERENCES

1. Riccardi VM. Neurofibromatosis: clinical heterogeneity. *Curr Probl Canc.* 1982;7:1–34.
2. Wimmer K. Neurofibromatosis type 1 (NF1). *Atlas Genet Cytogenet Oncol Haematol.* 2006;10(3):206–207.

3. Ruggieri M, Huson SM. The clinical and diagnostic implications of mosaicism in the neurofibromatoses. *Neurology*. 2001;56:1433–1443.
4. Lee S, Roh S, Kim S. Multiple segmental neurofibromatosis. *J Dermatol*. 2012 Sep;39(9):810–811.
5. Vaidya MK, Kullolli GK, Patil R. Segmental neurofibromatosis - a rare case report and review of literature. *Int J Sci Stud*. 2017;5(1):260–262.
6. Roth RR, Martines R, James WD. Segmental neurofibromatosis. *Arch Dermatol*. 1987;123:917–920.
7. Hager CM, Cohen PR, Tschen JA. Segmental neurofibromatosis: case reports and review. *Am J Acad Dermatol*. 1997;37:864–869.
8. Weleber RG, Zonana J. Iris hamartomas (Lisch nodules) in a case of segmental neurofibromatosis. *Am J Ophthalmol*. 1983 Dec;96(6):740–743.
9. Sloan J, Fretzin D, Bovenmyer D. Genetic counseling in segmental neurofibromatosis. *J Am Acad Dermatol*. 1990 Mar;22(3):461–467.
10. Dang JD, Cohen PR. Segmental neurofibromatosis and malignancy. *Skinmed*. 2010;8:156–159.