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Case report: a child with type 1 neurofibromatosis and intellectual disability



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ABSTRACT

Background: Neurofibromatosis is a genetic disorder that manifests as a tumor surrounding the nerves and several other pathologic presentations.

Case: Female, 11 years old, according to history, physical examination and supporting the investigation, was consistent with the diagnostic criteria of type 1 neurofibromatosis (NF-1). The patient also has an intellectual disability. A tumor on the foot region that was functionally disabling was found on the patient, and surgical treatment was performed. Cognitive disorder is the most common neurological complication in individuals with NF-1 and usually presents with a low intelligence quotient (IQ). There is no specific treatment to prevent the development of NF-1. However, early treatment can minimize and prevent further complications. Treatment for the patient involves multiple clinical disciplines.

Conclusion: A neurofibromatosis case can be diagnosed clinically alone, since many other systemic involvements require a multi-disciplinary approach.

Keywords: Neurofibromatosis, von Recklinghausen's, neurofibroma

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INTRODUCTION

Neurofibromatosis is a genetic disorder that manifests as a tumor surrounding the nerves and several other pathologic presentations.¹ There are three main types of neurofibromatosis based on clinical and genetic characteristics.² Type 1 neurofibromatosis (NF-1) is the most common condition, estimated to be 1 in 2500 to 3000 individuals regardless of ethnicity, race, or gender.^{3,4} Type 1 neurofibromatosis was first described by Frederich von Recklinghausen in 1882. The diagnosis of NF-1 can be made from clinical symptoms alone.^{5,6}

Cognitive deficit is the most common complication in children with NF-1. The frequency of intellectual disability in children with NF-1 is between 30 to 69%. Generally, further investigation is necessary to confirm an intellectual disability when an individual achievement is far below the expected standards for the age, school, and intellectual level.⁷

CASE REPORT

An 11-years old female presented with a complaint of multiple lumps all over the body. Initially, a large brownish patch appeared on the patient's right foot since birth, which then enlarged and grew bigger to form a large hanging lump. This condition caused difficulty in performing a daily activity. From 5-years before, multiple small lumps appeared on the body, both hands and limbs. The lumps were skin-colored, spongy and multiplied with brownish patches on the skin. There was a decreased cognitive function on the child, which was inappropriate for the age. There were no visual, hearing, or bone disorders. The patient's grandmother also had the same complaint.

The patient's general condition was good on physical examination, with compos mentis awareness. Vital signs and general status were within normal limits. Dermatologic status, there were multiple demarcated, round hyperpigmented macules (freckles) with a size of 0.2-0.5

cm on the facial and neck region. On the anterior et posterior of the thoracic region, axillary, and superior et inferior right and left extremities, there were multiple round tumors with a diameter of 0.5 – 4 cm, with spongy consistency, mobile and immobile, no tenderness, with buttonholing, multiple hyperpigmented macules to patches (*café-au-lait* macule) demarcated to geographic with a diameter of 0.1-2 cm and 0.5 x 3 cm, with discrete configuration and generalized distribution. There was a solitary tumor on the right foot region with an oval shape and size of 5 cm x 7 cm, with spongy consistency, resembling a "bag of worms" with multiple demarcated hyperpigmented macules with a size of 0.2 x 0.4 – 0.3 x 0.7 cm.

From the Pediatric department assessment, it was found that the GCS was E4V5M6, and there was no sign of neurological deficit. The computed tomography (CT) scan of the brain with contrast showed no sign of bleeding, infarct, or intracerebral space-occupying lesion (SOL). The result of the IQ

assessment was 76. The patient was assessed with a working diagnosis of intellectual disability.

The Plastic Surgery department has assessed the patient with a working diagnosis of type 1 neurofibromatosis. The patient was recommended for magnetic resonance imaging (MRI) examination of the foot region and was planned for a biopsy of the right foot region.

The working diagnosis from the Dermatology and Venereology department was type 1 neurofibromatosis. In this case, the patient was not given any treatment. We performed counseling provided information and education regarding the disease.

DISCUSSION

Type 1 neurofibromatosis (NF-1), also known as Recklinghausen disease, is a genetic disorder inherited in an autosomal dominant manner. This disease can present various clinical manifestations, including dermatologic, neurologic, endocrinologic, and orthopedic presentation.^{6,8} NF-1 is a much more common disease than previously predicted, with an incidence

of 1:2000 livebirths and a prevalence of 1/4000.^{9,10} The clinical manifestations can present in various forms. Many patients expressed a mild disease, but more serious complications can develop as the patient ages.^{2,11}

This disease is caused by a genetic mutation of chromosome 17q11.2 with a large coding protein called neurofibromin.^{2,10} This genetic mutation causes decreased neurofibromin protein expression. This protein regulates the signals for cellular proliferation and differentiation through the activity of the ras-guanosine triphosphatase enzyme. Neurofibroma developed due to uncontrolled cell proliferation when both alleles of NF-1 from the Schwann cells are mutated. The loss of function of both alleles will result in the manifestation of neurofibroma. This showed that neurofibromin acts as a tumor-suppressing gene.^{2,11}

The clinical manifestation of NF-1 includes systemic and cutaneous manifestation. The characteristic bone lesion usually occurs in the first year of life. An optic pathway tumor usually

develops; however, less than half of these patients will show symptoms.^{3,5} Lisch nodule found on the ocular examination will be helpful for diagnosis and will not affect visual function.¹²

Approximately 15% of children with NF-1 will develop into optic pathway tumors (OPT). The highest risk of symptomatic OPT development in NF-1 is during the first six years of life; the development of symptomatic tumor after six years commonly occurs. Thirty percent of children with symptomatic OPT will have an abnormal ophthalmologic examination without visual symptoms that lead to tumor findings. Because young children rarely complain about losing vision, even when it is severe, an annual eye examination is substantial in all young children with NF-1. There can be signs of ocular damage, including afferent papillae damage, optic nerve atrophy, papillae edema, strabismus, or color vision disturbance.^{3,12}

Diagnosis of NF-1 is mainly based on clinical findings. A genetic examination can be performed to confirm a mutation in NF-1. Histopathological examination is unnecessary to confirm the diagnosis of NF-1 since the clinical diagnosis of NF-1 is typically simple. Histopathologically, in neurofibroma, there are coil-shaped cells with an elongated nucleus and pale cytoplasm in between pale fibrillary tissue.^{12,13}

Other systemic clinical manifestations can also be found in NF-1. The inability to follow lessons is the most common manifestation found in approximately 30-70% of children. Brain tumors, such as meningioma, can affect 23% of patients with NF-1. Hypertension can also occur at a young age. The most common skeletal manifestation is tibial bone dysplasia (only affecting 1-4% of patients), pectus deformity (in 24% of patients), and scoliosis (in 10% of patients).¹³

Cognitive impairment is the most common neurological complication in individuals with NF-1 and generally presents with a low Intelligence Quotient (IQ). Thirty to sixty-nine percent of children with NF-1 will have learning difficulties, both verbally and non-verbally, and attention disorders. Therefore, they will fail to achieve their



Figure 1a-1c. Hyperpigmented macules (freckle) and multiple tumors.

full academic potential. These disorders include awkwardness, difficulty in reading/ writing, working memory impairment, and attention deficits.¹³ In this case, the patient was an 11-year old female who presented with complaints consistent with the diagnostic criteria of NF-1, with cognitive impairment. Upon examination, there was no visual, auditory or neurological impairment.

There is no specific treatment to prevent the development of NF-1. However, early treatment can minimize and prevent further complications. Treatments for patients involve multiple clinical disciplines to determine the progressivity of the disease detect organ involvement other than the skin tissue. Cutaneous neurofibroma can be treated if there is any itchiness or if it was functionally and cosmetically very disabling as what was found in this case.^{2,6,14}

The prognosis of this case is dubious. Until the last follow-up, there was other organ involvement, in the form of Lisch nodules found in both eyes, but it did not cause any visual disturbance. However, routine follow-up to monitor further complications such as optic pathway tumor is necessary. The patient also had an intellectual disability. Moreover, further treatment in the Plastic Surgery discipline and evaluation for other possible complications as the disease progresses is still necessary.

CONCLUSION

We reported a case of type 1 neurofibromatosis in an 11-years old female child. We found neurofibroma, café-au-lait macule, and Lisch nodules with intellectual disability in this case. The diagnosis, in this case, was made based on history and physical examination. A

neurofibromatosis case, in general, can be diagnosed by clinical assessment alone. However, a multidisciplinary approach is necessary since there are many systemic clinical involvements. Further evaluation of the disease progression is required. The prognosis of the patient is dubious.

ETHICS IN PUBLICATION

The patient received informed consent and agreed to share information and photography for publication and education.

CONFLICT OF INTEREST

None declared.

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AUTHORS CONTRIBUTION

Author EW and IAUP contributed to patient examination, follow-up treatment, manuscript preparation, and publication. Author NLPVK contributed to patient treatment and the theoretical approach for patient management.

REFERENCES

- Irvine A, Mellerio J. Genetics and genodermatoses. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. *Rook's textbook of dermatology* 8th edition. Singapore: Willey Blackwell; 2010. p. 15.15-15.20.
- Alves Júnior SF, Zanetti G, Alves de Melo AS, Souza AS, Souza LS, de Souza Portes Meirelles G, et al. Neurofibromatosis type 1: State-of-the-art review with emphasis on pulmonary involvement. *Respir Med*. 2019;149(January):9–15.
- Cannon A, Chen MJ, Li P, Boyd KP, Theos A, Redden DT, et al. Cutaneous neurofibromas in Neurofibromatosis type I: A quantitative natural history study. *Orphanet J Rare Dis*. 2018;13(31):1–7.
- Anonim. Buku Register Kunjungan Sub Bagian Dermatologi Anak Poliklinik Kulit dan Kelamin Rumah Sakit Umum Pusat Sanglah Denpasar tahun 2018 - 2019. 2019;
- Rabab'h O, Gharaibeh A, Al-Ramadan A, Ismail M, Shah J. Pharmacological approaches in neurofibromatosis type 1-associated nervous system tumors. *Cancers (Basel)*. 2021;13(15):1–18.
- Sirvaitis S, Sirvaitis R, Perusek T, Garcia-Zuazaga J. Early Cutaneous Signs of Neurofibromatosis Type 1. *J Dermatol Nurses Assoc*. 2017;9(4):191–3.
- Bergqvist C, Servy A, Valeyrie-Allanore L, Ferkal S, Combemale P, Wolkenstein P, et al. Neurofibromatosis 1 French national guidelines based on an extensive literature review since 1966. *Orphanet J Rare Dis*. 2020;15(1):1–23.
- Zulfiqar M, Lin M, Ratkowski K, Gagnon MH, Menias C, Siegel CL. Imaging features of neurofibromatosis type 1 in the abdomen and pelvis. *Am J Roentgenol*. 2021;216(1):241–51.
- Evans DG, Howard E, Giblin C, Clancy T, Spencer H, Huson SM, et al. Birth incidence and prevalence of tumor-prone syndromes: Estimates from a UK family genetic register service. *Am J Med Genet Part A*. 2010;152(2):327–32.
- Buchholzer S, Verdeja R, Lombardi T. Type I Neurofibromatosis: Case Report and Review of the Literature Focused on Oral and Cutaneous Lesions. *Dermatopathology*. 2021;8(1):17–24.
- Anderson J, Gutmann D. Neurofibromatosis type 1. In: *Handbook of Clinical Neurology*, 3rd ed. Washington: Elsevier; 2015. p. 75–86.
- Listernick R, Charrow J. The Neurofibromatoses. In: Goldsmith L, Katz S, Gilchrist B, Paller A, Leffel D, Wolff K, editors. *Fitzpatrick's Dermatology in General Medicine*, 9th ed. New York: Mc Graw Hill Education; 2019. p. 2465–79.
- Ruggieri M, Huson SM. The clinical and diagnostic implications of mosaicism in the neurofibromatoses. *Neurology*. 2001;56(11):1433–43.
- Salveti A, Ferrari V, Garofalo R, Gazzaniga P, Guerroni A, Metrucci A, et al. Incidence of herpes zoster and postherpetic neuralgia in Italian adults aged ≥50 years: A prospective study. *Prev Med Reports*. 2019;14(2019):1–7.



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