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BILATERAL NEUROFIBROMATOSIS IN MALE NIPPLE: CASE REPORT

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ABSTRACT
Neurofibromatosis type 1 (NF1) is a genetic disorder often diagnosed in childhood due to its early clinical manifestations, which include skin, eye, tumor, bone, and neurological changes. Also known as Von Recklinghausen's disease, it is an autosomal dominant genetic disorder that affects approximately 1 in every 3,000 individuals worldwide. This report discusses a typical case of neurofibromatosis type 1 with multiple café-au-lait spots distributed over the body, mainly concentrated on the trunk, abdomen, and back, and particularly on the patient's nipples. Surgical treatment was performed, with the excision of the nipple lesions showing good clinical progress.

Keywords: Neurofibromatosis type 1, Von Recklinghausen's disease, Neurofibromas, Skin nodules.

INTRODUCTION

Neurofibromatosis type 1 (NF1), also known as Von Recklinghausen's disease, is an autosomal dominant genetic disorder that affects approximately 1 in every 3,000 individuals worldwide. This condition is caused by mutations in the NF1 gene located on chromosome 17, responsible for encoding the protein neurofibromin, which acts as a tumor suppressor. The functional deficiency of this protein leads to the formation of multiple tumors along the nerves, known as neurofibromas, in addition to other diverse clinical manifestations.[1]

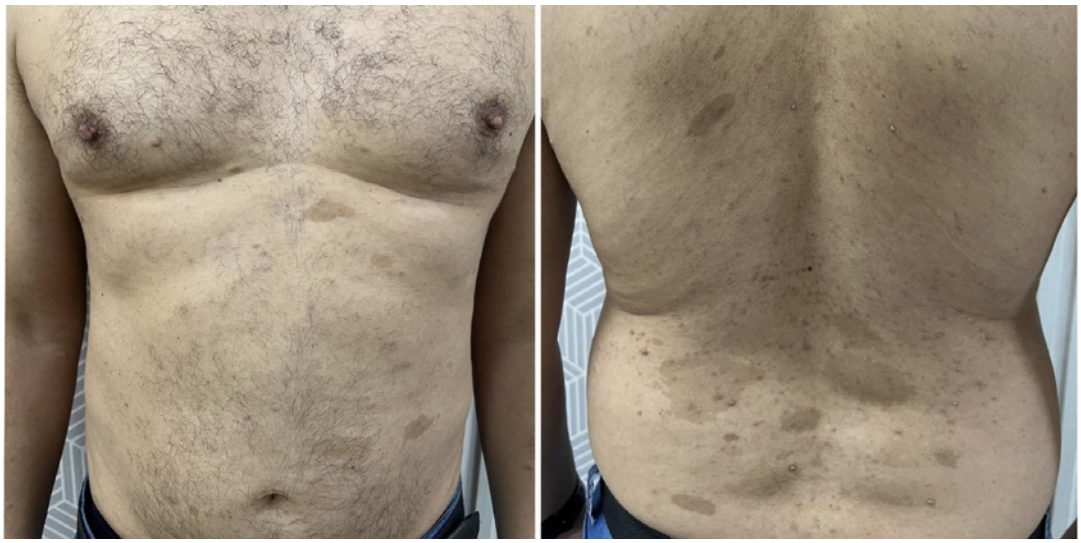
The signs and symptoms of NF1 vary widely among patients but typically include café-au-lait spots on the skin, axillary and inguinal freckling, optic gliomas, Lisch nodules (pigmented hamartomas of the iris), and a predisposition to developing both benign and malignant tumors. The complications associated with NF1 can be severe, involving the central nervous, cardiovascular, and skeletal systems, significantly impacting the quality of life of affected individuals. Cutaneous neurofibromas are one of the most visible manifestations of NF1. They can be classified as cutaneous, subcutaneous, and plexiform, each with distinct clinical characteristics. Cutaneous neurofibromas are the most common, presenting as soft nodules that can appear anywhere on the body. However, the location of neurofibromas can vary, and in rare cases, they can affect unusual anatomical regions such as the nipples.[2]

The presence of neurofibromas in specific areas can cause not only physical and aesthetic discomfort but also additional complications, depending on their location and growth.[1,2] Neurofibromatosis with breast involvement is particularly rare, and there are few reports in the medical literature about neurofibromas involving the nipples, especially bilaterally in male patients. This case report describes a rare presentation of neurofibromatosis type 1 with bilateral neurofibromas on the nipples in a male patient, highlighting the importance of recognizing this atypical manifestation and its implications for clinical and therapeutic management.

CASE REPORT

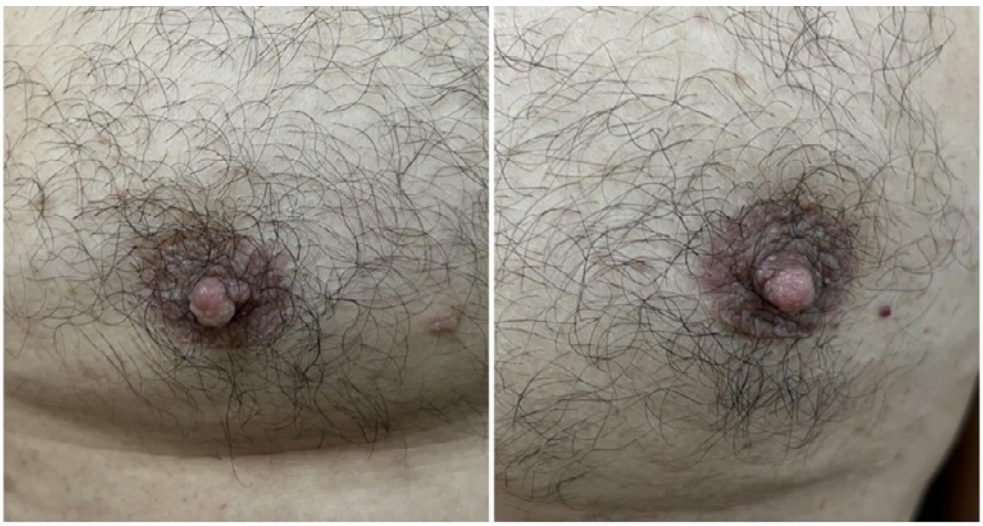
A 43-year-old male patient, P.M.C, from Brasília-DF, sought medical attention due to the presence of cutaneous nodules, including on the nipples. On physical examination, the patient presented with skin lesions clinically corresponding to neurofibromatosis type 1, with multiple café-au-lait spots distributed over the body, mainly concentrated on the trunk, abdomen, and back, as shown in (Figure 1).

Figure 1 - Images taken during the initial consultation showing café-au-lait spots distributed on the abdomen, trunk, and back.



Also observed were the presence of globular nodular lesions bilaterally on the nipples, with a fibrous consistency. The nodule on the right side was larger, suggesting neurofibromas (Figure 2).

Figure 2 - Images of nodular lesions on the nipples. A- Right nipple; B- Left nipple.



The conventional surgical excision technique was chosen for the removal of the lesions from each nipple, with the excised material from the right side sent for histopathological analysis. Both the histopathological and immunohistochemical analyses were compatible with nipple fibromas, consistent with neurofibromas.

DISCUSSION

Neurofibromatosis type 1 (NF1) is a genetic disorder often diagnosed in childhood due to its early clinical manifestations, which include skin, eye, tumor, bone, and neurological changes. The most notable skin features are café-au-lait spots and freckles. Café-au-lait spots, present in 95% of patients, are hyperpigmented, appear in the first year of life, and stabilize in adulthood. Freckles predominantly appear in intertriginous regions, such as the axillae and groin, between the ages of 3 and 53.

Patients with NF1 have a predisposition to developing various benign and malignant tumors due to the compromised function of the NF1 tumor suppressor gene. The most common benign tumors are neurofibromas, which can be plexiform, cutaneous, or nodular. Plexiform neurofibromas can be superficial or deep and are associated with hypertrophy of the skin and soft tissues. Cutaneous neurofibromas are soft, pruritic, and mobile to palpation, while nodular neurofibromas are firm masses under the skin that can cause pain and compress surrounding structures[3].

Neurofibromatosis in breast tissue is rare. Generally, breast lesions manifest as painless nodules of varying sizes, with colors ranging from pink to blue, and a consistency that can be gelatinous or fibrous. There is a tendency for tumors to be concentrated in the nipple-areolar complex. Malignant breast tumors have been observed in association with neurofibromatosis as well as mutations in the BRCA1 and NF1 genes, located on chromosome 17. In such cases, neurofibromatosis in the nipple-areolar complex can be treated by lesion resection, resulting in a good aesthetic outcome and a low risk of recurrence. Additionally, the surgeon should be aware of the risk of associated neoplasms in the breast parenchyma. Patients with neurofibromatosis require regular multidisciplinary clinical follow-up due to the variety of disease manifestations[4].

Lisch nodules, hyperpigmented spots on the iris, are a specific ocular manifestation of NF1, present in 90% of adults and 10% of children. Although they generally do not affect vision, an ophthalmological evaluation may be necessary[4]. Another benign tumor that can develop is an optic pathway glioma, with signs such as decreased visual acuity, proptosis, and optic nerve atrophy, typically arising in childhood. Neurofibrosarcomas, malignant tumors, often originate from plexiform or nodular neurofibromas and exhibit characteristics such as persistent pain, hardened consistency, and accelerated growth[3].

Patients with NF1 may also present with bone abnormalities, such as pseudarthrosis, bone dysplasia, increased fracture risk, short stature, scoliosis, and osteoporosis. Neurological alterations include cognitive deficits, learning difficulties, headaches, epilepsy, macrocephaly, and peripheral neuropathy[3].

The diagnosis of NF1 is clinical, based on the National Institutes of Health (NIH) criteria, which include the presence of six or more café-au-lait spots, two or more neurofibromas, axillary or inguinal freckles, optic glioma, two or more Lisch nodules, distinctive bone lesion, and a family history of NF1. Genetic testing for the NF1 gene mutation can be useful in doubtful cases[3, 5].

Clinical follow-up for NF1 complications includes evaluation for fractures and osteoporosis, early breast cancer screening starting at age 30, dermatological evaluation, and monitoring

for hypertension. Imaging exams should be requested based on clinical presentation, such as MRI in suspected cases of optic nerve glioma or neurofibrosarcoma[5,6].

The management of symptoms is adjusted according to the complications developed over time. Neurofibromas are generally treated conservatively, with surgical intervention only in cases of pain, bleeding, or aesthetic impairment. Optic pathway gliomas can be monitored radiologically or treated with chemotherapy. Neurofibrosarcomas are treated with surgical resection followed by radiotherapy[5,6].

The life expectancy of individuals with NF1 is reduced, with an average age of death around 54.4 years and a median age of 59 years, significantly lower than the general population. Quality of life and functionality can be significantly improved with early diagnosis and multidisciplinary follow-up. Although there is no specific treatment for neurofibromas, therapies such as the selective MEK inhibitor Selumetinib have shown promising results[6].

CONCLUSION

This report describes a typical case of neurofibromatosis type 1, with multiple café-au-lait spots distributed over the body, primarily concentrated on the trunk, abdomen, and back, and especially on the patient's nipples. Surgical treatment was performed with the excision of the mammary lesions, resulting in good clinical evolution.

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