

## CASE REPORT

# NEUROFIBROMATOSIS TYPE 1 IN A 32 YEAR OLD FEMALE: AN INTERESTING CASE REPORT

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## ABSTRACT

Neurofibromatosis (NF) is characterized by neuroectodermal tumours arising within multiple organs with autosomal-dominant inheritance. Neurofibromatosis type I (NF-1), known as well as Recklinghausen's disease, is the most common type of the disease accounting 90% of the cases. We present a case of 32-year old woman with NF-1. The disease started in childhood with the appearance of multiple hyper pigmented skin macules. At the age of 26 cutaneous tumours appeared all over the body surface. Because of progressive disfigurement, the patient came for a clinical examination at the age of 32 years. The point is to stress upon the fact that a diagnosis of NF1 is often delayed till the patient develops some disfiguring lesions or progressive visual or hearing problem.

**Keywords:** Neurofibromatosis, Neurofibromatosis type I, Recklinghausen's disease

## INTRODUCTION

Neurofibromatosis (NF) is a neurocutaneous syndrome, characterized by neuroectodermal tumours arising within multiple organs and autosomal-dominant inheritance. Neurofibromatosis type I (NF-1) is the most common type of the disease accounting 90% of the cases, and is characterized by multiple café-au-lait spots and the occurrence of neurofibromas along peripheral nerves, Lisch's nodules on the iris; etc. NF1 occurs across all ethnic groups and affects approximately one in 4000 individuals.

## CASE REPORT

A 32-year-old woman presented with multiple soft tissue growths all over the body including face for last 6 years resulting in gradual disfigurement. The disease started in childhood with the appearance of multiple hyper pigmented skin macules. From the age of 26 years cutaneous tumours appeared and started to increase in size all over the body surface especially on the face. Her mother was suffering from similar type of skin problems. Her hearing was not impaired and she had no visual problems. General examination revealed hundreds of soft cutaneous neurofibromas, the largest ones being on the back and limbs, ranging from a few millimetres to several centimetres in diameter (largest one being 5 cm diameter), some of them pedunculated; multiple café-au-lait spots with diameter >1.5 cm; axillary and inguinal freckling. The mucous membranes were not affected. Ophthalmological examination and hearing tests showed no posterior subcapsular cataract and conductive deafness respectively. Lisch's nodules on the iris of both eyes were not noted. The standard laboratory tests values including blood counts, renal and liver function

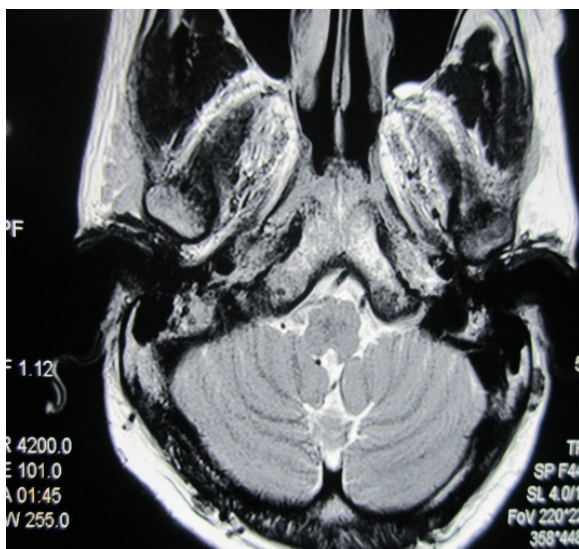
tests, and serum electrolytes were in the normal range. Facial X-ray and CT face were within the normal limits. MRI Brain did not reveal any optic glioma or acoustic neuroma. The diagnosis NF-1 was made according to the presence of three of the seven diagnostic criteria of the National Institute of Health Consensus Development Conference:

- Five or more café-au-lait spots larger than 5 mm in diameter in prepubertal patients; six or more café-au-lait spots larger than 15 mm in diameter in post pubertal patients
- Two or more neurofibromas of any type, or one plexiform neurofibroma
- Relatives in first degree with NF-I

Patient was referred to Plastic Surgery Department for possible excision of facial lesions.



**Figure 1: Multiple Neurofibroma on Upper Limb and Face and Café-Au-Lait Spot on Upper Limb**



**Figure 2: MRI Brain Revealing No Acoustic Neuroma or Optic Glioma**

## DISCUSSION

NF-I, also known as Von Recklinghausen's disease, is a neurodermal dysplasia, first described by the pathologist Friederich Daniel Von Recklinghausen in 1882. Two clinical forms of neurofibromatosis have been described: peripheral, type I (NF-I); and central, type II (NF-II)<sup>1</sup>. These are two different diseases both from the clinical as the genetic point of view.<sup>2</sup> The pathologic alterations that define the disease begin in the embryogenic period, prior to the differentiation of the neural crest<sup>1</sup>. NF-I is more frequent (90% of cases) than NF-II. It is manifested mainly by skin lesions (café au lait spots, multiple neurofibromas), as well as by bone malformations and central nervous system tumours<sup>3</sup>. It is the most frequent genetic human disease, affecting 1:3000 newborn and one of every 200 inhabitants with mental retardation. The genetic alterations are localized in the long arm of chromosome 17<sup>2</sup>. NF-I is an autosomal dominantly inherited genetic disorder with a penetrance of almost 100% and a variable expression. However, about 50% of cases are sporadic as a consequence of spontaneous mutations. The disease has one of the highest rates of spontaneous mutations within the genetic diseases<sup>2</sup>. There is no preference for gender or race in NF-I. Diagnosis of NF-I is based on clinical criteria According to the National Institute of Health Consensus Development Conference<sup>4</sup>, at least two of the following criteria must be present to make the diagnosis of NF-1:

1. Five or more café-au-lait spots larger than 5 mm in diameter in prepubertal patients; six or more café-au-lait spots larger than 15 mm in diameter in post pubertal patients
2. Two or more neurofibromas of any type, or one plexiform neurofibroma
3. Axillary or inguinal freckling

4. Optic glioma
5. Two or more Lisch's nodules
6. A distinctive osseous lesion (pseudo arthrosis of the tibia or sphenoid wing dysplasia)
7. A first-degree relative diagnosed with NF-1 in accordance with the above criteria.

Neurofibroma is a benign peripheral nerve sheath tumour<sup>5</sup>. Neurofibromas arise from Schwann cells and perineural fibroblasts. There exist two main clinical forms of neurofibroma: localized and plexiform neurofibromas. Localized neurofibroma is the most frequent one in NF-I. It develops along a peripheral nerve as a focal mass with well defined margins. It is rarely present at birth but appears in late childhood or early adolescence. Although skin is the predominantly affected organ, some others such as stomach, bowels, kidney, urine bladder, larynx or heart may become affected. In the head and neck, the most frequently affected. Plexiform neurofibroma spreads along the peripheral nerve and may affect some nervous rami. It is poorly-circumscribed. Café au lait spots are hyper pigmented maculae that may vary in colour from light brown to dark brown. Their borders may be smooth or irregular. They may appear anywhere on the skin, but they are less common on the face<sup>1</sup>. Inguinal and axillary freckles (Crowe's sign) are another salient feature. NF-I bone malformations such as kyphoscoliosis or pseudo arthrosis may appear, and the temporomandibular joint may be involved<sup>6</sup>. Skeletal deformities are frequently present in almost 40 % of patients with NF-I, with scoliosis being the most common skeletal pathology. Iris hamartoma, acoustic neurinoma, central nervous system tumours (glioma, glioblastoma), macrocephaly and mental retardation (up to 40% of cases) can also be found. Histologically, neurofibromas are composed of a mixture of Schwann cells, perineural cells, and endoneurial fibroblasts, and they are not capsulated<sup>1</sup>. Schwann cells account for about 36 to 80% of lesional cells. These constitute the predominant cellular type and they usually have widened nuclei with an undulated shape and sharp corners. Total or partial resection of neurofibromatous lesions is the treatment of choice to solve aesthetic or functional problems; it is advisable to wait for treatment until growth has been completed thus diminishing the risk of recurrence. Total resection with 1 cm margins whenever feasible is the treatment of choice for accessible and small tumours<sup>7</sup>. NF-I patients must receive genetic counselling since this is an autosomal dominantly inherited disease and the likelihood of transmission to the children is 50% in both sexes. Malignant transformation to neurofibrosarcoma bears a very bad prognosis and distant metastases are frequent, being the mean survival of 15% at 5 years<sup>8</sup>.

## CONCLUSION

The patient described here is a very typical case of NF-1. In such cases, a detailed patient examination and investigation is required, because of the possibility for

generalized involvement of other organs. The treatment of such kind of patient is surgical, seeking to achieve cosmetic improvement, and may be only palliative.

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