



## Case Report

# Multiple Plexiform Neurofibromas in Neurofibromatosis Type 1: A Case Report

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## Abstract

*Plexiform neurofibromas represent an uncommon variant (30%) of neurofibromatosis type 1 (NF-1). They account for substantial morbidity including disfigurement, functional impairment and may even be life threatening. More than one plexiform neurofibromas are uncommon in an individual of NF-1. We herewith, report a case of 50 years old female with NF 1 with multiple large plexiform neurofibromas over back, abdomen and left leg that began in early adulthood. Diagnosis of plexiform neurofibromas is usually made clinically, especially if classical signs of NF-1 are present. More than two diagnostic criteria for NF-1 were met, however in our case, the patient did not accept to undergo investigative work up and surgical resection and preferred to undergo clinical follow-up every 6 months. The current mainstay of the treatment of plexiform neurofibromas is surgical resection than medical therapy.*

**Keywords:** Plexiform neurofibromas, Neurofibromatosis type 1, café-au-lait macules.

## Introduction

Neurofibromatosis type 1 (NF-1) is a rare autosomal dominant genetic condition (1/3000 subjects), caused by mutations of the *NF1* gene, which is located at chromosome 17q11.2, characterized by multiple skin alterations such as café-au-lait macules, axillary freckling and by

tumoral growth along nerves, called neurofibromas.<sup>1</sup> Plexiform neurofibromas represent an uncommon variant of NF-1 in which neurofibromas arise from multiple nerves as bulging and deforming masses. It is considered pathognomonic of neurofibromatosis type 1 (NF-1). They are diffuse, painful and sometimes

locally invasive, generating cosmetic problems. It is uncommon for an individual with NF-1 to have more than one plexiform neurofibroma. We here report a case of multiple large plexiform neurofibromas involving back, left side of abdomen and leg, which presented also with classical hallmarks of NF-1 disease. Finally, we discuss clinical findings, diagnosis and therapy of this deforming disorder.

### Case Report

A fifty years old female presented to skin outpatient department with multiple progressive swellings over back, left side of abdomen and left leg, which started at early adulthood. Initially lesions were small which gradually increased over years to present size. She also had periods of occasional pain and functional impairment. She had no history of any systemic involvement. The patient reported positive family history of NF-1, but she had not undergone any clinical follow-up. Physical examination revealed multiple skin coloured nodules or diffuse mass of sizes ranging from 7x7 to 25x30 cm over back, left side of lower abdomen and left leg.[Figure 1,2,3] On palpation it had a typical feel of “bag of worms” seen in plexiform neurofibromas. Skin examination also showed "Café au lait" spots and numerous skin coloured nodules varying in size from 5mm to 20mm over trunk and extremities with “button hole sign”.

Other systemic and neurological examination was otherwise unremarkable. Patient did not prefer to undergo investigations other than routine laboratory tests, which were normal. However, despite the periods of pain and functional impairment, patient accept to come for follow up every six months than surgery.



**Figure 1.** Plexiform neurofibromas Over back along with numerous fibromas.



**Figure 2.** Large plexiform neurofibroma Over left side of abdomen.



**Figure 3.** large plexiform neurofibroma over left leg.

### Discussion

Plexiform neurofibromas occur in up to 30% of cases of NF-1, most frequently in the craniomaxillofacial region and are very rarely seen in other contexts. This entity may be

classified as a benign peripheral nerve sheath tumor that involves multiple nerve fascicles or branches of major nerves<sup>2</sup>. They often show considerable enlargement overtime resulting in severe disfigurement and functional impairment.

It is frequently located on the head and neck due to the rich innervations of the area; however, they have also been described in the extremities and trunk, where they follow the axis of a nervous track, appearing in a cord-like form.<sup>3-4</sup> Two main features stand out: hyperextensibility with a lack of elasticity and palpation that mimics a bag of worms. Plexiform neurofibromas can be nodular or diffused; the diffused form is known as *elephantiasis neurofibromatosa*. They are often painful to palpation.

Plexiform neurofibromas often appear in an infancy and early childhood mainly in craniofacial region. Thus far, most published cases reveal isolated plexiform neurofibroma in adults, affecting mainly the mouth. But our case had giant multiple plexiform neurofibromas that too in less commonly affected area (trunk and leg) responsible for difficulty in walking. However, other reports have described the condition in the orbit, hand, bladder, vulva, along with two cases in the leg (as in the present case).<sup>5-6</sup> Diagnosis of NF-1 is usually achieved when 2 or more criteria, developed by the National Institutes of Health (NIH), are met.<sup>7</sup> Plexiform neurofibromas are generally diagnosed clinically with appreciation of the typical features and histopathology is useful to exclude malignant transformation.

Therapy of plexiform neurofibromas is usually surgical, aiming at resecting deforming masses and cancerous tissue when malignant transformation occurs. However, these masses tend to recur in 20% of cases despite an appropriate approach.<sup>8</sup> In unresectable, progressive and symptomatic lesions, good results have been reported recently after the administration of interferon- $\alpha$ .<sup>9,10</sup> However, the prognosis is still unpredictable due to the high risk of progression of the disease and its variable expressivity.

### Patient outcome

In this case, her normal working was limited due to the giant multiple nodules as the result of progression of the disease. They are still growing. Despite this, the patient expressed the preference to avoid surgery and chose to undergo clinical follow-up every 6 months. Systemic therapy with interferon- $\alpha$  has been discussed as a possible future option.

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