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Case Report
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Giant and Recurrent Plexiform Neurofibromatosis in a Young Mexican: Case Study

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Abstract

Introduction: Plexiform Neurofibromatosis (PN) is a genetic disorder that typically results in benign tumors forming along nerve sheaths, affecting multiple nerve fascicles. These tumors may not always be visible externally, but imaging can reveal thickened areas within the nerves. PN is a rare condition, occurring in approximately 5% to 15% of patients with neurofibromatosis type 1 (NF-1). It is characteristic for these patients to present, before age one, with "café-au-lait" spots larger than 5 mm and neurofibromas, or nodules beneath the skin.

Case Presentation: We present the case of a young adult male diagnosed with PN, with a giant tumor located in the right gluteal and thigh regions. The patient has undergone at least 10 surgical interventions since 2013, with a cumulative resection of over 10 kilograms of tumor mass. However, the tumor continues to recur. Additionally, the patient has a coagulation disorder related to Factor VII deficiency, necessitating a conservative management approach due to the increased risk of bleeding.

Outcome: The patient currently reports moderate pain and paresthesia in the right gluteal region and lower extremity, limiting his functional abilities. As a result, a new surgical resection has been scheduled.

Discussion: As a genetic condition, PN lacks a curative treatment, though surgery can help alleviate symptoms. This patient presented at birth with a lesion suggestive of a melanocytic nevus in the right lower extremity. Subsequently, he developed a progressive increase in volume in the same region, leading to the diagnosis of PN. Notably, the patient did not exhibit the typical "café-au-lait" spots associated with NF-1, and the tumor has grown aggressively, necessitating multiple surgeries since 2013. Although his symptoms have improved post-operatively, tumor growth has not been arrested. The patient's Factor VII deficiency complicates radical tumor excision, limiting the scope of surgical intervention. A conservative surgical approach has been employed, and further surgery is planned to address pain and functional impairment.

Conclusion: Plexiform neurofibromatosis can present with unusual clinical progressions, complicating surgical management, particularly in patients with coexisting conditions, such as coagulation disorders, that limit surgical options. The prognosis remains guarded, and conservative treatment is advised, taking into account the tumor's histopathological characteristics.

Categories: Plastic surgery, resection of proliferative diseases.

Keywords: Plexiform neurofibroma; Giant tumor; Coagulation disorders; Reconstructive surgery

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Introduction

Type1 plexiform neurofibromatosis (NF-1), also known as Von Recklinghausen's disease, is an autosomal dominant hereditary disorder caused by a mutation in the tumor suppressor gene NF1. The global incidence is approximately 1 in 2,500 to 3,000 individuals. Typically, from birth or during the first year of life, patients present with hallmark features of the disease, such as café-au-lait macules, freckling in skin folds, and, in some cases, subcutaneous nodules known as neurofibromas.

Patients may also experience visual impairments (optic glioma or Lisch nodules) and distinctive bone lesions (such as sphenoid dysplasia or thinning of long bone cortices). Although NF-1 may be asymptomatic in many cases, symptoms depend on the location of tumor development [1-4].

The cause of PN is a mutation in the NF1 gene, located on chromosome 17, which typically produces a protein called neurofibromin that regulates cell growth. However, mutations in NF1 promote tumor growth, primarily affecting the peripheral nerve sheaths, though central nervous system involvement is also possible [5,6].

Histologically, neurofibromas in PN are benign peripheral nerve tumors, and occur in 20% to 50% of all NF-1 patients. Several authors estimate that these lesions may degenerate into malignant tumors in approximately 16% of cases [3,4].

The clinical presentation of PN varies significantly between individuals, even among members of the same family, ranging from mild forms that may go unnoticed to severe forms, which are the rarest. The clinical course of NF-1 changes with age, with symptoms typically absent at birth but gradually emerging over time. Some clinical reports indicate that neurofibromas are generally present later in life, manifesting either as small, painless but unsightly cutaneous growths (cutaneous neurofibromas) or as palpable nodules beneath the skin (subcutaneous neurofibromas), which can be painful and form long, tortuous masses of fibers, where surgical resection remains the only therapeutic option. Plexiform neurofibromas are comparatively rarer, and despite their congenital origin, they often do not present until adolescence, infiltrating nerves and adjacent tissues and causing significant morbidity related to the affected organs [7].

The treatment of PN is dependent on its classification and location, and requires a complex, multidisciplinary approach, as illustrated in (Figure 1) [1,2].

This report aims to analyze the progression of a rare presentation of PN and its surgical management.

Case Presentation

We present the case of a 27-year-old male from a southern state of Mexico, with a family history of a grandmother with skin cancer (non-melanoma). There is no family history of neurofibromatosis. The condition began at birth, with the appearance of a lesion suggestive of a melanocytic nevus on the right lower limb. Over time, this region experienced an increase in volume, leading to further studies that ultimately diagnosed the patient with Plexiform Neurofibromatosis (PN).

In 2013, the patient was referred to the National Institute of Pediatrics due to the size of the tumor and associated symptoms. A surgical resection was performed for the first time, during which a deficiency of factor VII was also discovered. The tumor recurred, and the patient underwent another surgery in 2014. Upon reaching adulthood, the patient was referred to the Plastic Surgery Department at the Manuel Gea González Hospital for continued management due to another recurrence.

By March 2015, the patient presented with a giant tumor in the right thigh region, accompanied by pain, difficulty walking, and impaired ability to maintain an upright posture as shown in (Figure 2). The tumor had irregular borders and firm consistency, measuring approximately 50 cm in diameter, extending from the posterior thoracic base and gluteal region down the entire posterior and medial aspect of the thigh to the popliteal area. It was limited to the midline of the anterior thigh. Surgical scars from previous procedures were visible, with no signs of inflammation and no tenderness on palpation. On March 18, 2015, a partial resection with primary closure was performed, involving a 45 cm × 20 cm excision and the removal of a 2,275-gram mass. The patient experienced 2,000 ml of blood loss, requiring a transfusion of packed red blood cells and plasma units. The patient was discharged four days later with clinical improvement.

Since 2015, the patient has undergone an additional eleven

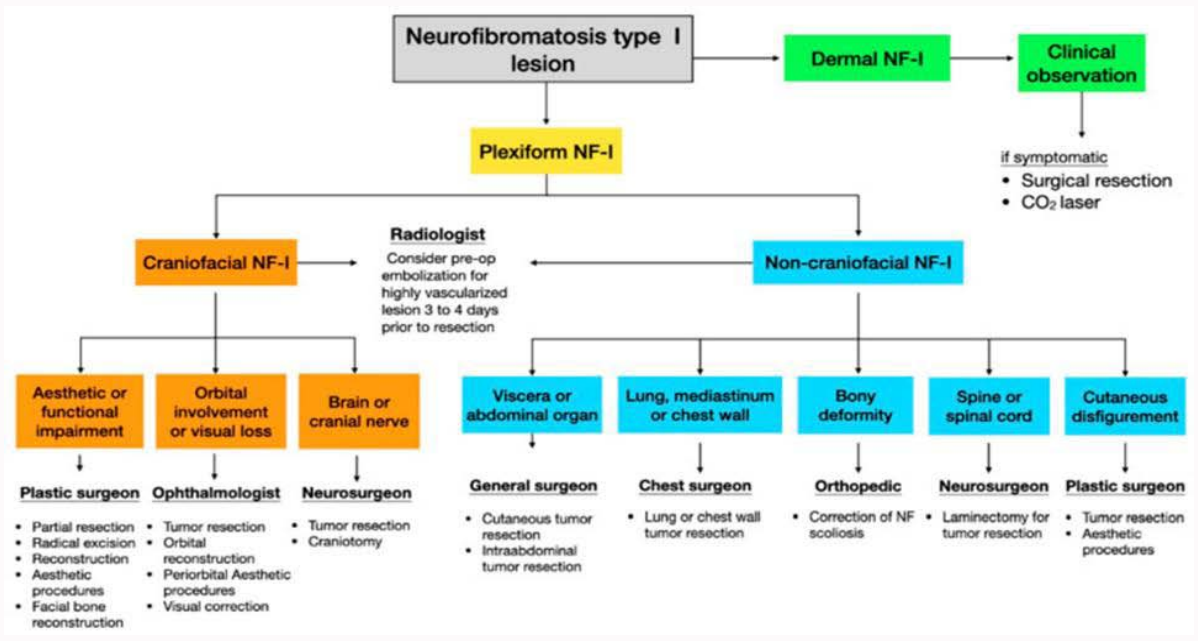

Figure 1: Treatment algorithm based on multidisciplinary teams for neurofibromatosis type I (NF-1), adapted from "The Number of Surgical Interventions and Specialists Involved in the Treatment of Patients with Neurofibromatosis Type I: A 25-Year Analysis" in Journal of Customized Medicine.

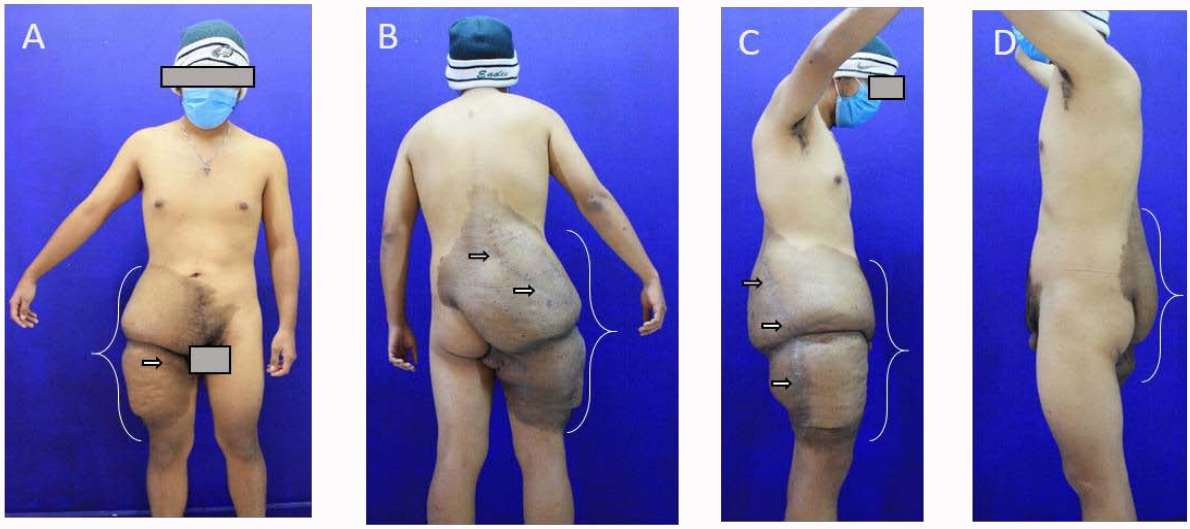

Figure 2: March 2015 photographs of the patient. A shows an anterior view, B a posterior view, C a right lateral view, and D a left lateral view. The bracket shows the size and location of the tumor. The arrows indicate surgical scars from previous procedures.

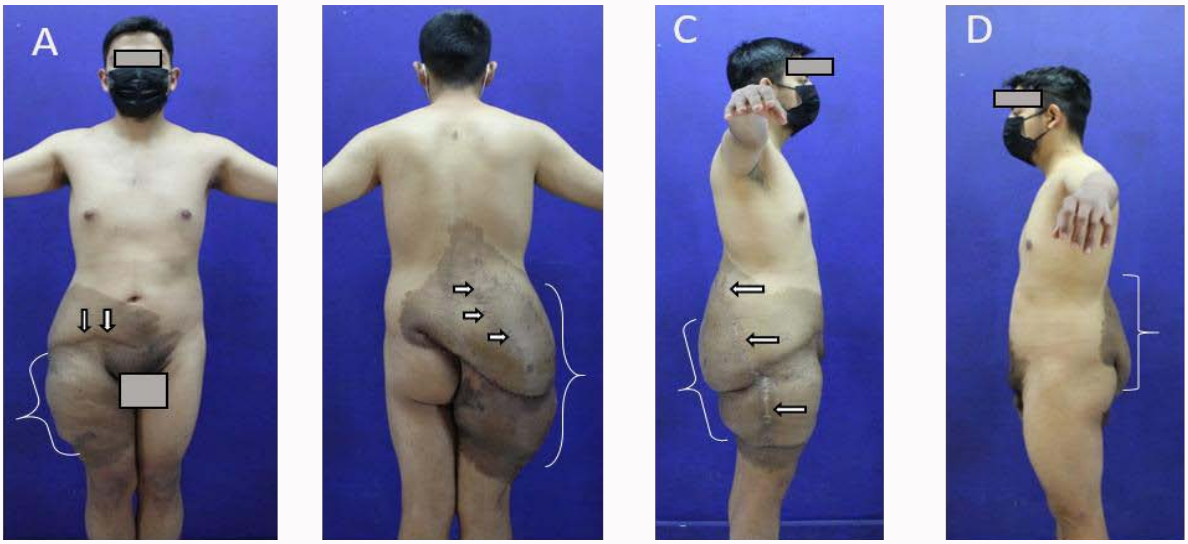

Figure 3: Currently, images of the patient. A shows an anterior view, B a posterior view, C a right lateral view, and D a left lateral view. The size and location of the tumor are shown in the bracket. The arrows indicate surgical scars from previous procedures.

surgeries, with a total of approximately 10 kilograms of tumor tissue removed throughout all procedures. The most recent surgery was performed on May 3, 2023. Due to the significant bleeding encountered during surgeries, the resections have been cautious, with moderate removal of tumor tissue.

Currently, the patient remains stable, with laboratory values within normal parameters, and has been scheduled for another surgery to address recurrent tumors. The patient is managed by a multidisciplinary team and reports improved self-esteem and quality of life.

Discussion

Plexiform Neurofibromas (PN) can develop along any peripheral nerve, and associated morbidities can range from mild disfigurement and pain to life-threatening complications, such as complete airway obstruction. Although generally benign, PN has the potential to transform into a malignant phenotype [3,4,7].

PN can present as either diffuse or nodular and well-demarcated. Nodular PN is primarily defined by imaging findings, with multiple firms and round discrete tumors arising from peripheral nerves. Diffuse PN spreads widely along connective tissue, surrounding normal structures with indistinct borders [7].

Recently, the concept of Distinct Nodular Lesions (DNL) has been proposed to describe well-defined round neurofibromas larger than 3 cm, with a loss of signal in the central core, a feature of classic PN. Rapidly growing DNLs are of particular concern due to their potential transformation into Atypical Neurofibromatous Neoplasms of Uncertain Biological Potential (ANNUBP). In such cases, a biopsy is required for differential diagnosis between benign PN and tumors with atypical or malignant behavior [7,8].

While there are some clinical trials with drugs aimed at treating

NF1-related alterations, surgical resection remains the standard treatment for neurofibromas [1,2]. Complete removal of symptomatic PN is often challenging due to significant risks of hemorrhage and neurological damage, especially in deep-seated tumors affecting multiple nerves [8,9].

Various surgical techniques have been proposed for diffuse PN to minimize intraoperative bleeding and facilitate tumor excision, including electrosurgical procedures, adhesive or thrombotic substances, or preoperative intravascular embolization [8,9]. Nodular PN, in comparison, tends to be more painful and involves sensory nerves. Superficial nodular PN resections typically result in sensory paresthesia, while deeper nodular PN resections can lead to motor paresis [8,9].

There is no single surgical algorithm that can fully address the complexity of NF-1 abnormalities. Many tumors are not fully resectable due to their location and partially resected PNs often recur [1-4]. Clinical management of neurofibromas focuses on monitoring disease progression and malignant potential via Magnetic Resonance Imaging (MRI), along with surgical removal when appropriate [7].

Imaging studies are essential for evaluating lesion location and extent. Ultrasound (US) is a valuable diagnostic tool for differentiating benign from malignant lesions, but its accuracy is limited, making MRI the gold standard for preoperative assessment [10]. In cases involving tumors larger than 10 cm, marginal resection is the treatment of choice, preserving the anatomy and functionality of the nerve and surrounding structures [11].

In this case, the patient also presented with a factor VII deficiency, complicating the surgical approach due to its role in blood coagulation. This rare autosomal recessive condition can lead to severe bleeding, requiring recombinant factor VII administration to prevent serious complications [13,14].

The patient had a large recurrent plexiform neurofibroma in the right lower limb, significantly affecting their quality of life. Surgical resection was complex due to the highly vascularized region involved and the patient's bleeding disorder. These tumors often induce vascular proliferation through angiogenic factors, infiltrating deep planes, and requiring the reconstruction of large tissue areas. Thus, proper preoperative planning using advanced technologies and a multidisciplinary approach is crucial for achieving satisfactory outcomes in functional restoration and improved appearance [15,16].

Finally, 8% to 15% of these lesions may undergo malignant degeneration into neurofibrosarcoma or malignant schwannoma, particularly following chronic treatment or incomplete surgical excision [1-4].

Conclusion

Due to the complexity and progression of this case, the patient will require continuous tumor resections to manage the tumor's size while minimizing the risk of hemorrhage. A multidisciplinary care model must be employed for this patient, involving healthcare professionals who can work together in a coordinated effort to provide comprehensive treatment, given the patient's challenging conditions [13,14,17].

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