An unusual plexiform neurofibroma confused with a vascular malformation: A case report

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ABSTRACT

Introduction: Neurofibromatosis type I, or Von Recklinghausen disease, is a multisystem disorder that primarily involves the skin and nervous system. Plexiform neurofibromas are one of the most pathognomonic and often the most disabling feature of the disease; generally benign, these lesions might degenerate into neurofibrosarcoma. They grow along peripheral nerves, and can be divided, on histological and biological bases, into two different groups: nodular / mass neurofibromas and Plexiform neurofibromas (superficial and deep). Despite the unique appearance of deep plexiform neurofibroma, especially on T2-weighted MRI, cutaneous and subcutaneous forms are more difficult to diagnose. The imaging findings of the superficial forms are different from the imaging characteristics of the deeper lesions and can be confused with a low-flow vascular malformation. Case Report: We report a 2-year-old boy, with diagnosis of neurofibromatosis type I, who came to our attention with a palpable swelling on the left nuchal region exhibiting ultrasonographical characteristics of a venolymphatic malformation. This lesion was histologically reported to be a superficial plexiform neurofibroma. Conclusion: A superficial plexiform neurofibroma may present imaging features of a vascular malformation. For this reason, the absence of the classical ultrasonographical appearance do not exclude a diagnosis of neurofibroma, especially in superficial location.

Keywords: Hemangioma, Neurofibromatosis type I, Peripheral nerve neoplasia, Plexiform neurofibroma, Schwann cells

INTRODUCTION

Neurofibromas are a common pathognomonic feature of neurofibromatosis type I (NF1). Its mortality and morbidity rates depend on proliferation and location, as well as growth in size and potential for malignant degeneration of the lesion [1–4]. Based on their histological and radiologic appearance, neurofibromas can be divided into two large groups: discrete mass / nodular forms and diffuse / plexiform variety, which is the most common [5–7].

These lesions are histologically defined as interdigitating network of enlarged nerves usually surrounded by a collagenous matrix representing the
diffuse involvement of a long nerve and its branches. They are composed by the same elements that compose peripheral nerves, including axons, fibroblasts and Schwann cells being the most significant (60%) [8–10]. These elements are located randomly within a myxoid stroma and occasionally they reach a size that is accountable for a disfiguring enlargement of the extremities, called “elephantiasis nevromatosa”.

Plexiform neurofibromas present with masses of variable size, often multiple, that might develop anywhere along a nerve course, although main locations are large nerve trunks and regions with high concentration of adipose tissue (e.g. orbit region) [2–3]. By location of their onset they are divided as superficial and deep with some lesions having mixed characteristics. Superficial plexiform neurofibromas can be cutaneous or subcutaneous and are common in NF1. Such lesions have imaging characteristics on ultrasonography (US) and magnetic resonance imaging (MRI) that often differs to the deep ones and this is the reason why they closely resemble a lymphatic or venous malformation, a hemangioma, or less commonly, a traumatic or inflammatory lesion of the subcutaneous tissues [11–13].

CASE REPORT

A 2-year-old boy, with diagnosis of NF1, came to our attention for a palpable swelling on the left nuchal region. The elements produced by ultrasonography were not significant in order to define the nature of the swelling: sonographic examination showed a inhomogeneous hypoechoic lesion of 1.5x1.3 cm in diameter, without posterior acoustic enhancement or shadowing and without peripheral nerve continuity but with numerous low-flow vessels at Doppler, compatible with a venolymphatic malformation. Due to the location and the ultrasound characteristics, the diagnosis of neurofibroma was (mistakenly) ruled out and a day-hospital exeresis procedure was planned. The excision showed a fibrous, white lesion, firmly attached to the skull. Because of the presence of numerous branches (Figure 1), the excision needed to be broadened in order for the lesion to be completely removed. This macroscopic feature, enhanced by the previous NF - I diagnosis, triggered the suspicion for neurofibroma: the post-operative histological examination proved to be a superficial (subcutaneous) plexiform neurofibroma. No local recurrence occurred after a 24 months follow-up.

DISCUSSION

Type I neurofibromatosis (NF1) or Von Recklinghausen disease is one of the most frequent genetic disorders [14–15]. It occurs with an incidence of 1/3000–4000 live births: nearly half of the patients suffer from the “sporadic” form, or report a non-verifiable family history. NF1 is an autosomal dominant disorder with high penetrance (almost 100%) within the fifth year of age; it has a wide clinical variability of expression and symptoms, even among members of the same family. There are four major clinical markers: “café au lait” spots, usually present at birth or within the twelfth year of age, axillary and/or inguinal freckling, which usually shows around 6-7 years of age and can increase until puberty; pigmented (yellow – brown) hamartomas of the iris, called Lisch nodules, that appear in puberty, in 85–90% of cases; cutaneous or nodular (subcutaneous) neurofibromas [9]. Minor clinical signs are sometimes associated with these, and can facilitate the diagnosis: macrocephaly (40–50%), short stature (30%), cyclopia (15%). The disease is generally asymptomatic, and occasional complaints affect a minority of subjects (around 20%) at a very young age or in specific age groups. Most recurrent disorders are: learning disabilities (40–60%), plexiform neurofibroma (25–30%), orthopaedic complaints, optic glioma (20%) around 4-6 years of age, Central nervous system (CNS) tumours (gliomas, ependymomas), convulsions (3–4%), cephalgia, stenosis, hypotension (6%), renal artery stenosis, pheochromocytoma) [16–17]. Even if Plexiform neurofibromas can occur throughout the body, the more common sites are thorax and abdomen (55%), arms (20%), lower limb (10%) and face (10%); the nuchal location, as shown in our case, is quite atypical [1].

Whereas NF1 can be diagnosed on the bases of specific clinical symptoms, superficial plexiforms neurofibromas are sometimes more difficult to detect due to the different imaging characteristics than deep ones. The role of T2-weighted MRI in deep neurofibromas is in determining

Figure 1: Intraoperative image of the plexiform neurofibroma in the left nuchal region. The large ramification differentiates it from a vascular malformation.
the nature (nervous) of the lesions and the extent of neurofibromas, visualizing the lesions through a signal with low to intermediate intensity, which tends to increase peripherally [2]. This target sign can be easily explained by the histological composition of neurofibromas; the low signal centre on T2-weighted images corresponds to dense fibrous and collagenous central zone and the high peripheral signal on MRI is related to the abundant myxoid material with high fluid content in the outer zones of the lesion [18–19].

The echographical aspect of a deep neurofibroma seems to depend on its size [11]. Smaller tumours tend to appear as homogeneous and hypoecogenic lesion that can show a posterior acoustic enhancement or shadowing mimicking a cystic lesion. Neurofibromas with a larger diameter tend to present with the same appearance of deep plexiform neurofibroma in MRI (increased signal intensity peripherally and decreased signal intensity centrally); peripheral hypoecogenic band and a more ecogenic core [20]. In both cases nerve continuity can be present. Lim et al. [11], in a multi - institutional study, have described different MRI characteristics for deep and superficial plexiform neurofibromas with 75% of deep ones demonstrating a target sign compared to 21% of superficial lesions. They further described the imaging features of superficial neurofibromas as unilateral or asymmetric diffuse lesion without any nodular or fascicular morphology corresponding to the ultrasonographical image of a heterogeneous hypoechoic lesion. The difference between deep and superficial neurofibromas can be related to the histology of infiltrating spindle cells (fibroblasts and smooth muscular cells) around normal superficial structures such as blood vessels, adipose tissue and skin adnexa [21–22]. In the present patient, the numerous low-flow vessels associated with diffuse thickening of subcutaneous tissue were believed to represent a venolymphatic malformation. In fact the prominent ectasic low-flow vessels in the lesion represented the rich vascularity that can be present in superficial neurofibromas.

CONCLUSION

In conclusion, a superficial plexiform neurofibroma can present ultrasonographical findings more similar to a vascular (venous or lymphatic) malformation than to a peripheral nerve sheath tumor. It is important to know that the absence of the classical ultrasonographical appearance do not exclude a neurofibroma, especially in a superficial and atypical location.

REFERENCES


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Author Contributions
Claudio Spinelli – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved
Gianmarco Elia – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved
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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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