CASE REPORT

A case of large diffuse cutaneous neurofibroma masquerading as plexiform variant: Diagnostic challenges

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Abstract

Diffuse Cutaneous Neurofibroma (DCN) is an infrequently encountered clinical entity that can be challenging to diagnose due to its variable clinical presentation, radiological findings, and histopathological features. We report an uncommon case of a large DCN located in the left gluteal region of a 31-year-old female. Initially it was diagnosed as a case of plexiform neurofibroma based on clinical findings. The diagnosis of DCN was rendered after evaluation of characteristic microscopic features and immunohistochemistry. This case highlights the importance of histological evaluation in distinguishing DCN from plexiform neurofibroma, given their differing associations with Neurofibromatosis Type 1 (NF-1) and malignant potential.

Keywords: diffuse cutaneous neurofibroma, soft tissue tumour, S100

Introduction

Neurofibromas (NF) are benign peripheral nerve sheath tumours that are composed of Schwann cells, perineural cells, fibroblasts, entrapped myelinated and unmyelinated axons. Multiple approaches have been proposed to categorize NFs according to their clinical presentation and histological characteristics, resulting in the publication of various classification systems [1]. According to the World Health Organization's (WHO) Classification of Tumours, 5th Edition: Soft Tissue and Bone Tumours, based on their anatomical location, growth pattern and relationship to nerves, NFs are classified into five types: localized cutaneous, diffuse cutaneous, localized intraneural, plexiform intraneural, and massive diffuse soft tissue tumours [2].

Diffuse cutaneous neurofibroma (DCN) can be difficult to diagnose because of its varied clinical, radiological, and histological characteristics. DCN, with or without adipose tissue, is infrequently observed in clinical practice and presents a diagnostic challenge [3]. Typically, it manifests in children and young adults, predominantly on the head or neck regions [4]. Only 10% cases occur in the setting of Neurofibromatosis Type 1 (NF-1), while the majority are isolated and sporadic [3].

We report an uncommon case of a large DCN located in the left gluteal region of an adult, occurring in the absence of any clinical features suggestive of NF-1. This case highlights the diagnostic challenges encountered with such atypical tumour locations, also emphasises critical role of histopathological evaluation in establishing a definitive diagnosis and guiding treatment.

Case Report

A 31-year-old female presented to the clinic with a gradually enlarging lesion in the left gluteal region, first noticed approximately 9 to 10 years ago. The patient now complains of stiffness in the affected area and increasing difficulty in walking and performing

routine activities. She reported a prior history of lesion at the same location, which was excised approximately 10-11 years ago, it was previously reported as spindle cell lesion. Unfortunately, the medical records and histopathology reports from the earlier procedure were unavailable for review. However, patient relates it with an injection site and the lesion was of sub-centimetre size.

On physical examination, a large, ill-defined, soft to firm swelling was noted over the left gluteal region, measuring 21 × 20 cm. The overlying skin was intact, without any ulceration or discoloration. The mass was non-tender, non-pulsatile and had vague 'bag of worms' feel on palpation.

Clinical examination revealed no café-au-lait spots or axillary freckling. Lisch nodules were not detected on ophthalmic examination. There was no family history suggestive of neurofibromatosis. MRI was not performed due to financial constraints and the clinician initially diagnosed the lesion as plexiform NF based on history and clinical examination. Excision with adequate surgical margins was done and the specimen was sent for histopathologic examination. Resected specimen consisted of skin covered glistening whitish mass measuring 24 × 21 × 6 cm which appeared to infiltrate into the surrounding tissue. Skin flap measured 24 × 22 cm. Deep surgical margin showed fat and fascia. No obvious areas of necrosis, hemorrhage, or cystic change were noted.

Microscopic examination revealed a dermal, infiltrative, poorly circumscribed tumor, displaying a mixture of bland-appearing spindle cells with wavy nuclei and fibroblasts, mast cells amidst several capillary sized blood vessels. Also seen were bundles of collagen, adipose tissue and adnexal structures amidst these cells. The tumour cells focally stained positively with S100 and CD 34, confirming the diagnosis of NF (Figure 1).

Post-surgery was uneventful. On follow up after 3 months of surgical excision, patient was asymptomatic with no signs of recurrence.

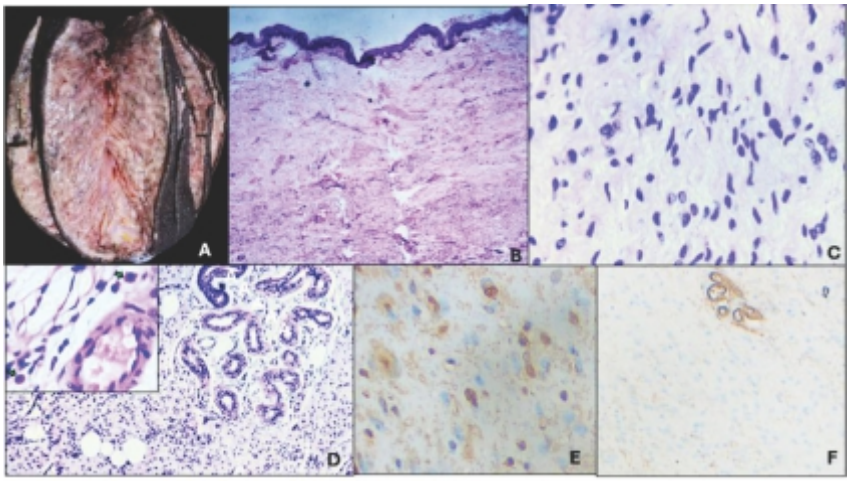

Figure 1: A) Gross specimen of DCN from left gluteal region showing skin covered glistening whitish mass. B) Infiltrative tumour in the dermis and subcutaneous tissue. (H& E, ×100) C) Tumour composed of bland spindle cells with wavy nuclei, (H& E, ×400). D) Mature adipose tissue and adnexal structures seen entrapped amidst the tumour cells, (H& E, ×200). Inset – Arrow pointing towards mast cells (H& E, ×400). E & F – Focal positivity for S 100 (×400) and CD 34 (×200).

Discussion

DCN is rare but distinctive form of NF, also referred as paraneurofibroma [5]. Previously it was considered predominant in young patients with head and neck involvement, whereas recent findings challenge this view [3]. Our case is uniquely located in the gluteal region, further emphasizing the widespread and atypical distribution of these tumours.

The present case was misdiagnosed clinically as plexiform NF, due to the location, history and examination findings. Diffuse and plexiform NF can be challenging to distinguish [6]. Numerous case reports have documented large slow growing plexiform NF in gluteal region, contributing to the diagnostic confusion in this instance, highlighting the critical role of histopathological examination for definitive diagnosis [7-8].

DCN are usually large, characterized by dermal and subcutaneous thickening. Microscopy reveals spindled tumour cells with fusiform nuclei in fibrillary collagenous matrix [5]. Tumour cells entrap adipocytes imparting a honeycomb effect and may show pseudomeissnerian-body-like structures [4].

Contrasting clinical and histomorphology findings between DCN and plexiform NF has been tabulated (Table 1). Plexiform NF are associated with a significant risk of developing to malignant peripheral nerve sheath tumour, whereas DCN has low malignant potential [4]. Hence, despite both being NF, prognostic and therapeutic implications are different making their distinction essential.

Immunohistochemistry (IHC) demonstrates a heterogeneous cellular composition, where only a fraction of the cells is S100 positive, creating a "spotty" or "dispersed" staining pattern alongside CD34-positive fibroblasts with fingerprint pattern. The fingerprint pattern of CD34 IHC helps to distinguish from early desmoplastic melanoma [1]. Due to diffuse infiltration into the subcutaneous fat, DCN may resemble dermatofibrosarcoma protuberans. Presence of Verocay bodies and strong S 100 positivity help to differentiate Schwannoma from DCN [9, 10].

Table 1: Differences between DCN and plexiform neurofibroma

Feature	DCN	Plexiform Neurofibroma
Clinical Feature	Younger age group Plaque -like lesion H&N region	Childhood tumour Large nerve trunks of the H&N, trunk, or extremities
Gross	Ill-defined dermal or subcutaneous nodule	Multinodular and serpentine nerve-like structures
Microscopic Features	Spindle-shaped tumour cells in a fibrillary to myoid matrix	Rounded to spindled cells in a myxo-edematous stroma with thick, haphazard collagen fibers (shredded carrot appearance)

Continued...

Cell Arrangement	Tumour cells entrap adipocytes (honeycomb effect)	Serpentine, multinodular pattern
IHC	S100 positivity Variable CD34 expression	S100 positivity Variable CD34 expression
Association with NF-1	Not strongly associated	Strongly associated
Malignant Potential	Low	High (MPNST)

DCN - Diffuse cutaneous neurofibroma; MPNST - Malignant peripheral nerve sheath tumour

Diagnosing DCN can be challenging, which may result in delayed treatment and potentially require more extensive surgical approach. Once diagnosed as a NF, it is essential to recognize it as a diffuse variant or DCN, as it is not usually linked to neurofibromatosis [6].

Management of large NF typically involves partial or complete surgical removal. Despite excision with clear margins, the tumour can recur because of its infiltrative nature [5].

Conclusion

DCN should remain a differential consideration for any indurated soft tissue mass, regardless of its location. The current case is reported for its rarity and distinctive presentation. Precise histopathologic subtyping of NF is essential to guide management and follow-up strategies.

References

1. Nagrani NS, Bhawan J. Histopathological variants of cutaneous neurofibroma: A compendious review. *Dermatopathology (Basel)* 2022; 10(1):1-19.
2. The WHO Classification of Tumours Editorial Board. WHO Classification of Tumours Soft Tissue and Bone Tumours. 5th ed. IARC Press; Lyon, France: 2020
3. Ravi AK, Ram R, Lindberg MR, Pandey T. Diffuse infiltrative neurofibroma: a clinical, radiological, and histological conundrum. *Skeletal Radiol* 2014; 43:1773-1778.
4. Magro G, Broggi G, Angelico G, Puzzo L, Vecchio GM, Virzì V, *et al*. Practical Approach to Histological Diagnosis of Peripheral Nerve Sheath Tumors: An Update. *Diagnostics (Basel)* 2022; 12(6):1463.
5. Kumar BS, Gopal M, Talwar A, Ramesh M. Diffuse neurofibroma of the scalp presenting as circumscribed alopecic patch. *Int J Trichol* 2010; 2(1):60-2.
6. Patil SB, Chatur KR. A histopathological study of neurofibroma and malignant peripheral nerve sheath tumors in a medical institute of Central Karnataka. *Int J Clin Diagn Pathol* 2021; 4(1): 81-85.
7. Sassi I, Bouida MA, Hasnaoui A, Zemni I, Ben Dhieb T. Giant gluteal and vesical plexiform neurofibromas in a patient with neurofibromatosis type 1: A case report. *J Med Case Rep* 2024; 18(1):15.

8. Mahipathy SRRV, Durairaj AR, Sundaramurthy N, Jayachandiran AP, Rajendran S. Large plexiform neurofibroma of the sacro-gluteal region – a rare case report. *Int J Sci Res* 2021; 10(8):30-31.
9. Jawalkar S, Patil V, Raj SS. A case of schwannoma in breast: A rare site. *J Krishna Inst Med Sci Univ* 2024; 13(4):185-188.
10. Manchanda J, Sood S, Gogia R, De R, Chopra P. A usual schwannoma at an unusual site – the mesorectum. *J Krishna Inst Med Sci Univ* 2016; 5(3):118-121.

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