

Understanding the Clinical Spectrum of Dermal Hyperneury

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Abstract

An uncommon medical disorder called dermal hyperneury (DN) is characterized by an overgrowth of nerve fibers in the skin. Small nodules or papules develop as a result, which can be uncomfortable or irritating. DN's actual etiology is unknown, however it is thought to be a result of aberrant nerve fiber development or a body's reaction to damage. In most cases, a biopsy of the afflicted region is used to make the diagnosis. The use of topical or systemic medicines, surgical excision, or laser therapy are available as treatments. Although cutaneous hyperneury is a benign illness, those who are affected by it may have discomfort and aesthetic concerns.

Introduction

The enlargement of dermal nerve fibers is a hallmark of DN. Although precise quantitative criteria have not been clearly established, it is histologically distinguished by extremely large and structured dermal or dermal/subcutaneous nerve tissue (Figure 1). The report of Winkelmann and Carney is thought to be the first exhaustive account of DN [1]. Research revealed that in clinically unaffected skin, dermal nerve fascicles in individuals with type 2b multiple endocrine neoplasia (MEN 2b) syndrome were 1.5 - 4 times greater than those in healthy persons. Within one high-power field (100), these nerve fascicles were infrequently deformed and were frequently observed closer to the epidermis than usual.

While researching 21 patients with Cowden syndrome, Starink et al. made a similar observation of hypertrophic nerves in epidermal tissue reports [2], and numerous mucocutaneous neuromas have been linked to PTEN hamartoma tumour syndrome [3]. MEN 2a syndrome and type 2 neurofibromatosis have also been linked to DN [4, 5]. Ieremia et al. reported a case of numerous skin lesions without a syndromic link [6]. DN often

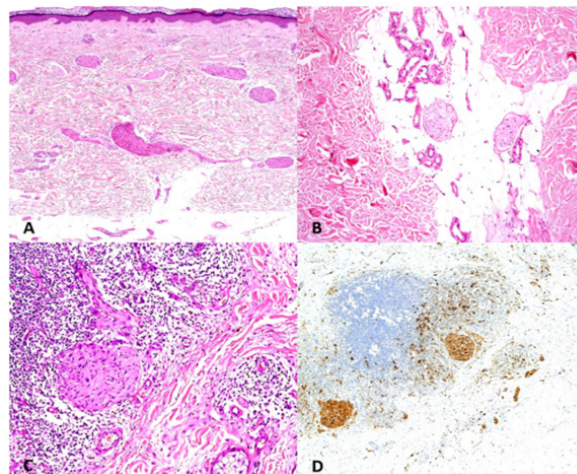


Figure 1: Histology (hematoxylin and eosin) of dermal hyperneury (DN) showing increased number of nerve fascicles or trunks at the dermal (A) and dermal/subcutaneous level (B). Increased number of nerves associated with plasma cells (C). Positive immunohistochemical reaction for S-100 in DN (D). Dermal Hyperneury

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manifests as solitary lesions outside of syndromic context. DN has only very rarely been described with lichen simplex chronicus/nodular prurigo and notalgia paresthetica, while it may occasionally be an incidental finding in epidermal tissue biopsy with other diseases such dermatofibroma and basal cell carcinoma.

Clinical Features

The eyelids, lips, and tongue of individuals with MEN 2b show characteristic periorificial mucocutaneous neuromas that are pathognomonic and manifest in infancy [7]. These neuromas can occasionally be found on cutaneous sites as well. These cobblestone-like, medically distinct lesions share certain histological characteristics with DN. On the other hand, there are no obvious clinical symptoms associated with the increased dermal nerve fascicles of DN found in MEN 2b individuals upon histological testing. On the trunk or extremities in other syndromes, DN generally manifests as skin-colored nodules or papules [4, 5].

Clinically detectable DN lesions have been seen in a variety of circumstances, both with and without associated symptoms. Multiple syndromic lesions are typical. In addition to MEN 2b, cutaneous neuromas that may be seen clinically, such as on the ear [8], face [9], and trunk [10], have been noted in some MEN 2b individuals, albeit infrequently. These dome-shaped lesions appeared on the upper lip, fingers, palms, and shins were painful, translucent, and ranged in hue from pink to skin-colored. Another illness that may be related to DN is neurofibromatosis type II [4], as shown by the development of painless cutaneous nodules with nerve enlargement in a 20-year-old patient with the condition. The patient exhibited bilateral auditory neuromas, several neurogenic tumours, and meningiomas, which are all strong indicators of neurofibromatosis type II. However, they also had papillary exaggeration and nodular protrusions on the tongue, which may be evidence of a mild or insufficient form of MEN 2b. The presence of DN has also been demonstrated in a mother and daughter with a verified RET mutation/MEN 2a syndrome, as well as in a MEN 2a patient with mucosal neuromas, macular amyloidosis, and medullary thyroid carcinoma. These findings were published in 2007 [5].

Nonsyndromic medically apparent DN might be localised or numerous in different contexts. Trauma [11], neurocristic hamartoma [12], notalgia paresthetica [13, 14], and prurigo nodularis [15, 16] have all been linked to it. It is perhaps overdone to say that DN is exclusive to prurigo nodularis and lichen simplex chronicus and is not seen in other pruritic dermatoses. According to studies [17, 18], neural hyperplasia only occurs in a tiny percentage of prurigo nodularis individuals, and hyperneury is not required for a correct diagnosis. Two seniors with actinic keratosis and basal cell carcinoma have DN as a fortuitous discovery [6]. One of the authors has made the additional discovery that DN can coexist with benign fibrous histiocytoma.

Idiopathic DN can manifest as a single lesion or many lesions. Numerous idiopathic cutaneous or mucocutaneous neuromas or hyperneury have been reported in case reports. Nine individuals with nonsyndromic, idiopathic DN, ranging in age from 44 to 74, made up the sole set of cases. A patient had two lesions, another four patients had a single lesion, and four instances had multiple lesions.

Pathological Features

Despite the fact that there is no established standard for the histologic quantitative measures, DN has been termed as the condition where the nerves in the skin are too large and prominent. The nerves frequently follow a convoluted path close to the epidermis and have a noticeable perineurium. They may also exhibit mucinous change, internal disarray, or an accompanying inflammatory infiltration [1]. At times, a degree of disarray resembling a neuroma of specific mucinous alteration inside the nerve fascicles, or an accompanying inflammatory infiltration made up of lymphocytes, histiocytes, and occasionally plasma cells [6]. S-100 positivity and EMA positivity surround the perineurium in the immunohistochemical profile of cutaneous hyperneury, which is typical of healthy nerve tissue. Immunohistochemistry results from none of the many idiopathic lesions described in the investigations indicated PTEN loss or RET amplification, nor did they reveal any clinical symptoms of associated illnesses [6]. MEN 2b and other disorders can cause neuromas, which can manifest in one of two ways. The first pattern resembles solitary circumscribed neuromas, which are distinguished by a well-circumscribed cutaneous tumour that is packed with Schwann cell and axonal fascicles. The second pattern, in comparison, is more diffuse and shows more DN overlap. Winkelmann and Carney [1] assert that the size of the lesion and the absence of a clinically obvious lesion in mucocutaneous neuromas distinguish them from swollen dermal nerve fascicles of DN among MEN 2b patients.

The numerous instances of multiple mucocutaneous neuromas that have been documented must be taken into account, both in cases that are connected with a recognised syndrome and those that are not, in order to have a thorough grasp of the various types of disorders related to DN [3, 19-23]. Some cases that have been diagnosed as neuromas may actually be deemed to be part of the category of DN based on their appearance because the concept of neuromas is not well established. Winkelmann and Carney claim that aside from size, mucocutaneous neuromas and hypertrophic nerves do not vary much histologically in individuals with MEN 2b [1]. Mucocutaneous neuromas can present as either single confined neuromas or convoluted and hyperplastic nerves that resemble DN in MEN 2b patients [23, 24]. Because of this, some lesions that have been labelled as "mucosal neuromas" or "cutaneous neuromas" may really come within the category of DN.

Diagnosis

Epithelial sheath neuroma (ESN) is an uncommon lesion that has several physical characteristics in common with DN, such as larger-diameter nerve fascicles [25, 26]. However, in cases of ESN, the perineurium of the nerve fascicles looks thicker and squamoid, which could be confused for squamous cell carcinoma perineural infiltration, and this is not present in cases with diffuse neuropathy. It's conceivable that dermal hyperneury is a kind of ESN.

Additionally, it has a distinctive perineural thickening that resembles squamous epithelium. This squamoid epithelial collar which covers the nerve fascicles could be so dense and obvious that it resembles the perineural invasion of squamous cell cancer. Although DN and ESN are both

benign, the treatment options is still significant since DN may be associated to a condition. Even if the perineurium may be thickened, DN lacks the distinctive squamoid perineural collar, which allows for differentiation.

Conclusion

Cutaneous nerve hypertrophy known as dermal hyperneury is seen in various syndromes such as MEN 2b, MEN 2a, Cowden syndrome, and NF 2, in addition to non-syndromic DN lesions, which can be singular or multiple. To find cancer in syndromic instances, meticulous surveillance is essential. To distinguish between syndromic and non-syndromic cases, it is imperative to understand DN as a unique entity and its primary clinicopathologic markers. Pediatric patients should have the proper diagnostic workup, including genetic testing, if a hereditary cancer condition is suspected.

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