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Topical Review

Abnormalities of Skin and Cutaneous Appendages in Neuromuscular Disorders

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ABSTRACT

OBJECTIVES: A thorough evaluation of the skin and its appendages is frequently outside the area of expertise of the neurologist who deals with neuromuscular disorders. However, the skin is more frequently affected in neuromuscular disorders and deserves more attention than so far acknowledged. **METHODS:** Review of publications by searching Medline dealing with skin disorders in neuromuscular disorders. **RESULTS:** Skin abnormalities are most frequently found in patients with dermatomyositis, myotonic dystrophies, mitochondrial disorders, muscular dystrophies, and neuropathies. The hairs and the sweat glands are the appendages most frequently affected in neuromuscular disorders. In myotonic dystrophies and mitochondrial disorders there are indications that the rate of skin neoplasms is increased compared with the general population. **CONCLUSIONS:** Skin lesions in neuromuscular disorders are not unusual. Neurologists should be aware of the cutaneous implications of neuromuscular disorders and should take a thorough history relative to cutaneous manifestations and complete a comprehensive investigation of the skin and its appendages. If there is evidence of a dermatological problem in a neuromuscular disorder, a dermatologist should be consulted. Dermatological involvement in neuromuscular disorders may contribute to the diagnosis of neuromuscular disorders and may help to differentiate between various entities. The skin should become a focus of the neurologist as well.

Keywords: cutaneous, dermis, sweat glands, hairs, dermatological, myopathy, neuropathy, neuromuscular transmission

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Introduction

Neuromuscular disorders (NMDs) comprise motor neuron disease, radiculitis, plexopathy, polyneuropathy, transmission disorders, and muscle disorders.[1] They may be hereditary or acquired. In the majority of the cases, only the α-motor neuron, the peripheral nerve, the motor endplate, or the muscle is involved.[1] However, some of the NMDs are accompanied by dysfunction of other organs and tissues and present as multisystem disease. The following review focuses on the skin and their cutaneous appendages (hairs, sweat glands, apocrine glands, sebaceous glands, nails) in NMDs and reviews the most recent findings of these manifestations.

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Methods

Data for this review were identified by searches of Medline, Current Contents, PubMed, and references from relevant articles using the search terms "skin," "dermatological," "cutaneous," "cutis," "hair," "hypertrichosis," "sweat glands," "sebaceous glands," "nails," and "apocrine glands" in combination with "neuromuscular," "myopathy," "muscular dystrophy," "mitochondrial disorder," "polyneuropathy," "motor neuron disease," "amyotrophic lateral sclerosis," "bulbospinal muscular atrophy," and "radiculopathy." Randomized (blinded or open-label) clinical trials, longitudinal studies, case series, and case reports were considered. Abstracts and reports from meetings were not included. Only articles published in English between 1966 and 2014 were considered. Appropriate articles were studied and discussed for their suitability to be incorporated in this review.

Results

Dermatological abnormalities in NMDs are more frequent than anticipated and occur particularly in NMDs with multisystem involvement such as in myotonic

dystrophies (MD1, MD2) or mitochondrial disorders (MIDs). However, a number of NMDs without multisystem manifestations in which nonetheless the skin or the hairs are affected. This is particularly the case in limb girdle muscular dystrophies resulting from mutations in the PLEC gene encoding for plectin, an organizer of the keratin filament cytoskeleton,[2,3] congenital muscular dystrophies resulting from COL6A1 mutations,[4,5] or in hereditary neuropathies affecting sensory or autonomic fibers.[6] Dermatological abnormalities reported in NMDs are listed in Table 1.[7-9] Diseases of the cutaneous appendages associated with NMDs are listed in Table 2.[7] The following sections present the data about skin and cutaneous appendage lesion in the various NMDs.

Dermatomyositis

Skin

Dermatomyositis (DM) is an idiopathic inflammatory myopathy (immune myopathies comprise polymyositis, DM, and necrotizing myopathy) in children and adults characterized by an inflammatory infiltrate primarily affecting the skin and the skeletal muscles.[10] Rash is a dominant feature of DM.[11] The most common and peculiar lesions show up as Gottron papules overlying knuckles, heliotrope rash of the eyelids, and erythematous rashes (Fig 1),[10,12] which can be found in most patients.[13] Patients with the systemic mucocutaneous phenotype may present with skin ulcerations, tender palmar papules, particularly at the lateral nail folds, finger joints (Gottron papules), and elbows.[11] Skin ulcerations in DM are usually if not always the result of cutaneous calcinosis and a tremendous problem particularly in pediatric DM. This problem is terribly difficult to treat once established and much better prevented if early recognized. Biopsy of palmar papules shows vasculopathy with vascular fibrin deposition and variable perivascular inflammation.[11] DM patients with anti-MDA5 antibodies frequently present with oral pain or ulceration, hand swelling, arthritis, or arthralgia and diffuse hair loss.[11] In addition to classical DM, amyopathic DM, hypomyopathic DM, postmyopathic DM, and DM sine dermatitis are differentiated.[10] Some patients present with generalized follicular hyperkeratosis and diffuse thickening of the soles and palms.[14] Histopathologically, these lesions present as keratotic plugging of the follicular infundibulum and features of arrector pili myositis.[14] Unlike adult DM, pediatric DM is not thought paraneoplastic, which may save expensive and generally unnecessary malignancy evaluations.

Appendages

Involvement of the scalp is common in DM and characterized by diffuse, violaceous, scaly, and symptomatic hair loss.[15] Alopecia in DM is usually nonscarring and generalized.[16] Another frequent manifestation of DM is intractable burning pruritus of the scalp.[17] In single patients with DM, trichomegaly of the eyelashes has been reported.[18]

TABLE 1.
Abnormalities of the Skin in NMDs

Skin Lesion	NMD
Acrocyanosis	MID
Rashes (exanthema)	DM, MID
Erythema	DM, MID (MELAS)
Dermal atrophy (lipoatrophy)	PNP
Epidermidolysis bullosa	LGMD2Q
Vitiligo	MID (MELAS), acyl-CoA DHG def.
Mottled pigmentation	MID
Reticulated pigmentation	MID (MELAS)
Hyperpigmentation	MID (KSS), PNP
Edema	DM, PNP
Psoriasis	MID, MD1
Gottron papules, palmar papules	DM
Ulcerations	DM, PNP
Hyperkeratosis	DM, PNP
Thickening sole/palm	DM
Seborrheic eczema	MID, PNP
Keloids	CMD (Ullrich)
Dysplastic nevi	MD1
Xerosis	PNP
Rubor	PNP
Telangiectasias	PNP
Angioma	PNP
Lipoma	MID (MERRF, MSL, NS)
Cutaneous leiomyoma	PNP
Pilomatrixoma	MD1
Squamous cell carcinoma	MD1
Basal cell carcinoma	MID (NS), MD1
Squamous cell carcinoma	MID, MD1
Cutaneous Paget	MID
Lymphoma	MD1

Abbreviations:
DHG = Dehydrogenase
DM = Dermatomyositis
MELAS = Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes
MID = Mitochondrial disorder
MSL = Multiple systemic lipomatosis
NMD = Neuromuscular disorder
NS = Nonsyndromic

TABLE 2.
Abnormalities of the Cutaneous Appendages in NMDs

Skin Problem	Appendage Abnormality
Premature graying of hair	MID (MERRF/PEO overlap), LGMD
Alopecia	DM, MID, LGMD2Q, CFTD
Madarosis	MID
Alopecia of the eyebrows	MID
Loss of hair cuticle	MID
Flattened shaft	MID
Brittle hairs	MID
Ridging of hairs	MID
Pili torti	MID
Hairs with longitudinal grooves	MID
Tiger tail hairs	MID
Trichothiodystrophy	MID
Hypertrichosis	MID (Leigh syndrome)
Trichomegaly	DM
Onychodystrophy	DM, MD1
Hirsutism	MID
Anhidrosis, hypohidrosis	PNP, glycogenosis, LES
Ichthyosis	PNP
Leukonychia	PNP

Abbreviations:
CFTD = Congenital fiber type dysproportion
DM = Dermatomyositis
LES = Lambert-Eaton syndrome
MID = Mitochondrial disorder
NMDs = Neuromuscular disorders