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Multiple skin neoplasms at one site (MUSK IN A NEST): collision tumor consisting of epidermal (macular seborrheic keratosis) and dermal (lichen amyloidosis) components

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Abstract

A collision tumor is a neoplastic lesion comprised of two or more tumors consisting of distinct cell populations in the concurrent location. Multiple skin neoplasms at one site (MUSK IN A NEST) is a term recently coined to describe two or more cutaneous benign or malignant tumors occurring at the same anatomic site. In retrospective studies, seborrheic keratosis and cutaneous amyloidosis have both individually been documented as a component of a MUSK IN A NEST. This report describes a 42-year-old woman who presented with a pruritic skin condition on her arms and legs of 13 years’ duration. Skin biopsy results showed epidermal hyperplasia with hyperkeratosis, hyperpigmentation of the basal layer with mild acanthosis, and evidence of amyloid deposition in the papillary dermis. Based on the clinical presentation and pathology findings, a concurrent diagnosis of macular seborrheic keratosis and lichen amyloidosis was established. A MUSK IN A NEST consisting of a macular seborrheic keratosis and lichen amyloidosis is likely a more common occurrence than implied by the paucity of published cases of this phenomenon.

Keywords: amyloidosis, benign, collision, keratosis, lichen, malignant, neoplasm, seborrheic, skin, tumor

Introduction

Seborrheic keratosis is an epithelial keratinocytic benign neoplasm. There are several clinical morphologies with corresponding pathologic changes. Occasionally malignant tumors, such as squamous cell carcinoma and melanoma, masquerade as a seborrheic keratosis, especially those that are hyperpigmented, reticular, or irritated [1].

Amyloidosis is a systemic disease characterized by the extracellular deposition of amyloid in multiple tissues or organs such as the heart, kidneys, liver, and blood vessels. Cutaneous amyloidosis has several clinical variants; some express the same amyloid proteins as systemic amyloidosis (amyloid AL) whereas others express keratin proteins (amyloid AA), [2]. Lichen amyloidosis is a pruritic dermatosis that is characterized by keratin amyloid proteins in the papillary dermis [3].

Cutaneous collision tumors, which has recently been designated as multiple skin neoplasms at one site (MUSK IN A NEST), consist of two or more neoplasms concurrently located at the same cutaneous location [4]. Seborrheic keratosis and amyloidosis have both been components of MUSK IN A NEST; although it is likely that a seborrheic keratosis and lichen amyloidosis have previously occurred as a collision tumor, to the best of our knowledge, a report of this phenomenon has not been published. A woman with a MUSK IN A NEST consisting of a macular seborrheic keratosis and lichen amyloidosis is described, and collision tumors of seborrheic keratosis and amyloidosis are reviewed.
Case Synopsis
A healthy 42-year-old woman presented for evaluation of a pruritic skin condition affecting her arms and legs of 13 years’ duration. Prior treatments included corticosteroid ointment, calcipotriene 0.005% ointment, oral prednisone, and oral antihistamines. The lesions would partially improve with therapy and subsequently recur after discontinuation of treatment.

Cutaneous examination showed lichenified, individual and confluently distributed, flat-topped, flesh-colored to tan, 2-3 millimeter papules predominantly on the extensor surface of her bilateral forearms, from the elbow to the wrist (Figure 1), and distal legs, from the knee to the ankle (Figure 2). In addition, on her right arm, there was a 2 centimeter brown superficial plaque overlying the papules (Figure 1A).

Skin biopsies of the right forearm (including the brown plaque and underlying papular lesions) and left arm (papules) were performed. Microscopic examination of the specimen from the right forearm, after hematoxylin and eosin staining, showed epidermal hyperplasia with hyperkeratosis. In the lateral portions of the specimen, there was sparse, non-compact, orthokeratosis overlying the epithelium and mild acanthosis. There was also hyperpigmentation of the basal layer (Figure 3).

Pink globular material recognizable as amyloid was located in the dermal papillae. Scattered melanophages were present in the upper dermis (Figures 3, 4). The periodic acid-Schiff (PAS) stain was negative for hyphae. Congo red staining highlighted the amorphous material in the papillary dermis (Figure 5). The biopsy from the left arm also demonstrated amorphous material in the dermal papillae.
Correlation of the clinical presentation and pathology findings established a diagnosis of lichen amyloidosis. In addition, the findings on the right forearm established a concurrent diagnosis of a macular seborrheic keratosis. Therefore, the right forearm was a MUSK IN A NEST consisting of not only a macular seborrheic keratosis, but also lichen amyloidosis.

Treatment was started with betamethasone 0.05% ointment twice daily; hydroxyzine 25mg each evening was also initiated for symptomatic relief of the itching. Within two weeks, there was significant flattening of the papules and relief of her itch. She was able to discontinue the oral antihistamine, and the topical corticosteroid ointment was progressively tapered over the next two months. Improvement consisted of flattening, but not complete resolution of the lesions. Topical care was maintained, and the clinical response persisted on follow-up.

**Case Discussion**

The clinical appearance of seborrheic keratosis may vary from a nearly flat plaque to a verrucous nodule. Lesions often develop in early-to-middle adulthood. Some individuals have few seborrheic keratosis whereas other people have hundreds [5].

The pathology of seborrheic keratosis typically shows varying degrees of hyperkeratosis (thickening of the stratum corneum). There is also acanthosis (thickening of the epidermis). In addition, keratin-filled pseudocysts (horn pseudocyst) and hyperpigmentation of the basal layer and/or the epithelium may also be present [5].

Amyloidosis of the skin can be skin-limited (primary cutaneous amyloidosis and secondary cutaneous amyloidosis) or a manifestation of systemic amyloidosis. Primary cutaneous amyloidosis...
includes lichen amyloidosis, macular amyloidosis, and nodular amyloidosis [2]. Secondary cutaneous amyloidosis is associated with a pre-existing skin condition or skin tumor, such as basal cell carcinoma, Bowen disease, mycosis fungoides porokeratosis, and solar elastosis [6,7].

Lichen amyloidosis is the most common form of primary localized cutaneous amyloidosis. It is more common in men and individuals with darker skin types. It typically presents around 50 years of age [8].

Lichen amyloidosis is a chronic pruritic condition. It is typically associated with rubbing and scratching the affected area. Eventually, papules develop [8].

Lichen amyloidosis is usually an isolated finding. It does not have any potential for malignant transformation. However, it can be associated with multiple endocrine neoplasia type 2A [8].

Pathologic changes of the lichen amyloidosis papules show amyloid deposition in the papillary dermis. The amorphous deposits can be visualized with hematoxylin and eosin staining. However, they are more readily identified with stains that highlight the amyloid such as Congo red and thioflavin T [2].

MUSK IN A NEST, initially referred to as a collision tumor, can consist of two or more malignant neoplasms, one or more malignant and benign disorders, or two or more benign conditions [4]. Seborrheic keratosis and cutaneous amyloidosis have both been a component of a MUSK IN A NEST [4,6]. We suspect that a collision tumor consisting of a seborrheic keratosis and lichen amyloidosis has previously been observed; however, to the best of our knowledge, this is the first report of a MUSK IN A NEST that consists of these two dermatologic conditions.

Seborrheic keratosis typically affects men more than women. They are observed in individuals who are greater than 65 years old. The most affected site is the posterior thorax [5].

Seborrheic keratosis is the most common benign tumor in a MUSK IN A NEST (Table 1), [9-13]. Mikhail and Mehregan reviewed 10,000 biopsies of seborrheic keratosis and found 14 cases to be associated with basal cell carcinoma [9]. Boyd and Rapini noted that a seborrheic keratosis was a component in 32% of collision tumors (22 of 69 cases) in their dermatopathology service; the other components were nevus, basal cell carcinoma, actinic keratosis, neurofibroma, adnexal tumors, and blue nevi in decreasing frequency [10].

In Cascajo et al., 54 malignant neoplasms in conjunction with seborrheic keratoses were characterized; they included basal cell carcinoma (N=43), Bowen disease (N=6), keratoacanthoma (N=3), and malignant melanoma (N=2), [11]. Vun et al. assessed 813 pathology specimens reported as seborrheic keratosis and found 43 to be associated with non-melanoma skin cancer, including intraepidermal carcinoma (N=36), basal cell carcinoma (N=4), squamous cell carcinoma (N=2), and both intraepidermal carcinoma and basal cell carcinoma (N=1), [12]. Moscarella et al. found that collision tumors were most associated with seborrheic keratosis (N=18), followed by basal cell carcinoma (N=13), nevi (N=7), melanoma (N=5), and squamous cell carcinoma in situ (N=4), [13].

Amyloidosis has frequently been described as a basal cell carcinoma-associated MUSK IN A NEST [14]. However, we are not aware of lichen amyloidosis coexisting at the same site as another cutaneous condition. The woman in this report had a macular seborrheic keratosis overlying and between her lichen amyloidosis lesions.

### Conclusion

Seborrheic keratosis is a benign intraepidermal neoplasm arising from epidermal keratinocytes and is a common lesion in aging skin. Lichen amyloidosis is the most common form of primary localized cutaneous amyloidosis; it is characterized by a chronic, pruritic eruption of hyperkeratotic, flesh-colored to tan papules. MUSK IN A NEST describes two or more cutaneous benign or malignant tumors occurring at the same anatomic site. Seborrheic keratosis has frequently been observed as a component of a MUSK IN A NEST. Amyloidosis has been noted in basal cell carcinoma as an incidental finding. Indeed, a MUSK IN A NEST consisting of a macular seborrheic keratosis and lichen amyloidosis...
expands the potential collision tumors encompassed by either seborrheic keratosis or lichen amyloidosis; however, the observation of a single skin lesion consisting of these dermatologic conditions is likely to be a coincidental occurrence that is more common than reflected by this single case report.

**Table 1. Seborrheic keratosis-associated MUSK IN A NEST***

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year of publication</th>
<th># of collision tumors</th>
<th># of SK</th>
<th>% of SK</th>
<th>Ref</th>
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<td>1982</td>
<td>14</td>
<td>14b</td>
<td>100</td>
<td>[9]</td>
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<tr>
<td>Boyd and Rapini</td>
<td>1994</td>
<td>69</td>
<td>22c</td>
<td>31.9</td>
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<td>1996</td>
<td>54</td>
<td>54d</td>
<td>100</td>
<td>[11]</td>
</tr>
<tr>
<td>Vun et al.</td>
<td>2006</td>
<td>48</td>
<td>48e</td>
<td>100</td>
<td>[12]</td>
</tr>
<tr>
<td>Moscarella et al.</td>
<td>2013</td>
<td>24</td>
<td>18f</td>
<td>75</td>
<td>[13]</td>
</tr>
</tbody>
</table>

MUSK IN A NEST, multiple skin neoplasms at one site; Ref, reference; SK, seborrheic keratosis; #, number; %, percent.

*This table contains some, but not all, cases of seborrheic keratosis-associated collision tumors.

In the study, seborrheic keratosis was associated with basal cell carcinoma (14 tumors, 100%).

In the study, seborrheic keratosis was associated with a nevus (14 tumors, 63.6%) and basal cell carcinoma (8 tumors, 36.4%).

In the study, seborrheic keratosis was associated with basal cell carcinoma (43 tumors, 79.6%), Bowen disease (6 tumors, 11.1%), keratoacanthoma (3 tumors, 5.6%), and malignant melanoma (2 tumors, 3.7%).

In the study, seborrheic keratosis was associated with intraepidermal carcinoma (36 tumors, 4.4%), acanthoma (4 tumors, 0.5%), basal cell carcinoma (4 tumors, 0.5%), squamous cell carcinoma (2 tumors, 0.2%), intraepidermal carcinoma and basal cell carcinoma (1 tumor, 0.1%), and keratoacanthoma (1 tumor, 0.1%).

In the study, seborrheic keratosis was associated with basal cell carcinoma (7 tumors, 38.9%), squamous cell carcinoma (in situ), (4 tumors, 22.2%), melanoma (3 tumors, 16.7%), a nevus (3 tumors, 16.7%), and basal cell carcinoma and dermal nevus (1 tumor, 5.6%).

**Potential conflicts of interest**

Ms. Laborada declares no conflicts of interest. Dr. Cohen is a paid consultant for ParaPRO; however, this activity is not a potential conflict of interest with regard to this manuscript.

**References**