Desmoplastic Melanocytic Nevus of Oral Mucosa

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Abstract The desmoplastic melanocytic nevus is an uncommon variant that easily may be confused with a fibrohistiocytic neoplasm or a desmoplastic melanoma. It is believed that the following report describes the first known example of a desmoplastic melanocytic nevus arising in the oral mucosa. The histopathologic and immunohistochemical features that allow separation from other microscopically similar pathoses are stressed.

Keywords Desmoplastic · Melanocytic · Nevus · Oral · Mucosa

Introduction

In their excellent review of spindle and/or epithelioid nevi, Paniago-Pereira et al. [1] appear to be the first to adequately describe a desmoplastic variant. This pattern was reported to occur in patients over the age of thirty and created histopathologic features that resembled dermatofibromas with spindle and/or epithelioid cells intermixed with thick collagen bundles. Many of the nevus cells demonstrated bizarre shapes, abundant cytoplasm, and prominent nucleoli. The cells were reported to be densely packed or sparsely distributed with little to no nesting. Melanin pigmentation typically was minimal or absent.

Two subsequent publications by Barr et al. [2] and by Mackie and Doherty [3] concentrated on this pattern and provided more complete histopathologic descriptions. The nevus cells were present within a desmoplastic stroma and frequently demonstrated unusual ganglion-like cells. Occasional cells with intranuclear vacuoles were noted and thought to contain invaginations of cytoplasmic material. Additionally, these nevi revealed little to no junctional activity, absence of the formation, and frequent lack of melanin pigmentation. The nuclei varied considerably in chromatin pattern, size, and shape with occasional bizarre mononuclear cells. In contrast to the earlier publication, a wide age range was reported with a number of patients presenting in the first decade of life. Both latter publications suggested the pattern represents a discrete entity and recommended the name Desmoplastic Melanocytic Nevus.

A PubMed search of the English language literature failed to reveal any previous description of a desmoplastic nevus of the oral mucosa. The following describes the clinical and histopathologic features of a desmoplastic nevus of the dorsal surface of the tongue.

Case Report

A 14 year old Caucasian male presented with a firm, sessile and dome-shaped enlargement of the dorsal surface of the tongue on the right side. The clinical alteration created an obvious well-defined, symmetrical, and raised circular lesion that measured approximately 1.5 cm in diameter. The lesion was normal colored and asymptomatic with an unknown duration. An excisional biopsy was performed with a clinical diagnosis of neuroma versus neurofibroma.

The gross examination mirrored the clinical description and revealed a nodule of mucosa that demonstrated a well

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circumscribed round dome-like elevation surrounded by normal-appearing filiform papillae. The histopathologic examination revealed a deep wedge of mucosa surfaced by stratified squamous epithelium with numerous filiform and fungiform papillae. The underlying lamina propria consisted of fibrous connective tissue with scattered vascular channels and neural bundles. The base of the specimen demonstrated numerous interlacing bundles of striated muscle. In the central area of the specimen, a proliferation of plump spindle cells was noted between the surface epithelium and the underlying muscle (Fig. 1). The cellular morphology resembled a fibrohistiocytic proliferation, but the distribution within the stroma was most unusual for fibroblastic neoplasm. The majority of the cells demonstrated minimal cytoplasm with elongated and plump nuclei that varied in size and chromatin content. The nuclei varied from small dark spindle cells to large vacuolated nuclei with prominent nucleoli (Fig. 2). Intermixed with these cells were scattered ganglion-like cells with extremely large pale-staining cytoplasm associated with large vacuolated nuclei and prominent nucleoli (Fig. 3). Intranuclear vacuoles were noted but difficult to find. Melanin pigmentation and cellular nesting were not observed.

An immunohistochemical panel was performed using the standard biotin-peroxidase method with appropriate positive and negative controls. Included in this panel were smooth muscle actin, CD31, S-100, HMB-45, Melan-A, factor XIII, Ki-67, p16, pancytokeratin, p63, and calponin. The smooth muscle actin and calponin demonstrated a similar pattern of reactivity and highlighted the muscle walls of the vascular channels and scattered spindle cells noted diffusely throughout the stroma. The number of

Fig. 1 Ill-defined proliferation of plump spindle cells noted between the surface epithelium and the underlying muscle (Hematoxylin and eosin, original magnification $\times 10$)

Fig. 2 Cellular infiltrate exhibiting nuclei that vary from small dark spindle cells to large vacuolated nuclei with prominent nucleoli (Hematoxylin and eosin, original magnification $\times 40$)

Fig. 3 Ganglion-like cell (delineated with arrow) exhibiting large pale-staining cytoplasm associated with large vacuolated nucleus and prominent nucleolus (Hematoxylin and eosin, original magnification $\times 60$)

positive spindle cells was increased in the stroma associated with the nevus cells and was judged to be intermixed reactive myofibroblasts. CD31 decorated the vascular channels but was not reactive with the cellular infiltrate. S-100 demonstrated diffuse strong reactivity (Fig. 4). The S-100 pattern highlighted the extent of the proliferation better than the H&E or any of the other immunoperoxidase reactions. The majority of the reactive cells paralleled the surface mucosa in the superficial stroma but extended into the muscle of the central portion of the specimen. The cellular infiltrate also was nonreactive for HMB-45, cytokeratin, and p63. Upon evaluation with Melan-A and p16, both reactants revealed numerous scattered large and

Fig. 4 Diffuse strong reactivity of the cellular infiltrate with antibodies against S-100 protein (Biotin-peroxidase method, original magnification $\times 4$)

irregular spindle-shaped cells with strong reactivity (Fig. 5). Factor XIII reacted with scattered cells of the normal stroma with the degree of reactivity increased dramatically in the area of the lesion that also was S-100 positive. Ki-67 reactivity demonstrated rare positive nuclei within the cellular proliferation. Although desmoplastic melanoma was considered, numerous features supported a benign diagnosis. The melanocytic proliferation did not demonstrate a junctional or intraepithelial component (Fig. 6). The spindle cells formed a symmetrical pattern and were not associated with an immune infiltrate. Although the cellular proliferation was not encapsulated and extended among the muscle bundles, the periphery of lesion did not demonstrate irregular infiltration of the nevus

Fig. 5 Numerous scattered large and irregular spindle-shaped cells demonstrating strong reactivity with antibodies against Melan-A (Biotin-peroxidase method, original magnification $\times 10$)

Fig. 6 Scattered spindle-shaped melanocytes present within the stroma and without an overlying junctional or intraepithelial component (Hematoxylin and eosin, original magnification $\times 10$)

cells into the surrounding parenchyma (Fig. 7). Areas of hyperchromatism and pleomorphism were present, but mitotic figures were not seen. These histopathologic features combined with low Ki-67 reactivity and diffuse positivity to FXIII, p16, and Melan-A led to the final benign diagnosis of Desmoplastic Melanocytic Nevus.

Discussion

As mentioned in the initial descriptions, the cellular infiltrate appeared fibrohistiocytic. In spite of this, a diagnosis of a collagenous neoplasm was low on the differential diagnosis due to the distribution of the cells within the

Fig. 7 Base of the lesion demonstrating a periphery without irregular infiltration by nevus cells (S-100, biotin-peroxidase method, original magnification $\times 4$)

stroma. Instead of an oval circumscribed proliferation, the cells were distributed over a wide zone of the superficial stroma parallel to the surface epithelium with a central involvement of the underlying muscle. Although the increased reactivity of stromal cells to FXIII supports a fibrohistiocytic neoplasm, that possibility was removed by the strong reactivity with S-100 protein and Melan-A.

Although located in an anatomic location without salivary glands, the possibility of myoepithelioma was considered due to the S-100 reactivity. Failure of reactivity with pancytokeratin and p63 removed myoepithelioma from consideration.

The lack of reactivity to HMB-45 in this nevus is not surprising. This reagent tends to demonstrate a reactivity pattern aligned with the maturation status of melanocytes. HMB-45 primarily reacts with epithelioid melanocytes, which frequently exhibit melanin pigmentation and are located predominantly within the epithelium or superficial stroma. Except for blue nevi, loss of HMB-45 reactivity often is noted in more deeply seated and spindled melanocytes which typically lack melanin pigment [4]. Similarly, loss of HMB-45 reactivity is noted in desmoplastic melanoma.

Results of reported HMB-45 reactivity in desmoplastic nevi are variable. Numerous cases have documented lack of HMB-45 reactivity in desmoplastic nevi [5–7]. In one study, 5/16 desmoplastic nevi demonstrated negative reactivity. Of the remaining 11, the reactivity was localized to the superficial portion of the nevus in 8/11 [7]. Investigators have suggested that desmoplastic nevi with HMB-45 reactivity represent sclerotic blue nevi, while nonreactive desmoplastic nevi represent a variation of a Spitz nevus or a unique nevus unrelated to both blue and Spitz nevi [5].

Once determined to be melanocytic, the primary differential diagnosis was a benign desmoplastic nevus versus a desmoplastic melanoma. Although desmoplastic melanomas typically arise in chronically sun damaged skin and demonstrate a significant mitotic index, examples not fulfilling these criteria occur. Immunoperoxidase reactions have proven beneficial in assisting in the separation of these two entities. Desmoplastic nevi typically demonstrate a significant increase in FXIII positive stromal cells while desmoplastic melanomas rarely reveal increased reactivity [8]. Studies of p16 expression have shown loss of reactivity in deeply invasive and desmoplastic melanomas, while strong cytoplasmic and nuclear reactivity has been reported in desmoplastic nevi [9]. Reactivity to Melan-A and Ki-67 also has been shown to be beneficial. In studies of desmoplastic nevi, greater than 90 % have demonstrated strong reactivity with Melan-A, while reactivity in desmoplastic melanomas has been reported to be less than 10 % [10, 11]. Ki-67 reactivity demonstrates a wide

variation of reactivity in melanoma but does not tend to exceed 10 % in desmoplastic nevi [10, 11].

These immunohistochemical findings combined with the previously described histopathologic features fail to support a diagnosis of melanoma.

The currently documented case is thought to represent the first reported example of a desmoplastic melanocytic nevus of the oral mucosa. A spindle and/or epithelioid nevus has been reported on the tongue but subsequently was reinterpreted as a malignant melanoma [12–14]. Whether previously reported desmoplastic nevi represent a distinct entity, sclerotic blue nevi, a variation of a spindle cell and/or epithelioid nevi, or a compilation of all three variants remain the subject of debate [15, 16]. Although the features of the current case suggest the possibility of a fibrohistiocytic neoplasm or a desmoplastic melanoma, the histopathologic findings and associated immunoperoxidase panel are sufficient to warrant a diagnosis of desmoplastic melanocytic nevus of the oral mucosa.

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