

## Desmoplastic Trichilemmoma: A Case Report with Immunohistochemical Characterization of the Extracellular Matrix Components

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The case of an unusual desmoplastic variant of trichilemmoma arising in the neck of a 56-year-old man is reported. The tumour was characterized by the presence of a densely sclerotic stroma, surrounded by lobules of epithelial cells with features of outer root sheath differentiation, including glycogen-rich, clear cytoplasm and peripheral palisading. In the central part of the tumour, irregular cords of epithelial cells entrapped in the desmoplastic stroma were found. Differential diagnosis of this rare tumour includes invasive squamous cell carcinoma, morphea-like type basal cell carcinoma, desmoplastic trichoepithelioma and desmoplastic trichoblastoma. By immunohistochemistry, the tumour epithelium stained with anti-cytokeratin antibodies while the stromal cells were positive with vimentin. The centro-tumoral extracellular matrix showed a diffuse and intense positivity for type I collagen and tenascin, whereas stains for laminin and type IV collagen were uniformly negative. We suggest that tenascin could be secreted by the epithelial neoplastic cells and play a role in the mesenchymal response, which results in desmoplasia.

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Trichilemmoma is a fairly common benign adnexal skin neoplasm, derived from the external root sheath of the hair follicle. It has been recognized either as a solitary entity or as multiple lesions, specifically associated with Cowden's disease (1-3). The tumour is generally found as a small smooth or keratotic papule in the face or neck of adult patients, affecting both sexes equally (1, 4, 5). Histologically, the lesion is characterized by trichilemmal differentiation in the form of a lobular growth of glycogen-rich clear cells, with peripheral palisade and a prominent basement membrane which sharply separates the lesion from the dermis (1, 5).

The presence of a prominent stromal desmoplastic component in an otherwise typical trichilemmoma was first described by Starink et al. in 1985 (6). Since then, to the best of our knowledge, only 29 cases of desmoplastic trichilemmoma have been reported (7, 8). We here describe an additional case, arising as a solitary lesion in the neck of a 56-year-old man. Immunohistochemical studies of the extracellular matrix components, including tenascin, laminin, type I and type IV collagen, were performed.

### CASE REPORT

A 56-year-old man presented with a slightly raised verrucous papule on the neck. He had first noticed the lesion 14 months prior to his

first consultation; no pruritus or other symptoms were present. On clinical examination, the lesion appeared as a solitary, firm, skin-coloured papule with a rough surface, measuring 0.5 cm in diameter. The clinical diagnosis included verruca vulgaris and papilloma. The lesion was surgically excised, and no recurrence was noted 1 year after the initial diagnosis.

### Histopathologic findings

Microscopic examination of the skin biopsy showed a well-circumscribed lobular proliferation of clear cells, surrounding an abundant desmoplastic stroma (Fig. 1). The lesion extended from the basal layer of the epidermis through the superficial dermis. The tumour lobules were composed of polygonal and cuboidal cells, with a clear cytoplasm and a central, round to oval nucleus, devoid of any cytologic atypia. The tumour lobules showed peripheral palisading of smaller, rather basophilic cells and were outlined by a homogeneous pale eosinophilic cuticle, which created a distinct boundary with the surrounding dermis. Rare small horn microcysts were also noted. Toward the center of the tumour, the lobular architecture changed into a more irregular pattern composed of narrow strands and delicate cords of epithelial cells, entrapped within a densely sclerotic stroma. The neoplastic clear cells were PAS-positive, PAS-D negative, and the hypocellular desmoplastic component contained an Alcian blue (pH 1.5) and PAS-positive, diastase-resistant material.

A streptavidin biotin immunohistochemical technique demonstrated that the tumour cells diffusely stained with anti-cytokeratin antibodies AE1/AE3 (Biogenex Laboratories INC, San Ramon, CA, USA), 34BE12 (Enzo Diagnostics INC., New York, USA) and KL1 (Immunotech S.A., Marseille, France), whereas the stromal cells were negative. Vimentin (Biogenex Laboratories INC) staining was weakly and focally distributed within the cellular stromal component and totally negative in the surrounding epithelium. Tenascin (Dako Corporation, Carpinteria, CA, USA) and type I collagen (DBA, Milan, Italy) stainings were distributed diffusely within the extracellu-



Fig. 1. Low power of the lesion, showing a well-circumscribed lobular epithelial growth composed of polygonal and cuboidal cells with clear cytoplasm. A central area of prominent desmoplasia is present (H&E, obj 2.5).

lar matrix of the central part of the tumour. Stains for cytokeratin CAM 5.2 (Becton Dickinson, San Jose, CA, USA), CEA (Zymed Laboratories INC, San Francisco, CA, USA), EMA (Dako Corporation), CD34 (Immunotech S.A.), laminin (Dako Corporation) and type IV collagen (Immunotech S.A.) were uniformly negative in both epithelial and stromal components (Fig. 2).

## DISCUSSION

Desmoplastic trichilemmoma is a rare neoplasm, which has been recently described in the dermatologic literature. Hunt et al. reported the largest series, with a clinical and histologic review of 22 patients (7). Subsequently, 7 other cases were described by Tellechea et al., including an immunohistochemical characterization of the neoplastic cells (8). The lesions occurred predominantly in males over a wide age range, being more frequent after the fifth decade (7, 8). The most common site was the face, followed by neck, scalp, chest and vulva (7, 8). The lesions were described as solitary small dome-shaped papules or nodules with a verrucous or smooth surface. Due to the rather nondistinctive clinical picture, most of the

cases were misdiagnosed as basal cell carcinoma, papilloma or verruca vulgaris (7, 8). Histologically, the most salient finding in all cases was an abundant desmoplastic stroma surrounded by a proliferation of epithelial cells with outer root sheath differentiation, including abundant glycogen-rich, clear cytoplasm and peripheral palisading of cells with subnuclear vacuolization (7, 8).

It is not yet clear whether the desmoplastic reaction is the result of a regressive-degenerative change of the epithelial component or a mesenchymal response histogenetically independent from its epithelial counterpart (7, 9). Hunt et al. (7) consider desmoplasia a secondary phenomenon in pre-existing trichilemmomas, whereas Tellechea et al. (8) suggest that it is a fibroblast-mediated, dendrocyte-independent process and not the result of an involutive epithelial change. We found a diffuse and intense positivity for type I collagen and tenascin around the epithelial elements embedded in the surrounding stroma, whereas collagen type IV and laminin were uniformly negative. Since collagen type I is widely distributed in the normal dermis and in several connective tissues, its diffuse expression in the

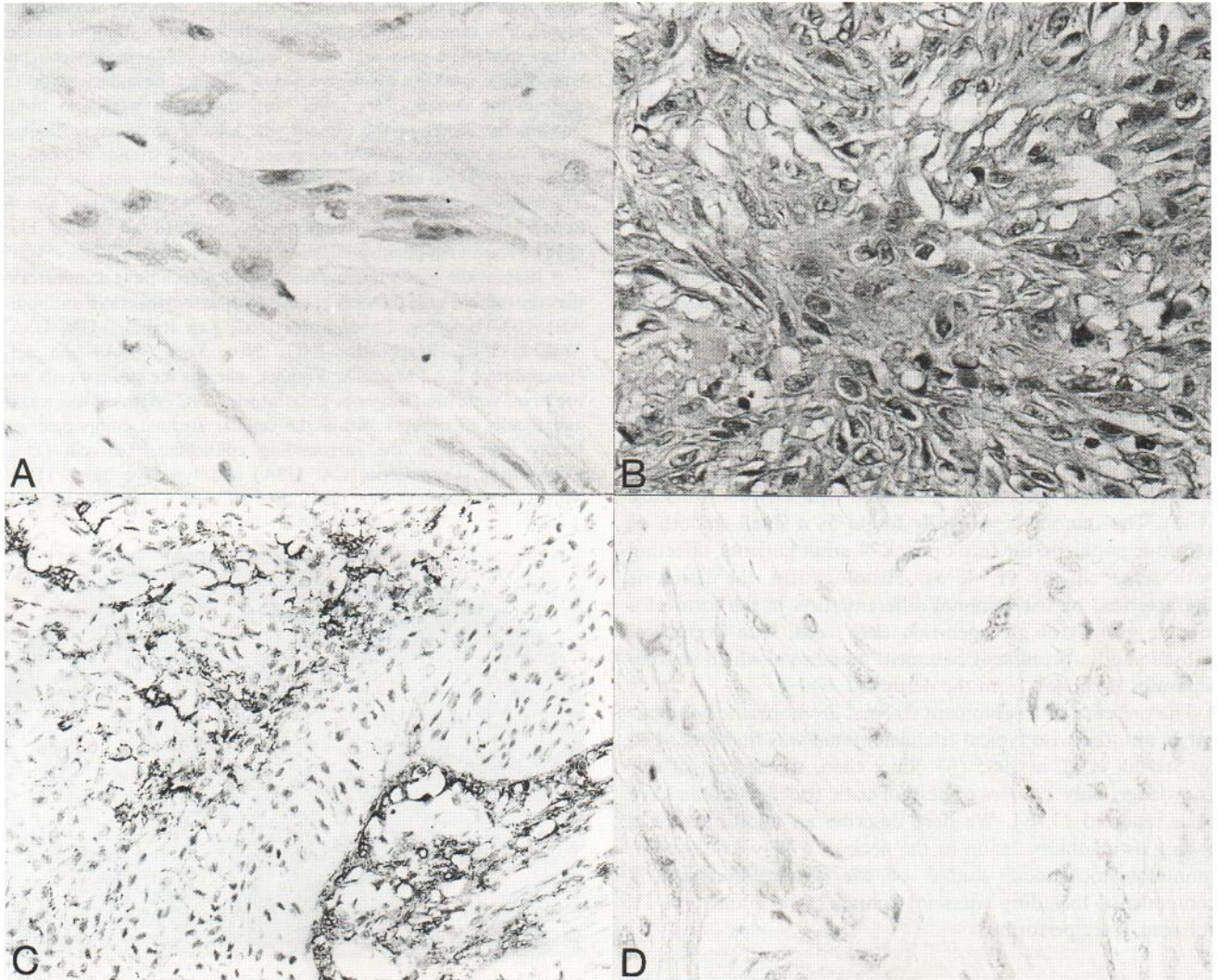


Fig. 2. (A) Weak and focal positivity for vimentin (obj 40); (B) diffuse extracellular and cellular positivity for type I collagen (obj 25); (C) intense and diffuse tenascin immunoreactivity at the epithelial-stromal junction (obj 10); and (D) no expression for type IV collagen is evidenced (obj 25).

desmoplastic areas was not surprising. Tenascin is an extracellular matrix component, which influences the morphogenetic interactions between the epithelial cells and the surrounding mesenchyme during morphogenesis and in several neoplasms. In normal skin, its expression is most pronounced in the dermal papillae, in association with the lower portion of hair follicles, sweat glands and blood vessels (10). Tenascin has also been detected in the stroma of many epithelial tumours of the skin, specifically in the epithelial-mesenchymal junctional areas (11–13). Although tenascin is considered to be mesenchymal in origin, it has been suggested that under certain circumstances it may be produced by epithelial cells (11). Thus, in desmoplastic trichilemmoma tenascin could be secreted by the epithelial neoplastic cells and play a role in the mesenchymal response. The absence of laminin and type IV collagen stainings probably reflects a partial loss of the ability to produce basement membrane components by tumour cells, as already observed in other types of pilar benign tumours, such as trichofolliculomas, trichoepitheliomas and pilomatrixomas (14).

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