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CORRESPONDENCE

Desmoplastic cellular neurothekeoma

Dear Editor,

A 39-year-old man presented for the evaluation and treatment of a 1-year history of an asymptomatic protruding nodule on his chin with slow progression in size (Figure 1A). He denied previous trauma or using any filler injections. He had no significant medical history. Physical examination revealed a firm skin-colored dome-shaped nodule with a telangiectatic surface on the chin. The clinical differential diagnosis included epidermal cysts and various adnexal neoplasms. The lesion was excised and pathologic examination showed a non-encapsulated and nodular tumor in the dermis. The lesion was composed of compact to confluent ill-formed small lobules, nests, and fascicles of plump oval, epithelioid or fusiform tumor cells harboring abundant pale pink cytoplasm, set in a matrix with a collagenous or myxoid feature. A large ill-defined central region of the tumor had a densely fibrotic matrix leading to a hyalinized and sclerotic feature. Multinucleated cells and frank nuclear atypia, enlargement, and pleomorphism were seen in some tumor cells. A few mitoses were found (Figure 1B–D).

Immunohistochemical studies revealed expression of vimentin, neuron-specific enolase, (Figure 1E), and collagen-IV. Very few individual cells showed focal and weakly cytoplasmic expression of epithelial membrane antigen (EMA). Few tumor cells were stained with actin, and all were negative for S100 and cytokeratin. A diagnosis of desmoplastic cellular neurothekeoma was rendered.

Cellular neurothekeomas are rare benign lesions that typically present as asymptomatic nodules on the face and neck in children and young adults with a slight female predominance. The lesions usually are found as solitary skin-colored nodules, 90% measured <2 cm.[1] Pulitzer and Reed[2] first labeled desmoplastic variant of neurothekeoma from 70 cases of neurothekeomas and three of their cases showed predominantly fibrous areas rather than typical myxomatous areas.[2] Hornick and Fletcher[1] analyzed 133 cellular neurothekeomas and only 4% showed stromal hyalinization. Desmoplastic cellular neurothekeomas also predominantly affect young female adults (mean age, 30 years) and are found on the head and upper extremities. During 24 months follow-up after surgical excision, there was no recurrence of distant metastases.

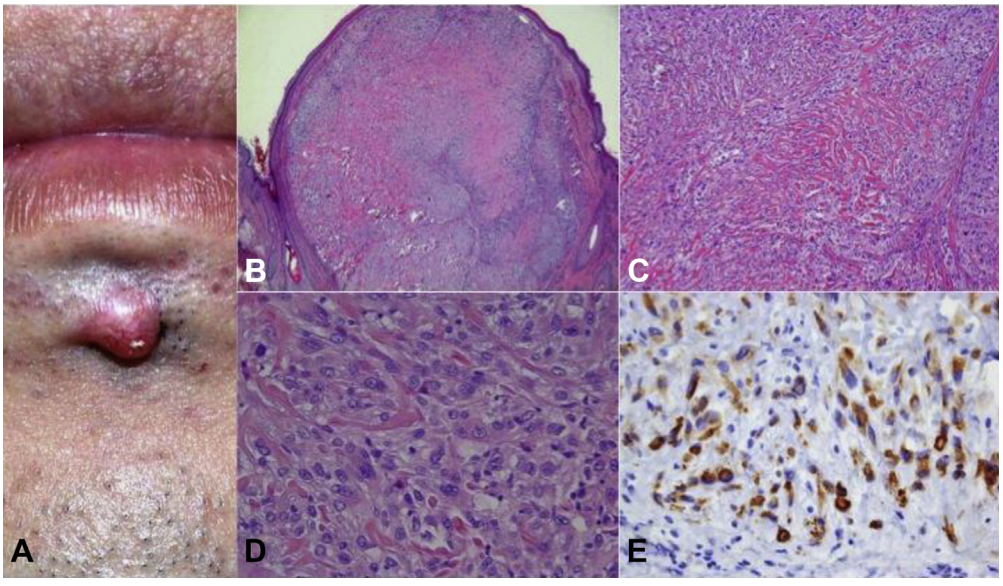

Figure 1 (A) An asymptomatic erythematous protruding nodule on the chin. (B) A dome-shaped tumor in the dermis with (C) desmoplastic hyalinized stroma and (D) plump oval, epithelioid or fusiform tumor cells. (E) The tumor cells are positive for neuron-specific enolase. (Hematoxylin & eosin, original magnification, A ×40, B ×100, C ×400; neuron-specific enolase, D ×400.)

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

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Table 1 Summary of the histological and immunohistochemical features of the lesions showing desmoplastic pattern.

Differential diagnosis	Clinical presentations	Histological findings	Immunohistochemical stains
Desmoplastic cellular neurothekeoma	On the face and neck in children and young female adults	Multinodular, fascicular arrangement of spindled and polygonal cells embedded in a sclerotic and hyalinized stroma	NKI/C3(+), vimentin(+), NSE(+) HMB45(−), S-100 (−)
Desmoplastic melanoma	Sun-exposed areas in older patients	An overlying atypical intraepidermal component	S-100 (+), HMB-45 (+), MART-1 (+)
Desmoplastic SCC	Sun-damaged or irradiated skin in elderly patient	Squamous differentiation and actinic change in the epidermis	CK (+)
Cellular dermatofibroma	Predilection for occurrence on the lower legs of women	Overlying epidermal induction predominant fascicular growth without lobulated/nested pattern	Expression of factor XIIIa, CD10, and NKI/C3
Plexiform fibrohistiocytic tumor	Frequently in the upper extremities in children and young adults	Low-power biphasic architecture generally deeper location (subcutis) greater degree of spindled/ myofibroblastic cells	Almost same as desmoplastic cellular neurothekeoma
Benign cutaneous plexiform hybrid tumor of perineurioma and cellular neurothekeoma	Solitary dome-shaped papules located on the lip	Nests or rounded neoplastic cells in a plexiform pattern	S100A6(+), NKI/C3(+), PGP9.5(+), EMA(+), and NSE(+)
Piloleiomyoma	Reddish firm papulonodules on the extensor extremities or trunk	Broader and more elongated and their cytoplasm are also more brightly eosinophilic	Desmin (+), SMA (+)

CK = cytokeratin; EMA = epithelial membrane antigen; HMB45 = human melanoma black 45; MART-1 = melanoma antigen recognized by T-cells 1; NSE = neuron-specific enolase; SCC = squamous cell carcinoma; SMA = smooth muscle actin.

Histopathological finding shows multinodular, fascicular arrangement of spindled and polygonal cells embedded in a sclerotic and hyalinized stroma. The cells consist of ample, eosinophilic, and vacuolated cytoplasm with vesicular nuclei and a single nucleolus. Sparse lymphocytes, plasma cells, and multinucleated cells infiltrates may be present. The mean mitotic rate is 0.67/10 high power fields. Cytologic atypia with nuclear variability and small nucleoli can exist.[3]

There are no specific immunohistochemical markers for desmoplastic cellular neurothekeoma. The cells express NKI/C3, vimentin, neuron-specific enolase, type IV collagen, laminin, CD68, and CD10. Focal cells are positive for smooth muscle actin or desmin. All tumors are negative for HMB45 and S-100.[1,3] The histogenesis is still uncertain. It is thought to be a type of nerve sheath tumor, but there is no good immunophenotypic evidence. Myofibroblastic or histiocytic origins were considered recently in some studies.[4,5]

The histopathologic differential diagnosis of desmoplastic cellular neurothekeoma includes melanocytic tumor (such as desmoplastic Spitz's nevus and desmoplastic melanoma), desmoplastic squamous carcinoma, cellular dermatofibroma,[6] plexiform fibrohistiocytic tumor, benign cutaneous plexiform hybrid tumor of perineurioma and cellular neurothekeoma,[7] and piloleiomyoma. They can be distinguished by clinical presentation, histological features, and immunohistochemical stains which are summarized in Table 1. Our case lacks the plexiform pattern, and its rare and sporadic weak immunohistochemical reaction for EMA is quite different from that of benign cutaneous plexiform hybrid tumor of perineurioma and cellular neurothekeoma.

Soft tumors with the most similar histological and immunohistochemical findings are plexiform fibrohistiocytic tumors. This type of tumor usually locates in the deeper dermis or subcutis. Only if distinctive biphasic architecture, nodules of macrophages, and osteoclastic giant cells surrounded by fascicles of fibroblastic spindle cells are present, are they helpful to distinguish them from desmoplastic cellular neurothekeoma. Plexiform fibrohistiocytic tumor has a reported local recurrence rate of 12–40% and rare regional or systemic metastases.[8]

In summary, we present a rare case of desmoplastic cellular neurothekeoma. Combined clinical, histological, and immunohistochemical information is essential for diagnosis. It is important to keep this uncommon entity in mind when encountering a desmoplastic lesion.

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