Immature trichoepithelioma: report of six cases


We report 6 cases of an immature variant of trichoepithelioma which histologically appears to show differentiation toward the primitive hair germ. The lesions presented in mature adults (mean age 44 years). Four occurred in men and 2 in women. Four lesions occurred on extremities, an unusual location for trichoepitheliomas. Histologically, the lesions were characterized by well-circumscribed, but unencapsulated, dermal collections of small tumor lobules composed of basalioid cells with invaginations resembling primitive dermal hair papillae. There was no adenoidal growth pattern or horn cyst formation. The separation of the immature lesions from those of classical trichoepithelioma and basal cell carcinoma can be made if multiple morphological features are considered; no one particular finding is diagnostic. The major differential features between the immature trichoepithelioma and basal cell carcinoma are circumscription, tumor lobule uniformity, occasional immature hair germs, and lack of retraction artifact of the tumor lobules from the stroma. The differential features between the immature and classical trichoepithelioma are less conspicuous. The immature form typically exhibits no horn cysts, displays fewer primitive hair structures, and lacks the adenoidal growth patterns of the tumor lobules which are usually present in the classical trichoepitheliomas.

Trichoepithelioma is a benign neoplasm with pilar differentiation. The tumor most commonly appears in adolescence as numerous small facial papules, inherited as an autosomal dominant trait. The solitary form of the disease, however, is not inherited and commonly appears on the face in adult life. These may be clinically and histologically confused with the classical basal cell carcinoma (BCC) that develops in the chronically sun-exposed skin of older individuals. In this report, we describe 6 cases of a histological variant of trichoepithelioma which may be confused with BCC on casual histological inspection. Because of its histological resemblance to the immature hair germ of embryonic skin, we have termed this histological subtype immature trichoepithelioma.

Material and methods

Five additional cases were obtained prospectively after recognition of the first case. Paraffin-embedded, hematoxylin & eosin-stained sections were reviewed on all cases. Follow-up information was obtained by contacting the referring physicians.

Results

The clinical data is summarized in Table 1. The patients ranged in age from 20 to 69 years (average, 44 years). Four lesions occurred in men and 2 in women. The lesions ranged in size from 2 to 10 mm; all were removed by excisional biopsy. Sites of oc-
Dermal lesion is circumscribed, unencapsulated, and consists of multiple, small epithelial lobules with interspersed fibrous connective tissue. The periphery of the lesion shows compression of adnexa and deep dermal structures.

Pathology

All cases showed similar histology; all were well circumscribed, non-encapsulated dermal tumors composed of collections of small basaloid cells within a loose cellular, fibrous stroma. The tumor recurrence included 2 from the face (chin), 2 from the shoulder, 1 from the leg, and 1 from the groin. Four of the 6 patients in which follow-up was available had no tumor recurrence from 1 to 8 years. One patient was lost to follow-up, and another was diagnosed just prior to this report.
Immature trichoepithelioma

**Fig. 3.**
(WU 87–7920) (H & E, ×90): Areas of the lesion show cystic acantholytic dyshesion within the tumor islands. Peripheral palisading of the lobules is also noted.

**Fig. 4.**
(WU 87–7921) (H & E, ×90): The stroma consists of loose, fibrous tissue "streaming" between the tumor islands. Retraction artifact, a prominent feature of BCC, is not seen.
nodules were single in each case and, in turn, were subdivided into smaller lobules by fibrous septae (Figs. 1, 2). The tumor lobules were uniform, with many displaying peripheral palisading. Other lobules contained dysesive areas with small cysts containing acantholytic cells (Fig. 3). No artifactual stromal retraction from the smaller lobules was noted. The stroma was only focally fibrotic, primarily in the central portions, and no obvious mucin was seen (Fig. 4). The periphery of a few lobules showed areas of slender dermal invaginations with disc-shaped accumulations of spindle shaped connective tissue cells recapitulating immature hair papillae (Fig. 5). Horn cysts or adenoidal growth patterns were not found.

Cytologically, the tumor cells were small and possessed a high nuclear/cytoplasmic ratio. Apoptosis was present focally within the lobules, though it was

5A (WU 87-7926) (H & E, ×260): A primitive epithelial island has central cystic change with slight invagination and condensed collections of horizontal fibroblasts, recapitulating the immature hair germ.

5B (WU 98-7925) (H & E, ×260): Two immature hair papillae are surrounded by condensed plate-like collections of small, oblong cells reflecting more advanced differentiation. This was a focal finding.
Table 2. Immature trichoepithelioma: Histological differential diagnosis.

<table>
<thead>
<tr>
<th></th>
<th>Immature trichoepithelioma</th>
<th>Trichoepithelioma</th>
<th>Basal cell carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall architecture</td>
<td>Circumscribed</td>
<td>Circumscribed</td>
<td>Variable, usually infiltrative</td>
</tr>
<tr>
<td>Overlying skin ulceration</td>
<td>Absent</td>
<td>Absent</td>
<td>Common</td>
</tr>
<tr>
<td>Perilobular stromal retraction artifact</td>
<td>Absent</td>
<td>Absent</td>
<td>Common</td>
</tr>
<tr>
<td>Primitive hair structures</td>
<td>Occasional</td>
<td>Common</td>
<td>Not found</td>
</tr>
<tr>
<td>Horn cysts</td>
<td>Absent</td>
<td>Common on face, less common on extremities</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Architecture of tumor lobules</td>
<td>Round or oval, usually solid</td>
<td>Stellate, usually lacylike, occasionally solid</td>
<td>Variable, many patterns</td>
</tr>
<tr>
<td>Acantholysis of tumor lobules</td>
<td>Common</td>
<td>Absent</td>
<td>Variable</td>
</tr>
<tr>
<td>Apoptosis of tumor cells:</td>
<td>Uncommon</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Nature of stroma:</td>
<td>Loose, fibrotic</td>
<td>Loose, fibrotic</td>
<td>Myxoid, except morphea</td>
</tr>
<tr>
<td>Inflammatory infiltrate</td>
<td>Variable</td>
<td>Variable</td>
<td>Usual</td>
</tr>
</tbody>
</table>

not seen in all tumors. Occasional mitoses were present.

Discussion

Trichoepitheliomas are classified as hamartomatous tumors of the hair germ, and occur either as multiple or solitary lesions (1). The multiple form was first described by Brooke and Fordyce, respectively and independently, in 1892 (2, 3); Wolters first described the solitary trichoepithelioma in 1901 (4).

Multiple lesions may be familial with an autosomal dominant mode of inheritance. They may first appear in childhood or adolescence as numerous small, flesh-colored papules usually located along the nasolabial folds, forehead, nose, or upper lip (1), and occasionally on the scalp, neck, and upper trunk (5). They rarely ulcerate and have no invasive growth; however, basal cell carcinoma and trichoepitheliomas have been described within the same tumor nodule (6). Multiple trichoepitheliomas usually range in size from 2 to 8 mm and rarely exceed 1 cm. The clinical differential diagnosis includes the angiofibroma of tuberous sclerosis, neurofibromatosis, syringoma, and BCC.

Solitary trichoepithelioma does not have a familial association, it develops as a single, firm, non-ulcerated, flesh-colored papule or nodule on the face of an adult. In most cases, the lesion is no more than 1.0 cm in diameter; however, it has been reported to growth to considerable sizes in some cases (7, 8). Although the solitary lesion is most commonly found on the face, other sites, including the neck, back, scalp, upper arm, and thigh can also be involved (1, 7, 8). The clinical differential diagnosis includes intradermal melanocytic nevus, dermato-fibroma, and BCC.

Both solitary and multiple trichoepitheliomas are histologically similar; thus, the location, number of lesions, and familial history are important pieces of clinical information one must utilize to arrive at the correct clinicopathological diagnosis.

Another variant of trichoepithelioma, the desmoplastic variety, consists of horn cysts and compressed epithelial strands within a dense, sclerotic stroma. It is most often confused with syringoma, morphea-like basal cell carcinoma, and desmoplastic metastatic tumors to the skin (9).

Trichoadenoma is considered a highly differentiated variant of trichoepithelioma, conceptually placed at the opposite end of the spectrum when compared to the immature form presented here. It often occurs as a solitary nodule on the face or trunk, and histologically consists of numerous cystic spaces lined by outer root sheath epithelium and displaying a prominent granular layer. Short epithelial cords may be attached focally, recapitulating hair root formation, though no true hair root or germ is seen (10).

Regardless of the clinical presentation, classical trichoepitheliomas, whether single or multiple, share similar histological findings in that they are dermal tumors composed of islands of basophilic cells showing peripheral palisading and multiple horn cysts in the majority of the cases located on the face. The horn cysts are less pronounced or absent in lesions from the neck and extremities (1). Most of the tumor lobules are arranged in an adenoidal or reticular pattern, but solid proliferations can also be seen. Both patterns may show focal areas in which tumor lobules display cup-shaped stromal invaginations reproducing hair papillae. In contrast, the immature variant described herein exhibits no horn cysts, occasional lobules show areas recapitulating the primitive hair germ prior to the induction of the dermal papilla, and tumor lobule acantholysis is commonly seen. BCC may be difficult to differentiate from either histological form of trichoepithelioma in some cases, but if one considers multiple factors, including overall architecture, retraction artifact, and differentiation toward the hair germ, the correct diagnosis can be made. Table 2 compares and contrasts the main histological features of immature and mature (classical) trichoepitheliomas with BCC.
In summary, we have identified a previously undescribed immature variant of trichoepithelioma, most likely nosologically situated at the less differentiated end of the spectrum of lesions originally proposed by Gray and Helwig (1), that may initially be confused with BCC. Conceptually, the immature trichoepithelioma may be considered a neoplasm of the primitive hair germ.

References

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