

## Trichoblastoma-Like Tumour with Follicular, Matrical and Sebaceous Differentiation: Involvement of Hair Follicle Stem Cells?

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Most cutaneous adnexal tumours show poor differentiation or differentiate toward only one adnexal structure. Trichoblastomas are benign tumours with hair germ differentiation. We describe here a trichoblastoma-like tumour appearing on the scalp of an elderly woman and propose that this tumour may have arisen from a multipotent hair follicle stem cell that is able to give rise to all elements of the cutaneous epithelium and adnexal structures.

### CASE REPORT

A 72-year-old woman presented with a painless nodule on her scalp. It was first noticed 20 years previously, and had been slowly increasing in size over the years. The patient had chronic hepatitis C infection, but no other medical history of note. She had previously worked indoors, and there was no history of frequent sun exposure or chronic arsenism. Clinical examination revealed a flesh-coloured nodule on the left parietal scalp, which was firm and non-tender, and measured 2.5 × 2 cm. No ulceration was present on the tumour surface, and no telangiectasias were seen. Cervical lymph nodes were not palpable.

On histological examination, there was a well-circumscribed, but unencapsulated, tumour extending from the upper dermis to the subcutaneous tissue (Fig. 1). The majority of the tumour was composed of islands of basophilic cells with poor differentiation (Fig. 1, inset). There was no connection with the epidermis. The tumour nests showed some peripheral palisading, but no retraction artefact could be observed. Stromal condensation could be seen around some tumour islands.

Serial sectioning revealed areas exhibiting multiple lines of differentiation, often in close proximity to each other (Figs 1 and 2). Follicular differentiation was evident in some areas, with formation of horn cysts (Fig. 2A). Eosinophilic shadow cells with distinct cell borders and well-defined areas of central pallor without nuclei were present in many regions, indicating matrical differentiation (Fig. 2B). Sebaceous differentiation was seen in many tumour islands, which contained many large foamy sebaceous cells and ductal structures (Fig. 2C). In addition, in some tumour islands there were elongated spindle-shaped basaloid cells with nuclei arranged in a palisading fashion, forming parallel rows of epithelial ribbons (Fig. 2D). These resembled the Verocay bodies found in neural tumours, such as schwannoma. There was no nuclear atypia, cellular pleomorphism, or abnormal mitoses. No evidence of vascular or neural invasion could be found. A diagnosis of trichoblastoma with multiple lines of adnexal differentiation was made.

Following complete surgical excision, the patient was followed up for 5 years. No tumour recurrence was noted over this time period.

### DISCUSSION

Most cutaneous adnexal tumours show only one line of differentiation (1), however, certain neoplasms have

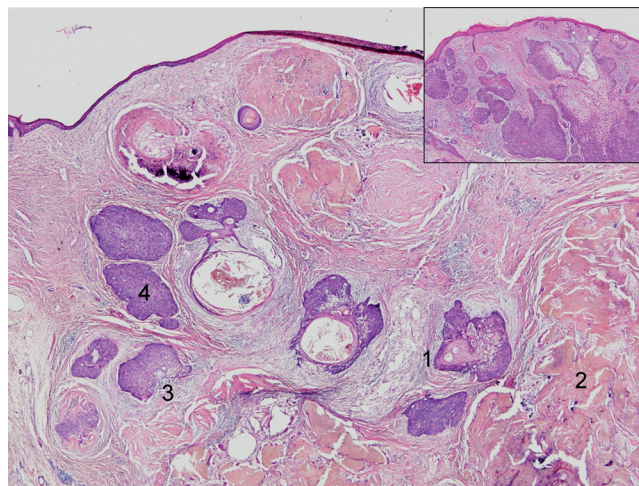


Fig. 1. The majority of the tumour was composed of islands of basophilic cells with poor differentiation (inset). Serial sectioning (main figure) revealed areas with follicular (1), matrical (2) and sebaceous (3) differentiation, as well as areas characterized by Verocay body-like central nuclear palisading (4). Haematoxylin-eosin stain, magnification ×10.

the potential to differentiate in more than one direction. Basal cell carcinomas in different patients may exhibit adenoid, sebaceous, or keratotic differentiation, and unusually two or more lines of differentiation may be present in a single tumour.

Trichoblastomas tend to be larger than most benign follicular neoplasms, and are usually greater than 1 cm in diameter. The head, particularly the scalp, is a common site of occurrence. They present as slowly growing, solitary, well-defined nodules. The age range is broad, ranging from the third to ninth decades. There is no gender or race predominance reported (2).

On histological examination trichoblastomas are large well-circumscribed, but unencapsulated, basaloid nodular tumours, often extending to the deep dermis and subcutaneous tissue. There is no epidermal connection. The tumour is composed of variably sized epithelial nests. Tumour cells are basophilic with small amounts of cytoplasm. Peripheral palisading is present, but there is stromal condensation around tumour islands, and retraction spaces are not a prominent feature (2).

The tumour described in this report could be differentiated from basal cell carcinoma due to lack of retraction artefact between the stroma and tumour nodules. It could be distinguished from trichoepithelioma,

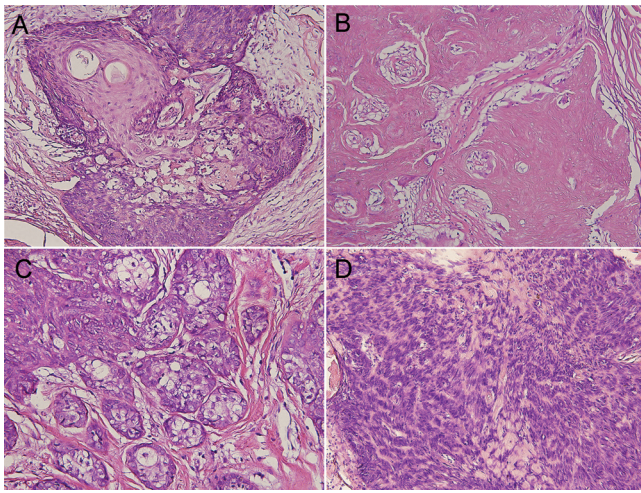


Fig. 2. Higher magnification images showing: (A) follicular differentiation with horn cysts; (B) matrical differentiation with eosinophilic shadow cells; (C) sebaceous differentiation with large foamy sebaceous cells; and (D) Verocay body-like central nuclear palisading. Haematoxylin-eosin stain, magnification A  $\times 100$ , B  $\times 100$ , C  $\times 200$ , D  $\times 100$ .

which is clinically much smaller and histologically characterized by smaller nodules with prominent keratinization and location in the superficial and mid-dermis without extension to the deep dermis and subcutaneous tissue (1).

Trichoblastomas may show poor differentiation or may differentiate toward one type of mature adnexal structure (2). A number of trichoblastomas exhibiting both apocrine and sebaceous differentiation have been reported previously (3, 4). In our case, a single tumour with combined follicular, matrical, and sebaceous differentiation was found. This has not been described previously.

It has been reported previously that multipotent stem cells are localized to the bulge region surrounding the outer root sheath of the hair follicle (5–9). This is different to the secondary germ, which is located at the base of the telogen hair follicle and which gives rise to the hair bulb.

During the hair follicle cycle, stem cells located in the bulge region normally give rise to all of the lower hair follicle epithelial cell types. In addition, hair follicle stem cells have been found to have the ability to give rise to all epithelial cell types within the follicle, as well as the epidermis and sebaceous gland (5, 10, 11). Most intriguingly, hair follicle stem cells isolated from the mouse hair follicle bulge area have been found to have the potential to differentiate into non-epithelial tissue, including Schwann cells and neurones (12, 13).

There is considerable evidence that basal cell carcinomas originate from hair follicle stem cells (5, 14, 15). This may explain why these tumours are composed of poorly differentiated cells with the capacity to differentiate into multiple adnexal structures.

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