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Histogenesis of Basal-Cell Epithelioma

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Introduction

We have been impressed by the almost constant presence of smaller and larger foci of keratin material in the epithelial cell nests of basal-cell epitheliomas. This study was undertaken to evaluate these keratinized foci and to see if any light could be shed on the morphogenesis of basal-cell epitheliomas and also to question the validity of the concept of basal-squamous epithelioma.

Methods

All of the basal-cell tumors seen in our laboratory during the past two and one-half years were reexamined and reviewed. The specimens were stained with hematoxylin and eosin, occasional ones with silver and PAS stains. Biopsy specimens of 147 lesions from 122 patients were studied. One patient had as many as nine separate lesions, removed, interestingly enough, from the back.

Gross and Microscopic Observations

Grossly, the tumors were either flat or slightly raised, forming low mounds. Only one lesion was polypoid and pedunculated. Basically, the lesions were characterized by various-sized solid nests of hyperchromatic oval- to spindle-shaped cells with the usual peripherally palisading and central haphazard arrangement. Almost without exception, in the tumor nests, there were irregularly placed larger and/or smaller foci of keratinization, at times forming small horny cysts and at times nearly filling the cytoplasm of cells, arranged in small whorls and resembling tiny pearls. Exag-geration of this process produced outspoken, large horny cysts. The pattern of keratinization forming the keratotic cyst was constant and striking. There was a whorled or laminated arrangement of the tumor cells about the central focus of keratin, producing a “cell-keratin complex” having an organoid appearance and resembling altered or abortive hair follicles. Frequently, within a single lesion the “cell-keratin complex” changes were such that a definite pattern was discernible and all stages of development, from small nests of keratin to fairly well-formed hair follicles, were easily seen (Figs. 1 and 2). In the rare lesion (only three) in which keratotic cysts could not be found, there was one or more foci within the tumors where the cells were larger than usual and had an increase of eosinophilic cytoplasm. These cells probably represented early keratotic changes and formed tiny pearl-like lesions mentioned above. Coarse pigment granules were commonly associated with, and in the centers of, the “cell-keratin complexes” (Fig. 3).

It was common to find the edge of the tumor cell nests extending around and apparently pinching off small portions of the stroma (Fig. 4). In approximately 10% of our series there was basophilic, myxoid change in the stromal inclusions within the tumor nests. In a few tumors the basophilic change was extensive, producing large pseudocystic spaces, thereby imparting an adenoidal appearance to the tumor (Figs. 5 and 6). In a few of the lesions there was an admixture of the more usual solid nests and the pseudocystic adenoidal form.

The tumors could be seen to arise from both the epidermis and the hair follicles. In our series there were no examples where the tumor was seen to arise from sweat
This process produced cutaneous cysts. The pattern of forming the keratotic cysts was striking. There was a laminated arrangement of the cysts about the central focus of the "cell-keratin complex" ganoid appearance and resembled abortive hair follicles. Within a single lesion the "cell-plex" changes were such that a pattern was discernible and all development, from small nests of early well-formed hair follicles, to a "cell-keratin complex" (Figs. 1 and 2). In the only three) in which keratotic features were not found, there was one or two in the tumors where the cells were less usual and had an increase in cytoplasm. These cells presented early keratotic changes and tiny pearl-like lesions mentioned above.

Coarse pigment granules were associated with, and in many, the "cell-keratin complexes" could be seen to arise from eccrine and the hair follicles. There were no examples where sweat glands were seen to arise from sweat glands.
Fig. 5 (upper left).—Pseudocystic adenoidal form of basal-cell epithelioma; $\times 100$.
Fig. 6 (upper right).—Pseudocystic form of basal-cell tumor showing varying degrees of degeneration of the stromal inclusions; $\times 450$.
Fig. 7 (lower left).—Nest of polyhedral cells with intercellular bridges in basal-cell epithelioma; $\times 100$.
Fig. 8 (lower right).—Area of pseudoepitheliomatous hyperplasia overlying basal-cell epithelioma; $\times 100$. 
Fig. 5 (upper left).—Pseudocystic adenoidal form of basal-cell epithelioma; $\times$ 100.
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Fig. 7 (lower left).—Nest of polyhedral cells with intercellular bridges in basal-cell epithelioma; $\times$ 100.
Fig. 8 (lower right).—Area of pseudoepitheliomatous hyperplasia overlying basal-cell epithelioma; $\times$ 100.

Fig. 9 (upper left).—Focus of calcification within nest of tumor cells; $\times$ 450.
Fig. 10 (upper right).—Portion of basal-cell epithelioma with large horny cyst and resembling hair; $\times$ 100.
Fig. 11 (lower left).—Epidermal germ buds in $\frac{3}{2}$-month fetus resembling superficial basal-cell tumor; $\times$ 100.
Fig. 12 (lower right).—Epidermal germ buds and early hair follicle in $\frac{3}{2}$-month fetus; $\times$ 100.
glands. In one case the tumor had its origin from an epidermal cyst.

We did not see intercellular bridges in the hematoxylin-and-eosin-stained sections of these tumors, except in one instance. In this lesion, which otherwise presented the usual solid nests of tumor cells, there was a single well-defined focus located at the deep aspect of the tumor, where the cells were abruptly changed into polyhedral cells with clearly defined intercellular bridges (Fig. 7).

The epidermis overlying the tumors was thinned or atrophic in the vast majority of cases, and in approximately one-half of these there was ulceration as well. The epidermis in the remaining lesions showed either no alteration or actual acanthosis, which at times was sufficiently pronounced to have the appearance of pseudoepitheliomatosus hyperplasia (Fig. 8). In general, the lesions were located in the upper half of the corium. A small number were of the superficial variety. In only two instances there was extensive penetration; in one case there was extension into and through cartilage of the ear, and in the second there was extension into underlying muscle. A mild to moderate inflammatory infiltrate, surrounding the tumor nests and composed principally of lymphocytes and plasma cells, was a rather common finding. In a few of the lesions the infiltrate was extensive, and in an additional few there was no inflammatory infiltration. Retraction of the nests of tumor cells from the surrounding stroma, as well as a basophilic appearance of the surrounding stroma, was frequently, though not invariably, seen. In four of the lesions there were well-developed foci of calcification within the tumor nests (Fig. 9). Two of the lesions had large areas of cystic necrosis within the neoplastic epithelial cell nests, giving the tumor a comedo appearance.

Comment

There was found, almost without exception, the presence of "cell-keratin complexes," which, while minimal in some lesions and hence when viewed singly could easily be unnoticed, when viewed collectively seemed clearly to show a tendency on the part of the cells in the basal-cell epithelioma to reproduce the pilar apparatus (Fig. 10). This was seen especially well in those tumors where all gradations between small and abortive keratotic nests and those nests which quite obviously were well-formed hair follicles were present. This is equally true in those tumors which were in continuity with the epidermis and had no apparent connection with the pilosebaceous apparatus or other skin appendages. It would seem reasonable to believe that there remain in the basal layer of the epidermis cells which are the anlage of the pilosebaceous structures, and that these could give rise to those basal-cell epitheliomas which are seen to be derived from the epidermis. Morphologically, there is a marked similarity between the primordial hair structures seen in the third- to-fourth-month fetus and the superficial, or intraepidermal, basal-cell epitheliomas (Figs. 11 and 12). Haythorn with silver stains demonstrated a similarity of the basement membrane around the basal-cell epithelioma and around the hair follicles. Though Montgomery questioned the value of silver stains in supporting the histogenesis of this tumor, preliminary studies in our laboratory, we feel, support Haythorn's observations. We hope to pursue this interesting facet in the future. If the basal-cell epithelioma were a tumor of undifferentiated basal cells, this would imply that it would pursue a more active biological course than the more differentiated squamous-cell carcinoma, whereas in most instances, as is well known, it actually does not.

Aside from morphological considerations, Lever and others have pointed to many interesting facts concerning the biological behavior of the basal-cell epithelioma which lend much support to appendageal origin of basal-cell epitheliomas. Lever points out that (1) basal-cell epitheliomas occur only in areas where skin appendages are present, i.e., the skin, with the exception of palms and soles (there are exceptions, however) and never from membrane epithelium; (2) basal-cell epitheliomas resemble primary epithelial structures seen in the third- to-fourth-month fetus; (3) presence in epitheliomas of differential structures such as hair follicles, sebaceous glands, signet cells, and trichoepithelioma; (4) basal-cell epitheliomas may be present with other adenomas such as nevus sebaceus, syringoma papilliferum, sebaceous cysts, or trichoepithelioma. Wallace and others feel that all basal-cell epitheliomas arise from hair follicles or hair anlage and suggest the designation of "trichoepithelioma" for these growths. We feel that our tumor does not support to this concept. Footprints are shown that those tumors with an adenoma pattern may have had their origin in eccrine sweat glands. However, an adenoma pattern in our series was apparent only when degeneration of stromal inclusion bodies occurred in these inclusions were followed by the development of the tumor, the edge of the tumor could be seen to surround small portions of these inclusions. The tumor cells, being at the center of the tumor, have the characteristic arrangement, which is maintained even when the process is completed. Stromal elements are apparent within the tumor nests. When the stromal elements are numerous, particularly when there is involvement of glandular structures, they may appear as though false. Teloh and West stated that definite evidence that basal-cell epitheliomas may originate from sebaceous glands was not seen in their series.

It seems striking that, though basal-cell epitheliomas arise from the skin, they are not seen on the palms or soles, lack pilar structures, and are not in the eccrine glands. There are rare exceptions, which prove the rule, and Ormsby and Sims have reported two cases where basal-cell epitheliomas were on the soles.

Ormsby and Montgomery found presence of squamous nests of epidermis.
and hence when viewed singly would be unnoticed, when viewed as a whole part of the cells in the basal-cell epithelioma to reproduce the pilar apparatus (Fig. 10). This was seen especially in those tumors where all gradations from small and abortive keratotic bases to those with more malignant features were present. The tumors with actual hair follicles were present in some cases. While acanthosis is commonly a feature of basal-cell epitheliomas of the skin, the absence of appreciable acanthosis in these tumors is of interest. The absence of basal-cell epitheliomas from the skin is a matter of degree and that the designation of basal-cell epithelioma should be restricted to those tumors with actual admixed basal-cell epithelioma and squamous-cell carcinoma, and that must be exceedingly rare.

**Summary**

In a review of 147 basal-cell epitheliomas, we found "keratin-cell complexes" in 144 and suggestive pearl formation in the remaining three. The general characteristics of these basal-cell tumors are described. The evidence for an appendageal origin of basal-cell epitheliomas is reviewed. It is our feeling that the presence of the keratin-cell complexes represents changes in the direction of the hair follicles and supports the origin of these tumors from either epidermal germ buds or hair anlage. We also feel that the diagnosis of basal-cell epithelioma should be restricted to those tumors with actual admixed basal-cell epithelioma and squamous-cell carcinoma, and that most of the tumors so designated are either examples of keratin-cell complexes of abortive hair follicles or squamous cells from...
areas of pseudopitheliomatous hyperplasia of the surrounding epidermis.

**BIBLIOGRAPHY**


Seabather's Eruption

JOHN S. STRAUSS, M.D., Philadelphia

Several reports of seabather's eruption have appeared since Sams' original description of this entity, but the causal relationship has not been definitely determined. Schistosome organisms have been considered to be the etiological agents. The causal relationship has not been beyond a doubt by recovery of schistosomes coincidentally with the clinical cases. During April and May approximately 75 persons were seen for a seabather's eruption following bathing in the area of Guantanamo Bay on the eastern shore of Cuba. The occurrence of seabather's eruption in this area has previously been described.

Clinical Studies

Almost all of the cases observed were bathing in the ocean at various locations on April 25, 1954. Sporadic cases were seen for the next three weeks. Only a small number of persons reported the occurrence of the eruption while in the water: the typical appearance of the lesions was seen usually 12 to 24 hours later. The lesions were follicular, and the lesions did not appear for several days. The characteristic site of the eruption was submitted for publication Oct. 22, 1954.

The personnel of the Tropical Medical Laboratory, U.S. Army, Fort Jum, Puerto Rico, performed the follow-up, serological tests, skin tests, etc.

From the Department of Dermatology, University of Pennsylvania School of Medicine. Fellow of the University of Pennsylvania School of Medicine, formerly Lieutenant (M. C.), U.S. Navy, attached to the U.S. Naval Base, Guantanamo Bay, Cuba.

* References 2 to 5.
† References 6 and 7.