BENIGN CALCIFIED EPITHELIOMA

BY

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[WITH SPECIAL PLATE]

Since Malherbe (1880) first gave an account of a circumscribed calcified lesion of the skin and named it "épithélioma calcifié" a number of papers have been published on this interesting condition. The more useful in the English language are Ch'in's (1933) comprehensive review of the world literature, and papers by Côté (1936), Highman and Ogden (1944), and King (1947), all in journals of pathology. The standard textbooks of general pathology make no reference to the condition, Willis (1948) alone giving a brief description and discussing its aetiology. Of the standard textbooks of surgery consulted only Aird (1949) mentions it, quoting Willis.

For this reason the lesion is rarely, if ever, recognized clinically, and yet it is not uncommon, as the following eleven cases show, ten occurring in 11,330 surgical specimens examined during 1943 to 1949 in the histological laboratory of a general hospital, and one found from the records of another hospital.

Clinical Findings

Analysis of the case records of the present series (see Table) reveals several characteristic features. The lesion

Table Showing Details of Cases

Case No.	Sex	Age	Site	Injury	Clinical Diagnosis	Viable Epith.	Calcification	Bone	Giant Cells	Pigment
1	F	7	Arm	+	Implantation dermoid fat necrosis	-	+	+	+	-
2	M	49	Leg	-	Fibroma	-	-	-	-	+
3	F	29	Neck	-	Calcified sebaceous cyst	-	+	+	+	-
4	F	14	Face	-	Calcified gland	+	+	-	+	+
5	F	60	"	-	Sebaceous cyst	+	+	-	+	+
6	F	7	Arm	-	"	+	+	-	+	-
7	M	65	"	-	Secondary "carcinoma"	-	+	+	-	-
8	M	19	"	+	Cyst	-	+	+	+	-
9	F	11	Face	+	"	-	+	-	+	-
10	F	24	"	+	Foreign body	-	+	-	+	-
11	F	63	Chest	-	Sebaceous cyst	+	+	-	+	-

may occur at all ages, the youngest in this series being 2½ years and the oldest 65, but half the cases were subjects under 20. This low age incidence has been noted previously, and may be of importance in considering the aetiology.

Females predominated over males in the proportion of 8 to 3, and four cases were girls under 14 years of age. In Côté's series, however, males were more common, and in those of Ch'in and of Highman and Ogden the sexes were equal. There does not appear to be any significance in the sex distribution, though Côté suggests that females may seek advice more often for cosmetic reasons.

Length of history varies from months to years and increase in size is slow. In three cases there was a history of injury some years previously. Pain was rarely complained of, and the tumour was removed for reasons of appearance or because of its uncertain nature.

The physical characters were constant. The lesion was a well-defined nodule in the subcutaneous tissue, varying from 5 to 25 mm. in diameter. It was usually described as hard or firm and when excised was finely nodular with a gritty cut surface (Fig. A). Attachment to the skin was commonly noted but never to the deeper structures.

The usual distribution was confirmed, the nodule occurring in five cases about the head and neck, four times on the arms, once on the leg, and once on the chest.

Diagnosis and Treatment

If these characteristics are borne in mind a confident diagnosis of benign calcified epithelioma should be possible, but it is not made because the condition is not sufficiently well known. Reading through the case records it can be seen that the clinicians were impressed by the two factors of hardness and attachment to skin. On these grounds the most frequently made diagnosis was calcified sebaceous cyst, usually preceded by several queries. Yet it is of interest that during the seven years under review only one specimen of this condition was submitted to microscopy.

In one case the lump was thought to be a secondary deposit from carcinoma of the bronchus and was removed for biopsy. Other diagnoses, usually tentative, were sequestration dermoid, foreign body, subcutaneous fat necrosis, and the ubiquitous fibroma.

Treatment is by surgical excision, usually under local anaesthesia, but a general anaesthetic will be necessary for a child. Recurrences have been reported, but these probably follow incomplete removal due to ignorance of the nature of the condition at the time of operation.

Histology

The cases here reported all showed in some degree the characteristic histological features previously described by other authors. Decalcification was usually necessary in the preparation of the material. Microscopical examination of the lesion showed in each case masses of epithelial cells surrounded by a well-defined fibrous capsule. The cells had undergone necrosis, their nuclei failing to stain, but still retained their faint cell outlines with "ghost" nuclei, a change sometimes termed mummification and the most typical feature of the condition (Plate, Fig. 1). There may be areas of viable epithelium, smaller in extent and sometimes absent altogether, which retain their normal staining reactions (Fig. 2).

Patchy calcification of the mummified epithelium is nearly always present in varying amount, but is not

FIG. A.—Cut surface of the tumour, showing patchy calcification.

essential to the diagnosis and was absent in Cases 2, 5, and 6. Ossification also occurs (Fig. 3), and was present in four cases in this series (Cases 1, 3, 7, and 8). A well-marked fibrous stroma is present in which foreign-body giant cells are a frequent occurrence. Melanin-like pigment was noted in Case 4 and has been recorded in previous series. In Case 2 eleidin granule pigment was demonstrated, and no previous references to this have been found in the literature.

Discussion

The essential feature of the lesion seems to be an encapsulated proliferation of epithelial cells, followed by their death. Calcification and later ossification can be considered as secondary changes apt to occur in any dead tissue. The result is easily recognized under the microscope, but the origin of the condition is obscure and many theories have been propounded.

Côté considers it to be a neoplasm of low malignancy, intermediate in type between a sebaceous cyst and a basal-celled carcinoma, founding his theory on the presence of mitotic figures and a supposed basal origin for the epithelium. This supposition is disputed, for in cases in which viable epithelium was present this appeared to be squamous-celled in origin. Confirmation was afforded in Case 5 by the presence of prickle cells and keratinization; in Case 2 eleidin granules were present, which normally occur in the stratum granulosum, and are further evidence of the squamous nature of the epithelial cells. No mitotic figures were noted in the present series. Moreover, it is unusual for sebaceous cysts or rodent ulcers to occur in the low age group of benign calcified epithelioma.

Highman and Ogden found brown pigment resembling melanin in three cases out of twelve, and suggested that the primary lesion is an epidermoid cyst arising from a hair follicle, with which pigment is often associated.

Willis regards the condition as being due to degenerative changes in the proliferating epithelium of a sebaceous or epidermoid cyst and does not think the lesion is a true tumour.

King differentiates two types—one derived from squamous cells proliferating in an epidermoid cyst, and the other, much less common, of basal cells with mitotic figures. In support of his first suggested form he found transitional types showing the characteristic changes of mummification occurring in an otherwise typical epidermoid cyst.

Epidermoid cysts may arise from epidermal cells implanted by injury, from sebaceous ducts or from hair follicles. The histological appearances in this series are consistent with an origin from such a cyst and do not support an origin from basal cells or indicate any neoplastic change. A history of trauma in three cases and the usual occurrence of the lesion in situations exposed to minor injury suggest that the cyst may sometimes be of the implantation variety.

Summary

Eleven new cases of benign calcified epithelioma are reported.

The clinical findings and histology are described.

The nature of the lesion is discussed and evidence presented in support of an origin from proliferation of squamous cells in an epidermoid cyst.

A plea is made for the wider recognition of a not uncommon skin condition.

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GLINSKI AND THE AETIOLOGY OF SIMMONDS'S DISEASE (HYPOPITUITARISM)

BY

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In studying the literature for early observations on lesions of the pituitary gland, Simonds (1922) referred to a German abstract of a paper by Glinski (1913b) in which two cases of post-partum necrosis of the pituitary were described; this abstract was later mentioned by Sheehan (1937). I was unsuccessful in tracing in this country the original Polish paper, but further references were kindly supplied me by Dr. J. J. Keevil, librarian keeper of the Royal College of Physicians of London. These papers, however, also could not be traced in this country. An approach was then made to the Director, Army Medical Library, Washington, D.C., and as a result three papers by Glinski, two of which are in Polish, have been traced (1913a, 1913c, 1913d), the microfilms of them seen, and translations made.

Glinski's Investigations

Glinski's papers provide most interesting reading, particularly when it is appreciated that they were written some 37 years ago. He drew attention to work which had been done on such properties of extracts of the posterior lobe of the pituitary as the production of increased arterial blood pressure, peripheral vasoconstriction, slowing of the pulse, contraction of smooth muscle, especially of the uterus and urinary bladder; and the lack of work done on the properties of anterior-lobe extracts. This he ascribed to the difficult procedure of obtaining extracts, and he warned against the danger of drawing conclusions from impure or contaminated extracts.

In other words, the extract of a gland was not necessarily the secretion of the gland. "In my opinion, therefore, we should not, at the present stage of our knowledge, overestimate the effects of the hypophysial extracts, and, in spite of many contradictory findings based on these investigations, I still regard the anterior glandular part of the pituitary as the active and more important division of the gland." He based his views on an extensive study of the anterior lobe, its "incomparably greater blood supply," and the

I. GILLILAND: KIMMELSTIEL-WILSON LESION

FIG. 1. — Kimmelstiel-Wilson lesion, Group 1. General picture. (H. & E. $\times 60$.)

FIG. 2. — One large and several small islands. (H. & E. $\times 173$.)

FIG. 3. — Both afferent and efferent arterioles are affected. (Periodic acid of Schiff. $\times 205$.)

FIG. 4. — Fatty changes. (Sudan IV. $\times 205$.)

FIG. 5. — Argentophil nodules. (Gordon and Sweet's modification of Wilder. $\times 205$.)

FIG. 6. — Arteriosclerotic kidney, Group 2. (H. & E. $\times 205$.)

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FIG. 1. — Mummification with "ghost" nuclei. ($\times 1,000$.)

FIG. 2. — Areas of viable epithelium. ($\times 400$.)

FIG. 3. — Bone formation. ($\times 400$.)