Squamous epithelium in the human thyroid gland

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SYNOPSIS Four cases are reported in each of which squamous epithelium was an incidental finding in surgically excised thyroid gland tissue. The occasional thyroid cyst lined throughout by squamous cells probably represents a persistent ultimo-branchial body, but the evidence indicates that the usual source of such cells in this gland is metaplasia of the follicular epithelium. An explanation is offered for the infrequency of this transformation in the thyroid, despite the frequent occurrence of the changes which predispose to epithelial metaplasia at other sites. There is no evidence to suggest that squamous cells arising in this gland by either of these means have any sinister significance.

Squamous epithelium was first described in a human thyroid gland by Nicholson (1922); he attributed this finding to metaplasia of the follicular epithelium induced by severe chronic inflammatory and fibrotic changes in the gland. Epithelial metaplasia occurs in response to altered function or at least as the result of altered environment (Boyd, 1961). Such conditions are a feature of many of the pathological states affecting the human thyroid; nevertheless, although it has been reported in some of these, squamous epithelium remains an unusual finding in this gland. Whilst metaplasia remains as a possible explanation for its presence (Wegelin, 1926; Jaffe, 1937; Klinck and Menk, 1951), there is evidence that such epithelium may represent a persistent vestigial remnant or congenital rest (Meeker, 1925; Goldberg and Harvey, 1956).

This paper records four cases in which clusters of squamous cells were an incidental finding in surgically excised thyroid tissue and discusses the factors determining their presence and their significance.

CASE REPORTS

CASE 1 A 56-year-old woman complained of a gradual loss of weight for two years and a diffuse goitre enlarging progressively for a year; the swelling first appeared on the left side after a severe cold and then slowly spread to include the right side, always being temporarily exacerbated by menstruation. She found increasing difficulty in keeping warm and had noticed slight exophthalmos, but there was no dyspnoea, dysphagia, hoarseness, or other symptom. Her mother and sister both had a goitre.

The two lobes, particularly the left, and the isthmus of the thyroid were enlarged, nodular and hard. Radio-iodine uptake studies were normal but serological anti-body tests were positive (ADT: +ve on second day; TCH: 1:250,000; CFT: 1:250). The provisional diagnosis was Hashimoto’s disease; a biopsy was taken from the right lobe with a wedge resection of the isthmus.

Histology Sections of the rock-hard, pale fawn tissue show abundant, interwoven, thick bands of hyaline collagen. Within the meshwork so formed there are dense foci of plasma cell and lymphocyte infiltration. Small numbers of tiny follicles in various stages of degeneration and solid clusters of epithelial cells lie amidst this infiltrate; occasionally the cells are of Askanazy type. Towards the periphery of some of these foci there are small groups of non-keratin-forming squamous cells (Figs. 1 and 2); an occasional cluster of similar cells is embedded in the collagen but there is no evidence of neoplasia.

CASE 2 A 43-year-old woman gave a history of one month for a slowly enlarging, firm, slightly mobile, solitary nodule at the lower pole of the left lobe of the thyroid. There were no other symptoms or signs and there was no family history of goitre. The nodule was excised for histological examination.

Histology The nodule, 1-6 cm. in all external diameters, includes an irregularly shaped degeneration cyst filled with turbid, brown fluid and bounded by a wall of varied thickness. It consists of occasional small foci of atrophic follicles embedded in a collagenous tissue infiltrated by moderate numbers of plasma cells, lymphocytes, and haemosiderin-laden macrophages. There are also larger groups of both small and moderate sized colloid-filled, follicles, some of which are undergoing degeneration; in an occasional follicle a cluster of squamous cells interrupts the usual cuboidal or flat cell lining with transition between the two types (Fig. 3). In addition a few similar clusters, some with keratin plugs, are embedded in the collagen but with no continuity between them and the degenerate cells lining the cavity of the cyst.
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FIG. 2. Case 1. Higher-power view of a group of squamous cells showing inter-cellular bridges but no keratin. Haematoxylin and eosin × 450.

FIG. 3. Case 2. A cluster of squamous cells forms part of the lining of a large, colloid-filled follicle. Haematoxylin and eosin × 325.
CASE 3 A 60-year-old woman gave a 20-year history of a tense swelling in the left lobe of the thyroid; during the last six months she had become increasingly agitated but the swelling had not changed its characteristics. There were no other symptoms or signs. The lesion was provisionally diagnosed as a cyst and a partial hemithyroidectomy performed.

**Histology** A multilocular cyst, $3.0 \times 3.0 \times 2.5$ cm, enclosed by a wall of irregular thickness, was embedded in normal thyroid tissue. The cavity is incompletely lined by epithelium, usually flat and non-secretory but here and there pseudostratified or squamous (Figs. 4 and 5). Substantial areas of the supporting wall are formed of dense collagen amidst which are atrophic follicles and occasional cholesterol deposits; elsewhere there are zones of loose connective tissue containing small and moderate sized, colloid-filled follicles lined by a single layer of flat cells (Fig. 4), and small numbers of chronic inflammatory cells.

A few small follicles almost devoid of colloid and partially lined by pseudostratified, but not squamous, epithelium are embedded in the collagen of the thinner parts of the cyst wall, but there is no continuity between this epithelium and that lining the cyst.

CASE 4 A 58-year-old man with a five-month history of progressively increasing hoarseness culminating in a total loss of voice was found to have a paralysed left vocal cord and a solitary, firm, almost immobile, nodule in the left lobe of the thyroid. There was no abnormality in the other systems. The nodule was suspected of being a carcinoma and a hemithyroidectomy was attempted.

**Histology** A unilocular cyst, approximately $3.5$ cm in all diameters, containing turbid yellow-red fluid was partially embedded in the posterior part of an otherwise normal left lobe of the thyroid. The cyst wall is composed of two zones each of uniform width (Fig. 6). The inner one is lined by a thin layer of squamous epithelium and includes numerous islets of squamous cells, some with a central plug of keratin, enmeshed in fibrous tissue infiltrated by small numbers of chronic inflammatory cells. There are no hair follicles or sweat glands nor is there any continuity between the islets and the cyst lining.

The outer zone of the wall consists of mature fibrous tissue containing clusters of atrophic follicles (Fig. 6); one area includes several moderate sized bundles of nerve fibres and a fragment of parathyroid tissue. There is no evidence of neoplasia.
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FIG. 6. Case 4. The cyst wall clearly divided into an inner and outer zone. A thin layer of squamous epithelium lines the cyst with islets of squamous cells enmeshed in fibrous tissue forming the inner zone. Haematoxylin and eosin × 70.

DISCUSSION

Squamous epithelium is undoubtedly an unusual finding in the human thyroid gland; these four cases are the only examples of this occurrence in over 1,200 consecutive thyroid biopsies examined in this laboratory, an infrequency supported by the literature. No other type of non-thyroid epithelium was found in this series.

Alterations in the conditions of life of the cells lining the thyroid follicles may result in metaplasia just as they do with epithelial cells at other sites, the transformation probably representing an adaptation to these changes. There is no evidence of disturbed function in any of the cases being reported, but the chronic inflammation and fibrosis present in all four would have produced an altered environment for small groups of follicular cells. Chronic inflammation and fibrosis are frequent findings in the abnormal thyroid; however, in addition to such antecedent factors, for epithelial metaplasia to occur it is necessary that while old cells degenerate, young and as yet not fully differentiated cells proliferate (Lubarsch, 1930). Degeneration of the follicular cells is not uncommon in disease of the thyroid, but the usually slow rate of cell turnover indicated by the rarity of mitoses, and the negligible uptake of tritiated thymidine in experimental animals, may make metaplasia of the follicular epithelium unlikely. It is of interest that in most of the reports of squamous change in this gland it is associated, as in case 1, with chronic thyroiditis, an abnormality in which foci of epithelial regeneration are occasionally found.

The vast majority of cysts in the thyroid arise by degeneration of the parenchyma and show no evidence of epithelial regeneration, either in their lining or wall. Nevertheless, the finding of occasional small foci of squamous cells in continuity with those of follicular type, as in cases 2 and 3, leaves no doubt that metaplasia can occur; in both cases the squamous epithelium lies on chronically inflamed collagenous tissue, whilst the immediately adjacent epithelial cells are less degenerate than those usually found in such cysts.

By contrast the features of case 4, in particular the almost complete lining of the cyst by squamous epithelium and the numerous islets of similar epithelium embedded in the inner zone of the wall, are similar to those seen in the thyroid cysts reported in a variety of animals (Badertscher, 1918; Mason, 1931; Van Dyke, 1943 and 1944) and in two human cases (Goldberg and Harvey, 1956). There is no indication of recognizable thyroid epithelium either in the lining or in the adjacent zone of the wall in this case; furthermore, the site of the cyst and the presence of parathyroid tissue and bundles of the recurrent laryngeal nerve in part of its wall support the suggestion that such a cyst originates in a remnant of the ultimo-branchial body. This structure usually disappears at an early stage in the development of the human thyroid (Kingsbury, 1939) but is believed to persist occasionally at the exact location where these cysts are found.

Primary squamous cell carcinoma of the thyroid is even more infrequent than the finding of squamous epithelium (Harcourt-Webster, 1965); with both categories the total number of recorded cases is insufficient to allow any definite conclusion on relationship, and there is no published evidence to support the opinion of Jaffé (1937) that epithelial metaplasia is the source of squamous cell carcinomas of the thyroid gland. Similarly, there is no justification for attaching any sinister significance to the finding of squamous epithelium in either chronically inflamed thyroid glands or their cysts.

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