TUMOUR OF THE PALM HAVING THE STRUCTURE OF A MIXED TUMOUR OF THE SALIVARY GLANDS

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The neoplasms most frequently arising in the glands adjacent to the mucosa of the face and neck have been designated as mixed tumours because of the complex epithelial and connective tissues of which they are composed. Tumours of this type are usually located in one of the large salivary glands, notably the parotid. They occur, also, in the small accessory salivary glands of the mouth, in the nasal fossae, the pharynx and nasopharynx, on the skin of the face, on the scalp, in the lacrimal glands and the tracheobronchial mucosa. Only a few such tumours located elsewhere than in the cephalic region have been recorded.

Kreibig has reported two cases in which growths having the structure of these salivary gland tumours were found elsewhere than in the head and neck. His first patient was a man thirty-eight years of age who, six years previous to hospital admission, had received a severe trauma to the anterior part of the tibia between the median and the lower third. At the point of injury there appeared a hard nodule, which was well encapsulated and increased progressively in size. At the time of examination it was as large as a hen’s egg. In Kreibig’s second case, that of a man thirty years of age, the tumour, the size of a hazelnut, had appeared three years previously on the proximal part of the forearm. In both instances the diagnosis was mixed tumour.

Tessman, quoted by Kreibig, described a tumour which he called a chondro-endothelio-myxoma, which would appear to be a mixed tumour. It had grown for four years on the back of the hand of a middle-aged woman.

Hirsch has reported a mixed tumour in a negress, thirty-eight years of age. The tumour, as large as an apple, arose in the connective tissue of the thigh, above the patella.

Vidari saw a tumour in the calf of the leg, in a man forty-eight years of age. It had been present from childhood and recently had assumed rapid growth. It was readily enucleated, and microscopically resembled a mixed tumour of the salivary glands.

Gaehtgens described a tumour which for two years had grown very slowly on the fourth finger of the right hand of a woman sixty years old. The growth was the size of a cherry, was well encapsulated, and multilobular. It was diagnosed histologically as a neoplasm presenting the structure of a mixed tumour of the salivary glands.

Scharla recently added another case to those mentioned above. In his patient, a woman thirty years of age, the tumor was located on the fifth finger.

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of the right hand. It was the size of a hazelnut, was hard, lobulated, well defined, and movable. One year after removal there had been no recurrence. Under the microscope the tumour was seen to be composed of connective tissue—myxoid and sarcomatoid—mingled with glandular or massive epithelial strands. It contained no cartilage.

Such mixed tumours of the salivary type—called heterotopic—are, as appears from this brief review, quite rare. It seemed of interest, therefore, to report a case recently studied and suggesting an origin which has not here-

![Cross-section of the tumour](image)

**Fig. 1. Cross-section of the tumour.**
Low magnification. Hemalum, erythrosine, saffron.

to before been mentioned for tumours of this type located in parts other than the cephalic region.

**Case Report**

A woman seventy-six years of age consulted Prof. B. G. Bourgeois (to whom we are indebted for the clinical notes) in October 1936, regarding a tumour of the left hand. The tumour was located in the hypothenar region and was the size of a pigeon's egg. It was covered with skin, was hard and resistant to pressure, and was attached to the deeper tissues. It had appeared ten years previously as a small subcutaneous nodule, which grew slowly but progressively. The tumour, which was well defined, was easily removed under local anesthesia. It was of a grey colour and of the consistency of gelatin. Its exact dimensions were $50 \times 45 \times 42$ mm. A year and a half after the operation there has been no recurrence.

*Histologic Description:* Under low magnification the tumour, which has been cut transversely to its long axis, is found to be oval and surrounded by a capsule which is fairly
thick on one side and thin on the other. At one point the capsule is missing, and the limits of the section are occupied by the tumour tissue itself.

Magnified to this degree, the tumour is seen to be of irregular structure. The greater part is made up of clear areas of varying dimensions, combined with darker zones which are either isolated or united one with another. The clear parts correspond with areas of a mucous substance, the darker ones with epithelial and connective tissues (Fig. 1).

We shall, first of all, describe the epithelial tissue and its different aspects, showing the relationship between the different types; secondly, we shall study the connective tissue and endeavour to explain the origin and the modifications of the fundamental or supporting substance.

(A) Epithelial Tissue: The first type of epithelial tissue, and the most familiar, is made up of malpighian strands, the cells of which are united by protoplasmic filaments; some of

![Fig. 2. Strand of Malpighian Cells United by Protoplasmic Filaments; Eleidin Granulations and Horny Cells (Hemalum, Erythrosine, Saffron)](image)

these become loaded with eleidin granulations and differentiate into typical squamous cells (Fig. 2). These malpighian strands extend in numerous directions, with foci of large oval cells slightly distorted by reciprocal pressure. These cells have an abundant homogeneous cytoplasm, sometimes red, again light blue with the trichrome (iron haematoxylin, ponceau-fuchsin, aniline blue) and light yellow with Mallory's phosphotungstic haematoxylin stain (Fig. 3). Similar cells are frequently found in mixed tumours of the salivary glands, where they have been given, by Masson and Peyron, the name of naeviform cells, on account of the resemblance they bear to cells of pigmented naevi. We have observed them also in tumours of the sweat glands.

Occasionally, in the centre of these naeviform areas, the cells flatten and arrange themselves concentrically, one over the other, around a narrow cavity, an arrangement recalling the intra-epidermal portion of the excretory ducts of the sweat glands.

Between these naeviform cells are sometimes found a few cellular bridges; more often
they are joined together by a coarsely fibrillar substance arranged in the manner of cement between the stones of a wall (Fig. 3). This substance is stained dark violet with Mallory's phosphotungstic haematoxylin, and yellow with ponceau fuchsin. It does not seem to be elastin because it fails to take Weigert's fuchselin stain. At many points, this interepithelial substance seems to liquefy and to transform itself into a mucoid substance which is stained with mucicarmine. The epithelial cells then detach themselves from one another and become round, thus meriting, by their appearance, the name of naeviform cells. These cells seem to represent an undifferentiated type of malpighian cell in which the protoplasmic bridges have degenerated into a mucoid substance.

The malpighian and naeviform areas are also in continuity, at several points, with strands of smaller cells which have a dense hyperchromatic nucleus and a clear, seemingly hollow cytoplasm. These cells at times occur in uniform areas, without definite cellular grouping. At other times they arrange themselves in narrow strands surrounding an area of typical malpighian cells (Fig. 4). This latter aspect closely resembles the hair sheath with its outer layer, rich in lipids and glycogen, surrounding the inner layer of flattened or polygonal cells. The clear cells which we have just described also show, with the scharlach R and Best's carmine, a cytoplasm loaded with fats and glycogen.

The whole area of epithelial tissue, heretofore described, may be designated as the malpighian and pileous region.

The second type of epithelial tissue is made up of glandular formations (Fig. 5), which are distant one from the other and resemble sweat-gland glomeruli. The cells are cubical or low cubical, and contain in their cytoplasm a substance which is stained pink by mucicarmine. Some of them have acidophilic granulations similar to those of the cells of apocrine glands. A few glandular cavities are filled with a dense homogenous secretion of a mucoid or colloid character. These glandular tubes are connected here and there with a few narrow tubes resembling excretory ducts.
Fig. 4. Malpighian and Pileous Formations (Laidlaw's Reticulin Stain, Ponceau-Fuchsine, Light Green)

Fig. 5. Glandular Formations (Hemalum, Erythrosine, Saffron)
Adjacent to these glandular formations and sometimes surrounding them are vast areas of clear cells containing in their cytoplasms a few glycogen granulations and a substance stained pink by mucicarmine. This mucoid substance, secreted by the cells, accumulates between them and separates them. At many points it becomes abundant and forms large pools of firm brittle mucus (Fig. 6), stained a deep red by mucicarmine. Throughout this mucus are scattered many mucinous epithelial cells, some of which degenerate and become pyknotic.

This second area of epithelial tissue may be designated as the glandular and muciparous region.

To summarize, it may be said that the epithelial areas of the tumour closely reproduce almost all of the epithelial tissues of the skin; malpighian epithelium with granular and squamous cells, pileous formations rich in lipids and glycogen; sweat-gland glomeruli and ducts. There is, in addition, a secretory character: the mucous secretion of certain epithelial elements, a phenomenon which is not found in the normal skin but is the appanage of the salivary glands, which, like the epithelia of the skin, are derived from the ectoderm.

(B) Connective Tissue: The connective tissue of the capsule is dense and rich in parallel collagen fibres. There are few fibroblasts. The vessels, arterioles and veins are also few in number. The capsule contains atrophied sweat-gland acini.

In the tumour itself the vessels are abundant. Most of them are in the form of large distended capillaries, surrounded by endothelial cells. There is evidently passive congestion in the circulatory system of the tumour.

The composition of the connective tissue of the tumour is variable. In the first place, it is represented by coarse and sinuous strands of collagen fibres, lacking in fibroblasts, but rich in elastic fibres which run from the capsule between the epithelial agglomerations. These strands no doubt represent old local connective tissue which has been buried and preserved in the tumour.
The connective tissue which surrounds the epithelial formations is almost devoid of fibroblasts and is reduced to a reticulinic and collagenous fundamental or supporting tissue. It is applied and adapted to the epithelial elements, with which it forms an ensemble which may be qualified as "organoid." This collagenous fundamental substance, contemporary with the tumour, but already old, like the tumour itself, thickens in certain places and at its edges comes in contact with oedematous areas with which, in sections stained by ordinary methods, it seems to have no relation. In reality, as is seen in sections treated with silver carbonate, the oedematous areas, rich in albumin, contain a dense network made up of delicate reticulin fibres which extend to the reticulin fibres enclosed within the periepithelial collagenous sheaths. There is, therefore, continuity between the fundamental substance which is adapted to the epithelial formations and the reticular felting of the oedematous areas. This continuity between older periepithelial collagenous substance and the more recent reticular felting is strikingly suggestive of the mode of formation and growth of the stroma of the tumour.

Into the midst of the oedema is precipitated a reticulin network, the fibres of which grow, thicken, and are transformed into collagen fibres. The reticulin and its transformation into collagen are well shown by Laidlaw’s silver method followed by Lumière’s green, the reticulin fibres being stained black and the collagen fibres green.

This fibrillar precipitation is also seen in the mucous areas, where, with ordinary stains, numerous epithelial cells appear free and naked. With silver carbonate each cell may be seen surrounded by a network of anastomosed fibres, bristling with outgrowing points, which seem to arise from the mucous substance (Fig. 7). There is probably a precipitation of the mucoid substance under the action of the secretion of the epithelial cells.

Another aspect of the fundamental substance or supporting tissue is represented in Fig. 8. Amid the mass of epithelial cells described above, which have a clear protoplasm containing mucus, are found narrow strands of fundamental substance, at times anastomosed and attached to the capsule, at others independent and with round or oval outlines. These strands are small, but irregular in size; they are completely devoid of fibroblasts and are
composed of fine fibrils. With silver carbonate followed by light green they are stained black and green in the centre. With mucicarmine the outer fibrils are stained rose, while those in the centre remain colourless. It would appear that around the collagen fibres there is a precipitation of fine reticulin fibres. At the periphery of the strand, the new reticulin fibres are argyrophile and mucicarminophile; when they are older and are, in turn, submerged by new fibres which appear at the periphery of the strand, they are transformed into green collagenous fibres. In fact, we have here a process which is identical with the one described in connection with the isolated cells in the mucus. In that case, there was a precipitation around epithelial cells; in this, the precipitation appears near the epithelial cells but around small collagen fibres. It is worthy of mention that in both cases the precipitation occurs in the presence of epithelial cells which secrete a mucoid substance. We have found these growing collagen strands, also, in sweat-gland tumours.

Still another type of fundamental substance appears in the form of cartilaginous nodules (Fig. 9), scattered over naeviform areas or near the mucus-secreting cells. These nodules are either isolated in the connective tissue or are in continuity with the epithelial masses. Their fundamental substance is composed of a dense felting of very fine fibrils which are revealed by silver carbonate but can be seen only under oil immersion. The larger fibrils form an irregular network that is stained violet with Weigert's fuchselin. The whole fibrillar substance, stained with mucicarmine followed by yellow metanil, varies from red to yellow, according to the quantity of mucine. This latter is especially seen around the cells, where it forms a halo in the pallial substance ("Chondrinballen").

The cells are round or oval; their cytoplasm contains mucine, which is either diffused in the protoplasm or clumped into irregular granulations. The glycogen is sometimes diffuse, sometimes accumulated at the periphery under the cellular membrane. It also contains lipidic granulations.

There can be no doubt as to the nature of the tissue just described; it is cartilage. But where does it come from? On examining the edges of some of these cartilaginous nodules, it may be seen that they are at several points attached to epithelial muciparous

FIG. 8. OUTGROWING STRANDS OF COLLAGEN AND RETICULIN, DEVOID OF FIBROBLASTS, IN LARGE AREA OF MUCINOUS CELLS (LAIDLAW'S RETICULIN STAIN, FUCHSIN, LIGHT GREEN)
masses, with which they are in direct continuity. Moreover, on passing from the epithelial parts towards the cartilage, it is seen that the epithelial cells are segregated by the mucus they secrete, and that there appear in the mucus, secondarily, fine fibrils of fundamental substance. This precipitation of fibrils in the mucus imprisons the epithelial cells, which assume progressively the character of cartilage cells (Fig. 10). The fibrillar fundamental substance subsequently becomes dense around the cells and forms the "Chondrinballen" which are rich in mucine. This precipitation occurs far from any connective tissue, in the absence of fibroblasts.

There is, therefore, a metaplasia of epithelial tissue into cartilage, in the presence of mucus which is secreted by the cells and into which is precipitated a chondrinic fundamental or supporting substance.

Finally, at the periphery of the large mucous areas mentioned above, fragments of collagen fibres immersed in the mucus reveal, at their edges, a dislocation, and, at the same time, an affiliation on the part of their fibres for mucicarmine.

**FIG. 9. TWO CARTILAGINOUS NODULES ENCLOSED IN THE CONNECTIVE TISSUE (HEMALUM, ERYTHROSINE, SAFFRON)**

To summarize our study on the fundamental substance, we may say that the collagenous substance, immersed in mucus, sometimes undergoes a dislocation and a mucous transformation. On the other hand, a new fundamental substance, reticular, collagenous, or chondrinic, is being formed in and between certain epithelial masses, surrounding glandular formations and isolated cells, and in the middle of oedematous areas. Most of the time, this production of fundamental substance occurs in the presence of mucus secreted by epithelial cells and in contact with these.

**DISCUSSION**

The authors mentioned at the beginning of this paper, who have reported cases of so-called heterotopic mixed tumours, quote the observation of Fischer-Wasels, who long ago described an adamantinoma of the tibia which he believed had its origin in an adamantine heterotopy.
Without taking a stand, Kreibig and Vidari express the opinion that heterotopy with salivary potentiality may give rise to a mixed tumour of the salivary type occurring elsewhere than in the cervico-facial region.

Gaehgtgens and Scharla also consider their mixed tumours as having a dys-embryoplastic origin. They explain the presence of the multiple connective tissues—myxoid, mucous and cartilaginous—by the morphogenetic action of the embryonic epithelium on preexisting local connective tissue. This is Spemann's theory of organizers applied to a dysgenetic tumour. Schumann, Pfluger and Norrenbrock have likewise attempted to explain the genesis of the various constituents of mixed tumours of the salivary glands.

It is not our intention to discuss here the different theories which have been advanced to explain the origin of mixed salivary gland tumours. Our purpose

![Fig. 10. Edges of an Epithelial Mass Being Transformed into Cartilage](image)

At the left the epithelial cells are segregated by mucus; at the right they are transformed into cartilage cells. High magnification. Hemalum, erythrosine, saffron.

is to endeavour to give an explanation of the various structural aspects of our tumour in the light of comparative oncology and of histophysiology, without recourse to the hypothesis of a misplaced embryonic salivary tissue. Such an explanation may aid in the understanding of the polymorphous aspects of mixed tumours of the salivary glands.

It is worthy of mention that most of the authors have recourse to the theory of the inclusion of embryonic cells or tissues to explain tumours which are paradoxical in their structure and location. For the most part it is the theory of inclusion that has been put forward for tumours resembling the one described above, and let us say here that it cannot be deliberately set aside. It still remains a theory, however, and one which is not particularly fruitful as regards the study of tumours.
It is no less logical to admit that our tumour has arisen from local epithelial elements, and that the various aspects of the fundamental substance result from the action of the secretion of the epithelial cells on the connective media.

There is nothing paradoxical as regards the various epithelial structures of our tumour. Malpighian areas with cellular bridges and horny cells, clumps of pileous arrangements, naeviform cells, and glandular masses may be found in certain carcinomas of the epidermis and in sweat-gland adenomas and carcinomas. All of these aspects represent several selective differentiations, which may be observed separately or together in tumours of the epidermis and its adnexa. Pathologists who have had the opportunity of studying sweat-gland adenomas are familiar with the epithelial polymorphism of these tumours. The polymorphism of cutaneous epithelial tumours recalls the great variety of tumours of the breast, a gland which also is a derivative of the ectoderm. This idea of multiple varieties of epithelial differentiation is familiar to those who make whole histological sections through carcinomas of the breast. In such sections are frequently found, in the same carcinoma, mingled areas of multiform glandular carcinoma, of atypical carcinoma, of papillary carcinoma with a more or less abundant stroma, according to location. It would seem that such polymorphism is one of the foremost characteristics of carcinomas arising from derivatives of the ectoderm.

We admit then freely that our tumours arise from a local epithelial element of the palm, most probably from a sweat-gland. Nor is mucous secretion a serious objection. Many carcinomas of the derivatives of the ectoderm secrete a mucous substance, as the cylindromas and mucoid carcinomas of the breast.

This mucous secretion brings us to consider the different aspects of the fundamental substance. The greater part of the tumour is made up of mucus. We have already seen that some of the epithelial cells contributed, by their secretion, to the accumulation of a mucous substance in the interstices of the cells. It is likely that this mucus does not invariably come from the epithelial cells. The imbibition by the mucus of the collagenous fibres, at certain points, seems to transform these gradually into a mucoid substance, which is added to the secreted mucus: the collagen fibres are dislocated in contact with the mucus, and are stained at their periphery by mucicarmine. These are the same structural and tinctorial modifications as are found in the cylindromas and in mucous carcinomas of the breast. The mucous substance would then have a double origin: epithelial and collagenous.

This mucous substance undergoes elsewhere, under unknown physicochemical conditions, in contact with epithelial cells, a precipitation under the form of reticulin fibres which later become collagenous.

It remains to explain the origin of the cartilaginous nodules. From the morphological standpoint, they are indisputably made up of cartilaginous tissue: the fundamental substance has all the characters of chondrin and the cells it contains have the structure and properties of cartilage cells. The point which has given rise to numerous controversies is the origin of that tissue which is so frequently found in mixed tumours of the salivary glands. Some are of the opinion that it is due to a metaplasia of the connective tissue, of the
FIG. 11. CARCINOMA OF THE BREAST WITH THE STRUCTURE OF A MIXED TUMOUR; LARGE EPITHELIAL MASSES SECRETING MUCUS AND UNDERGOING TRANSFORMATION INTO CARTILAGE (HEMALUM, ERYTHROSINE, SAFFRON)

FIG. 12. TUMOUR SHOWN IN FIG. 11 UNDER HIGHER MAGNIFICATION
At the left, in gray, is the connective tissue wall; at the right of the wall is the periphery of a carcinomatous mass progressively transformed into cartilage, to the right. Hemalum, erythrosine, saffron.
stroma of the tumour; others, on the contrary, believe that it represents an absolute metaplasia of the epithelial tissue into cartilage.

We have already described the transformation of the epithelial masses into cartilage. It must be emphasized here that there can be no question of invasion of the carcinomatous tissue by a common connective tissue which later becomes cartilage. The phenomenon of metaplasia begins in the absence of any fibroblast: the cartilage is only secondarily in contact with the connective tissue through its outgrowth. It is in the midst of epithelial masses, under the probable action of the mucous secretion of the epithelial cells, that the chondrinic substance appears and grows. The imprisoned epithelial cells are gradually transformed into cartilage cells.

This interpretation is identical with the one previously put forward by Masson and Peyron to explain the origin of cartilage tissues in mixed tumours of the salivary glands. It is contrary to the opinion of the advocates of cell specificity, but it rests on facts which are so evident that it cannot be ignored without having received serious study. Moreover, this metaplasia of epithelial tissue into cartilage belongs not only to mixed tumours of the salivary glands; it may be found also, occasionally, in carcinomas of the breast in women (cf. Schultz-Brauns: Die Mischgeschwülste der Brustdrüse in Henke and Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, vol. 7, part 2, pp. 351–352 and 396–398). A case in Professor Masson’s collection is of interest in this connection. A tumour removed from the upper right quadrant of the breast of a middle-aged woman was found to include two parts: one an atypical muciparous carcinoma; the other a chondroma made up of irregular nodules separated by common connective tissue. Between the carcinoma and the chondroma lay an intermediate area in which the carcinomatous masses were undergoing a cartilaginous transformation, beginning at the centre (Fig. 11). Certain regions in this growth are particularly revealing in that they show, in the same mass, that the cartilaginous tissue, which is located in the centre, is in direct continuity with the carcinomatous tissue located at the periphery (Fig. 12).

Similar facts may be observed in comparative oncology. It is known that in the bitch there frequently occur tumours of the breast (Peyron) containing cartilaginous nodules which have caused to be given to these lesions the name of mixed tumours. The mechanism of the production of cartilage is probably the same in our tumour, in mixed tumours of the breast (woman and bitch), and in mixed tumours of the salivary glands.

This epithelio-cartilaginous metaplasia is therefore not peculiar to mixed tumours of the salivary glands; it may occur in neoplasms of ectodermal derivatives and seems to be closely related to the mucous secretion of the epithelial cells. In fact, the mucous secretion, as has been shown by Guyon, appears to be an important if not indispensable phenomenon in the genesis of normal cartilage.

Other facts derived from embryology, such as the histology of the adamantine organ, the epithelial origin of the iris muscle and of the myoepithelial cells, the cartilaginous transformation of the notochord (Masson and Peyron), the neural crest origin of the branchial cartilages in Batrachians (Stone), the ectodermic origin of the mesectoderm, may all be compared with the epithelio-
cartilaginous metaplasia of the so-called mixed tumours in general. These facts of normal and experimental embryology contradict the old theories of specific and independent sheaths. They are to embryology what epithelio-cartilaginous metaplasia is to oncology.

The so-called mixed tumours arising from ectodermic derivatives should therefore be considered epithelial in their origin but mixed in their evolution, and it may not be necessary to have recourse to the theories of germ or cell inclusions to explain their origin.

A general idea comes out of our histological description and the facts of comparative oncology which we have cited: the presence of cartilage in epithelial tumours has a connection with the mucous secretion of the epithelial neoplastic cells, and seems to be determined by that secretion.

There are some tumours in which the cartilage is of mesenchymatous origin; they are the true dysembryoplastic tumours (gonadal, coccygeal, mediastinal, or cranial) which differ entirely from ours in their origin and composition.

SUMMARY AND CONCLUSIONS

A case is reported of a tumour of the palm having the structure of a mixed tumour of the salivary glands. From the histologic study, it would appear that the tumour may have a local origin, arising from the sweat glands. Epithelial at first, it acquired the structure of a mixed tumour through selective differentiations of the epithelial tissue, through modifications of its stroma and metaplasia of epithelial tissue into cartilage. These modifications and metaplasia appear to have some connection with the mucous secretion of the epithelial neoplastic cells.

BIBLIOGRAPHY