MYOBLASTOMA

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In 1926 Abrikossoff (1) described, under the name "Myoblastenmyome," several tumors of presumably myogenous derivation. Almost simultaneously Diss (2) and Keynes (3) reported single instances of identical tumors occurring in the tongue, as rhabdomyomas of a peculiar type. Subsequently a number of case reports and reviews have appeared indicating the increasing recognition given these neoplasms. A comprehensive survey of the still limited number of reported cases was published by Klemperer (4) in 1934, making a complete review of the literature here unnecessary.

We have had opportunity to study five tumors which answered the description of myoblastoma, the term now most commonly used. The clinical and histologic features of these cases closely resemble those observed and reported by others.

CASE I (Jewish Hospital, Surg. Path. No. 4719, Dr. M. G. Seelig): A white woman, thirty years old, noticed in the anterior portion of her tongue a tumor which had been growing slowly and painlessly for about five months until it had attained the size of a hazelnut. It appeared as a smooth, dome-shaped protrusion on the dorsum of the tongue underneath the intact mucosa. Upon section it was found to be embedded in the muscle. Its color was yellowish and its consistency firm and elastic. Microscopic section showed a nodular neoplasm developing in the uppermost layers of the muscularis and spreading into the submucosa. The tumor cells were large, polyhedral, slightly granular, well surrounded by a network of fine connective-tissue fibrils. Some of these cells appeared to fuse with the muscle fibers of the tongue. Tumor cells were particularly conspicuous in the papillary projections of the submucosa. Up to the present time, nine years after operation, there has been no recurrence.

CASE II (Jewish Hospital, Surg. Path. No. 9105, Dr. E. Fischel): A white male, thirty-five years old, had noticed a rather rapidly growing tumor on the left edge of his tongue for about six months. This patient suffered from allergic rhinitis and believed that he had bitten his tongue on several occasions during sneezing spells. The tumor measured about 6 mm. in diameter and was located in the submucosal layer. The mucosa appeared grayish but intact. The histologic findings were identical with those of Case I. No recurrence was observed within six years, although the tumor was excised with only a small margin.

CASE III (Jewish Hospital, Surg. Path. No. 13263, Dr. C. T. Eckert): A white female, fifty-five years old, complained of a tumor growing slowly and painlessly on the left side of her chest below the mammary fold. The skin was reddened over the tumor. The excised neoplasm measured about 15 mm. in diameter, was well encapsulated, very firm, grayish in color, and was located in the cutis layer. Microscopic examination revealed a fibrous capsule surrounding a growth composed of large cells with a poorly staining, coarsely granular cytoplasm. A network of fine connective-tissue fibrils was present, surrounding complexes of several cells rather than individual cells. There were no transitional cell forms and no striation was observed in any of the cells, which maintained a uniform appearance throughout the section. Fat stains were negative.

CASE IV (Jewish Hospital, Surg. Path. No. 13665, Dr. W. Bartlett): A white woman, thirty years old, complained of a tender, slightly elevated nodule, the size of a pea, which

1 Aided by an anonymous cancer research fund.
she had observed on her tongue for about a year and a half and which had remained without any definite change. The overlying mucosa was intact. Upon section a small yellowish, fairly well demarcated tumor was seen, and diagnosed grossly as myoblastoma. Microscopic examination showed, immediately below the mucosa, a nodular accumulation of large cells with a coarsely granular cytoplasm (Fig. 1). The arrangement of the connective-tissue fibers, the presence of spindle-shaped cells with striation, and the lack of a tumor capsule were features identical with those observed in Cases I and II (Fig. 2). This patient has been observed for three years since the operation and has remained free from recurrence.

CASE V (City Hospital, Surg. Path. No. 2396, Dr. H. Maas): Clinical details for this case are not available, except that the large, encapsulated tumor was removed from the breast of a white woman, in the Out-Patient Department. The tumor measured about 10 cm. in diameter, had a grayish color and a firm consistency. Microscopic examination showed a thin fibrous tissue capsule surrounding a neoplastic growth of polyhedral cells, which appeared to be identical with those found in the previous cases. The connective-tissue stroma arrangement was similar to that seen in Case III.

Myoblastomas, as exemplified by these specimens, are generally considered to be characterized by the following microscopic picture. Large polyhedral cells measuring between 20 and 60 micra, occasionally even more, predominate in a nodular neoplastic cell accumulation. Their cytoplasm stains only very faintly with eosin and contains coarse neutrophilic granules. Because of this cytoplasmic structure these cells may be mistaken for xanthoma cells, but the specific lipoid stains do not reveal the presence of fatty substances. The nuclei of the tumor cells are rather small, at least in comparison with the unusual dimensions of the cytoplasm, and, while not exactly uniform, never display the irregularity which one associates with malignancy. Surrounding the tumor cells, individually or groupwise, is a slender network of connective-tissue fibers, which may require a contrasting stain after Van
Gieson or Masson for better definition. There may or may not be a tumor capsule; if not, the tumor cells are sometimes seen to blend with the striated muscle fibers of the surrounding structure.

The sites of these tumors are widespread. The accompanying table summarizes the topographic data. It is condensed from the survey made by Klemperer (4), augmented by a few cases reported since. The 77 tumors here recorded occurred in 10 different locations, the tongue alone accounting for 44 per cent. Of the remaining tumors, those in the lip, jaw, vocal cord and upper esophagus could by some stretch of the imagination be considered related to the lingual tumors, because these organs, like the tongue, develop from the primitive oropharyngeal cavity and its surrounding branchial structures.

For the histogenesis of this supposedly new tumor entity more or less plausible explanations have been offered. The first observations of Abrikossoff, Diss, and Keynes were made on neoplasms of the tongue. In these particular tumors transitional cell forms linking the tumor cells with skeletal muscle fibers were quite regularly observed. Abrikossoff interpreted the tumor cells as juvenile muscle cells, believing that they resembled the primordial muscle elements found in the myotomes of embryos. He suggested that these cells develop in consequence of reparative regenerative tissue reactions, possibly following some mild trauma of the muscle fibers, and not, as the supposedly juvenile appearance of the cells might indicate, from persistent embryonal cell complexes.

A new issue was injected into the discussion of the etiology and nature of the myoblasts when Klinge (16) reported as myoblastomas a number of tumors of apparently similar cellular composition, but in locations devoid of
autochthonous striated muscle tissue. Abrikosoff (17) and others (see discussion following Klinge’s paper, 16) accepted Klinge’s tumors as myoblastomas. Obviously, the regenerative theory suggested by Abrikosoff could not be applied to them, however. Klinge found no difficulty in explaining these heterotopic myoblastomas on the lines of Cohnheim’s tumor theory, which Abrikossoff had mentioned in his original paper but had rejected. Taking the resemblance of the tumor cells to primordial muscle elements as proof of their embryonic nature, he explained their appearance in various odd sites by a dysontogenetic accident. During the early stage of development, the primordial muscle cells and the cells which later on form the connective-tissue layer of the skin lie together in two symmetrical and segmental cell cords along the spinal column, in the so-called myotomes. Subsequently, the cells destined to form the cutis migrate to the periphery, while the primordial muscle cells still remain for a certain time grouped around the spinal column. The appearance of myoblasts in the skin or mucosa may be explained by an incorrect separation of these two cell groups constituting the myotome, some muscle cells being included in those cell complexes which migrate to the periphery in order to form the corium.

Although Klinge’s theory has been generally accepted, we feel that his and to a certain extent Abrikossoff’s deductions are insufficiently supported by evidence.

The first debatable point seems to be the presumption that the various intracutaneous, submucous, intramuscular, and lingual tumors described as myoblastomas are oncologically identical. Such contention rests entirely on the similarity of the large granulated cells so conspicuously present in these different tumors, and implies that the tumors are really imperfect rhabdomyomas. Convincing evidence of their uniformly myogenous nature is, how-

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**Table I: Topographic Classification of Cases**

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<th>Author</th>
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<th>Lip</th>
<th>Alveolar process of maxilla</th>
<th>Mandible</th>
<th>Vocal cord</th>
<th>Upper esophagus</th>
<th>Breast</th>
<th>Skin</th>
<th>Subcutis of oral region</th>
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ever, lacking. Only in the lingual tumors have transitional cell forms been found which can be considered as proof of a relationship between the tumor cells and striated muscle fibers. Of the five tumors which furnished the material for Abrikossoff’s first publication, three were lingual tumors, of which two contained such transitional cell forms. Of the remaining two, one was located in the lip and one in the musculature of the calf. In neither of these were transitional cell forms or striated muscle fibers seen. While a myogenic origin was at least suggested for the tumor located in the gastrocnemius muscle on account of its location, no such circumstantial evidence could be adduced for the lip tumor, because it was neither surrounded by nor attached to muscle.

Histologic features indicating a rhabdomyomatous nature are likewise lacking in all of the tumors subsequently described as extralingual myoblastomas by various authors (Table I) who follow the precedent set by Abrikossof and Klinge. Only in a most indirect manner can a connection with rhabdomyomas be assumed, and then for but one type of extralingual myoblastoma, namely that of the maxilla. Before the introduction of the tumor genus myoblastoma, these maxillary new growths went under the term of congenital epulis of the newborn. Abrikossoff (17) Ceelen (18), Volkmann (19), and Meyer (20) claimed them for the myoblastoma group because of their large granular cells giving no reaction with lipid stains. They originate with a narrow pedicle from the alveolar process of the maxilla in the region of the incisor teeth and thus suggest a connection with the premaxillary anlage. Here, as in the other myoblastomas not located in the tongue, the occurrence of definitely rhabdomyomatous elements has not been ascertained.

Richter (21) described a tumor in an adult which developed from the tooth socket of the upper right central incisor, previously removed for infection. It had developed concentrically around the apex of the root and attained the size of a bean. Microscopically it consisted of a fibrillar and moderately cellular connective tissue and a scant layer of cross-striated muscle fibers in a more peripherally located stratum. No mention is made of any cells of the myoblast type. Even this tumor we do not believe furnishes satisfactory evidence for the myoblastoma theory of the congenital epulis. Its development after infection, its location at the apex of a root remnant and, furthermore, its lack of any cellular elements even remotely reminiscent of the myoblasts, are all unfavorable to an analogy with the congenital tumors. It is described in some detail, however, because it is the only instance known to us which could be regarded as a possible proof of the myogenous origin of the congenital epulis, and we wished to put on record our negative opinion concerning its theoretical significance for the histogenesis of these tumors in particular and the extralingual, heterotopic myoblastomas in general. It seems more probable that the cells of these epulis-like tumors are non-descript mesenchymal cells or histiocytes of unusual size, laden with products of the cellular metabolism. It would seem preferable to retain the non-committal term congenital epulis until the histogenesis is definitely established.

Because we consider unwarranted a histogenetic diagnosis based on some vague resemblance of cells which exhibit conspicuous degenerative changes, we have subsequently revised our views upon Cases III and V, described above
as heterotopic myoblastomas. It is true that the cells in Case V (Fig. 3) resemble to a certain extent those seen in the lingual tumors. Abrikossoff (17) and Meyer (20) have reported similar tumors of the breast as myoblastomas. In some of the sections from various parts of the large tumor, however, areas could be seen in which the arrangement of the stroma was slightly more suggestive of an adenoma than of a myoblastoma of the type encountered in the tongue. Occasionally even a mammary duct was found among the nodes of neoplastic cells, and at times the cellular arrangement was suggestive of tubules. Thus we gained the impression that this tumor may have developed from the glandular structures of the breast.

The relationship to the breast parenchyma was less definite in the smaller tumor (Case III), as ducts were only found close to the tumor capsule but not within the tumor itself; but the connective-tissue arrangement here too was somewhat indicative of an adenomatous growth because it encircled cell groups rather than the individual cells.

In contrast to the problematic histogenesis of many of these tumors, the myogenous nature of the cells in the lingual tumors is usually quite patent. Indeed, here the transition between tumor cells and muscle fibers is so impressive that quite a number of them have probably been recognized as myogenic neoplasms before reports of myoblastomas or myoblastenmyomas appeared in the literature. Our Case I, for instance, was diagnosed as rhabdomyoma in 1926. The usual interpretation of the sequence of cellular transition has been that the myoblasts, in their capacity of juvenile cells, attempt to develop into mature muscle fibers. The details of the microscopic picture, however, do not indicate such evolution. There is no evidence that the tumor cells produce muscle fibers or their precursors. On the contrary, one can ob-

![Figure 3. Case V: A Characteristic Section of the Mammary Tumor Showing the Large Granulated Cells in an Arrangement Suggestive of Glandular Tubules](image)

In the right upper part of the field is a duct. Hematoxylin and eosin stain. × 100
serve that the granulated cells issue from fully developed, usually large muscle fibers located in the normal stratum of the muscular tissue and forming an integral part of the same. Towards the periphery of the neoplasia, i.e., where the cells have infiltrated into the subepithelial papillary projections of the submucosa, no muscle fibers nor transitional cells are ever seen. The characteristic fibrils with their cross- striations appear abruptly and fully developed within some of the tumor cells; no pre-stages nor cytoplasmic aggregations initiating the structural differentiation of the contractile substance can be found. It is reasonable, therefore, to conclude that the tumor cells originate from mature muscle cells, but do not develop into such.

The proliferation of the tumor cells remains unexplained, but it seems that it is preceded by a dedifferentiation of the sarcoplasm. This process may perhaps be pictured as a disturbance in the equilibrium between the contractile substance in the central portion and the trophic protoplasm on the surface of the muscle fibers. The reactivation of the non-contractile outer layer, its increase and the subdivision of this syncytium into individual cells are often observed after injury to muscle fibers. Admittedly, the cells in the lingual tumors cannot be considered identical with the newly formed cells in the reparative stages following traumatic, toxic, or infectious damage. Moreover, the cell formation in the myoblastomas is definitely a neoplastic process which, according to an observation of v. Meyenburg (22), may even progress to malignancy. In v. Meyenburg’s case a recurrence appeared after the removal of what was considered to be a typical myoblastoma of the tongue and became locally destructive with erosion of the blood vessels in the floor of the mouth. The comparison of the microscopic sections showed that the cells had later

**Fig. 4. Section from a Case of Circumscribed Hypertrophy of the Lingual Submucosa**

In the center of the section several muscle fibers are seen in the stage of granular dystrophy. Hematoxylin and eosin stain. × 250.
on assumed a malignant character as reflected in the polymorphism and size of their nuclei.2

On the other hand, degenerative changes of muscle fibers may occur with little or no concomitant cell proliferation. Heurtaux (24) described such findings in a small tumefaction removed from the surface of the tongue, and we observed similar changes on two occasions. One of our specimens was a protrusion 5 mm. in diameter, resembling a hypertrophic papilla, removed (by Dr. E. L. Keyes) from the edge of the tongue. Microscopically we found, besides localized edema and hypertrophy of the submucosa, several swollen and opaque muscle fibers. In a few places the eosinophilic sarcoplasm was replaced by a very lightly staining and coarsely granular cytoplasm. Here the cell borders became distinctly demarcated (Fig. 4).

Granular degeneration of this type is by no means common in the tongue. We could discover only one other instance in a series of 20 specimens of carcinomas and simple ulcerations. In this case the main pathology was a non-specific ulceration. The granular muscle degeneration and subdivision into cells were found in a limited area only (Fig. 5). Definite myoblastomatous cell proliferations were not encountered in this series, although some authors have reported squamous-cell carcinomas of the tongue associated with myoblastoma.

We are inclined to believe that granular degeneration of the muscle fibers in the tongue is of rather infrequent occurrence and that the neoplasia of large granular cells, conventionally called myoblasts, is in a yet undetermined manner related to this process.

The degenerative aspects of the histologic picture in the lingual tumors must have impressed Roffo (5), who, apparently not acquainted with Abrikossoff's publication, described a typical case of so-called myoblastoma as "nodular myolysis of the tongue." Meyer (20) likewise considered a degenerative process in the muscle fibers etiologically implicated in the lingual myoblastomas.

These observations point towards an etiology of the lingual tumors which does not pertain to the other myoblastomas. Abrikossoff, too, was reluctant to abandon his traumatic theory of the tumors of the tongue after Klinge had suggested a common dysontogenetic etiology for the enlarged scope of intramuscular and heterotopic myoblastomas. Gander (8) likewise favored a traumatic explanation for the lingual tumors while relegating the dysontogenetic explanation to the other myoblastomas.

We believe that much of Klinge's theorization could have been spared and possibly a confusion in tumor classification avoided if he had not so readily accepted Abrikossof's comparison of the tumor cells with embryonic myoblasts. Abrikossoff based his analogy on the description of the development of muscle tissue in the embryo by Godlewski (25), but perusing this reference we were by no means impressed by this supposed resemblance. Furthermore, the studies of myogenesis by Zechel (26), Franz (27), and Marcus (28) make no reference to granular polyhedral cells which could be compared with the tumor cells. We have also tried to discover Abrikossoff's myoblastoma

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2 Morpurgo (23) attempted to produce myoblastomas of the tongue in rats by injecting tobacco extracts. In 1 out of 10 rats a tumor supposedly resembling this malignant myoblastoma developed nineteen days after the first and three days after the third injection.
cells in serial sections of human and laboratory animal embryos, but were unable to recognize anything suggestive of such cell forms.

If we agree that embryonal or primordial muscle cells do not look like the tumor cells, then the designation of the latter as myoblasts is untenable. We believe that no conclusion concerning their origin can be made from their appearance and that their histogenesis must be established in the individual tumor from a demonstrable relationship to parental cells. For the cells in the lingual tumors, this may be convincingly done; for the other two tumors reported here, degenerated glandular epithelium must be considered as the most likely parent tissue in one case, and perhaps in both. In general, one can say that in the so called myoblastomas the cells look engorged and encumbered with products of cell katabolism rather than juvenile and fast-growing. Such description agrees with clinical experience, for myoblastomas are slow-growing or stationary tumors, while tumors containing immature striated muscle cells are generally of a high degree of malignancy. The one malignant recurrence recorded by v. Meyenburg is possibly an exception, or this particular tumor was really a malignant neoplasm originally, a rhabdomyosarcoma.

Conclusions

Under the term myoblastoma, a number of tumors have been described composed of large polyhedral cells with a coarsely granular cytoplasm.

Because of the presumed resemblance to embryonal skeletal muscle, the histogenesis of these tumors was considered established. This comparison, however, seems to be unwarranted, and therefore the term myoblastoma should be discarded for this tumor group.

Many so called myoblastomas occur in the tongue. In these tumors the

![Figure 5. Section from a case of non-specific ulceration of the tongue.](image-url)

In the center two muscle fibers are seen with granular cytoplasm and increased number of peripherally located nuclei. Hematoxylin and eosin stain. × 500.
myogenous nature of the tumor cells can be ascertained; however, they do not impress one as immature muscle cells, but as cells that develop from muscle fibers undergoing necrobiotic changes.

The myogenous derivation of non-lingual myoblastomas is questioned.

Bibliography