MALIGNANT MIXED TUMOR OF THE THYROID GLAND WITH SKELETAL MUSCLE FIBERS

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Malignant tumors with an intimate mixture of cellular components from two germ layers, such as epithelium and mesothelium, in varying proportions, are of special interest because of their rarity, and because their tissues contain surprising and bizarre combinations of cell structures. Such tumors originating in the thyroid gland, in the mammary gland, and elsewhere, have been reported as carcinosarcomas (Mason and Wells; Küchens; Saltykow). Wegelin’s recent review of these tumors of the thyroid mentioned only a few, and the structure of these varied considerably. Antedating Wegelin’s review by several years was the report by Schuppisser in which he stated, as have others, that true carcinosarcomas of the thyroid are rare. He mentioned the two tumors reported by Förster, those reported by Kocher, Jr., Simmonds, Albrecht, and Schmorl, and one in a dog reported by Wells. These summarizing statements and those in the recent account by Mason and Wells indicate how few indeed are the reports of malignant mixed cell tumors of the thyroid.

The variations in histologic structure seem to depend upon the degree of differentiation of the epithelial and mesothelial tissues and the proportion of each entering into the composition of the primary growth and its metastases. Some of the accounts report a fairly complete separation of the tissue derivatives in the primary growth, in the recurrence, or in the metastases, so that in these various places elements of only one of the two germ layers were found.

The co-existence of tissues from two germ layers, such as epithelium in tubules and osseous tissues, has established clearly the mixed tissue composition of some of the tumors, but this security does not exist, as Woglom and Mason and Wells have stated, when the mesoblastic components have attained only the differentiation of spindle cells. Cartilage and bone are the only complex mesoblastic tissues that have been described either in
the malignant mixed cell tumors or sarcomas of the thyroid. There seems to be no record, as yet, of a malignant thyroid tumor with mesoblastic tissues having skeletal muscle characteristics, although certain teratomas (Koerner)—tumors not considered in my report—have contained smooth and striated muscle tissues, a circumstance which suggests displacement of muscle elements into the thyroid gland.

There is the possibility, if only speculative, that some of the large spindle cells described in certain reports of mixed cell tumors of the thyroid were myogenic, and that such cell qualities could have been demonstrated by suitable staining procedures. Koehler, for example, described a tumor of the thyroid the structure of which in the primary growth and in the metastases resembled closely that of the tumor described in my report except that the large spindle cells of his tumor were not described as having cross striations although cells with glycogen were abundant. The tumor of my report and the metastases, as the succeeding paragraphs relate, had spindle cells with the staining reactions of myoglia; the longitudinal fibrils of the individual cells were mottled by alternating light and dark bands, and had all the minute details of embryonic skeletal muscle structure, even to the narrow Krause's membrane in the light bands.

H. N., a white man, aged twenty-one years, unmarried, an electrician by occupation, entered the service of Dr. S. C. Plummer under the care of Dr. H. I. Meyers at St. Luke's Hospital, December 2, 1929, because of an enlargement of the thyroid gland and cervical lymph nodes during the five months preceding his entrance. He also complained of pain and numbness of the left leg, of a loss of seventeen pounds in weight, and of insomnia of a month's duration.

The notes of the physical examination record a symmetrically enlarged thyroid gland, the right lobe hard and irregular; paresthesia of the left leg from the hip to the toes; markedly enlarged cervical lymph nodes, smaller axillary and inguinal lymph nodes; and absent left knee and Achilles tendon reflexes. The urine on December 3, 1929, contained 10 mg. of albumin per 100 c.c., a few hyaline and granular casts, and 25 to 30 leukocytes per high-power field. The hemoglobin of the blood was 70 per cent (Sahli), the red blood cells 3,620,000, and the leukocytes 9,350 per c.mm. These constituents of the blood changed by December 28, 1929, to hemoglobin 34 per cent, red blood cells 1,900,000 and leukocytes 10,100 per c.mm.

On December 11, 1929, Dr. Meyers removed the left lobe of the thyroid gland and a cervical lymph node, and on December 20, the markedly enlarged lymph nodes of the left axilla. The roentgen examinations on February 10, 1930, by Dr. E. L. Jenkinson, demonstrated a
metastatic growth in the lower third of the left ulna, many metastases of the lungs, and metastases of the sacro-iliac regions and of the right ilium. The patient lapsed into a lingering illness, the left arm became markedly edematous, ascites and hydrothorax developed, small metastases appeared in many parts of the skin, and death occurred at 1:45 A.M. February 25, 1930. The details of the examinations of the tissues removed by Dr. Meyers are recorded with the histological report of the tissues obtained by the post-mortem examination.

The post-mortem examination was started seven hours after death, and was limited to the tissues of the neck and trunk. The essential portions of the anatomic diagnosis are: primary malignant mixed tumor of the thyroid gland; marked tumor tissue compression of the esophagus and trachea; multiple metastases of the myocardium, cervical and tracheobronchial lymph nodes, sternum, parietal pleura, lungs, aortic lymph nodes, left suprarenal gland, pancreas, left testis, left ulna, peritoneum, and the skin; anasarca of the left arm; bilateral hydrothorax; bilateral hypostatic hyperemia and edema of the lungs; acute catarrhal bronchitis and tracheitis; marked diminution of the lipoid substance of the cortices of the suprarenal glands; cloudy swelling and fatty changes of the kidneys and liver; hyperplasia of the spleen; healed thyroidectomy scar of the neck; healed surgical scar of the left axilla.

Excerpts from the essential portions of the post-mortem record follow. The emaciated body of this young white man weighed 113½ pounds and was 176 cm. long. There was a nodose thickening of the front and sides of the neck so that it was 38 cm. in circumference at the level of the thyroid gland. The width of the neck was 11.8 cm., and the thickness, 11.8 cm. The nodular enlargement on both sides of the neck extended from the angles of the jaw to the clavicles, had a length of 10 cm., a width of 7 cm., and protruded 2.5 to 3 cm. A similar thickening extended across the midline just below the laryngeal cartilage, and in the skin of the neck 2.5 cm. above the clavicles was a curved thyroidectomy scar. The left arm was markedly edematous and in the anterior fold of the left axilla, equally on the arm and chest, was a narrow curved and puckered surgical scar 12 cm. long. There were many flat, slightly elevated thickenings about 1 cm. in diameter in the skin of the upper parts of the trunk, involving about 10 per cent of the surfaces, and more numerous on the chest than on the abdomen.

The sternocleidomastoid and other superficial muscles of the ventral portion of the neck were anterior to the nodular masses. After these muscles had been reflected, there was a nodular mass of tough white fibrous-like tissue, 14 cm. wide and 11 cm. long, that encircled the upper part of the trachea and the structures of both carotid sheaths. It was closely adherent to the trachea and extended around on both sides so as to compress the esophagus. Under the lining of the upper part of the esophagus were a number of tumor masses as large as 3.5 cm. that markedly narrowed the lumen. Enlarged cervical lymph nodes extended on the right side to the base of the cranium, on the left only to the angle of the jaw. Those on the left side were smaller than those on the right.
By block dissection a mass of tissue 12 cm. long was removed which included the upper part of the esophagus and trachea and the larynx. The trachea was opened dorsally and the lining was smooth. The firm tissue in front of the trachea was 4 cm. thick, and on surfaces made by cutting it was tough and white with interlacing fibrillar markings and whorls, resembling much the appearance of fibromyoma tissues. There was no red-brown lobulated thyroid tissue. The lumen of the trachea was narrowed by compression. The right axillary lymph nodes were not enlarged. The tissues of the left axilla were chiefly fibrous, containing a pocket 5 to 7 cm. long and 2 to 3 cm. in diameter filled with a clear yellow fluid. Under the peritoneum of the bowel were a few small tumor metastases. The enlarged spleen weighed 460 grams. The mesenteric lymph nodes and the groin lymph nodes were small. The right pleural space contained 1,450 grams of a clear yellow fluid, the left, 1,930 grams. A tumor metastasis 5 by 3 by 0.5 cm. in diameter had destroyed the upper part of the body of the sternum; another 4 by 3 by 0.7 cm. had destroyed much of the manubrium. The clear yellow pericardial fluid weighed 220 grams. On the ventral surface of the right ventricle of the heart there were several flat and slightly rounded, pearly-white metastases distributed about the root of the pulmonary artery, 20, 12, and 11 mm. in diameter. Another toward the apex on the right side was 18 mm. in diameter, a fifth near the apex and the septum was 13 mm., several on the outside of the left ventricle were 10, 7, and 8 mm. in diameter, and a number of others were only several millimeters in diameter. The peritracheal and peribronchial lymph nodes were markedly enlarged. They contained firm white tissue blackened with carbon.

Evisceration of the trunk disclosed extensive subpleural metastases on both sides of the spine that formed confluent nodules of moderately firm white tissue which were more abundant and thicker in the upper part of the chest, extended from the spine laterally 10 to 20 cm., and were larger on the right side than on the left. The periaortic lymph nodes contained an abundance of similar tissues. There were many flat subpleural and a few visceral nodules of the lungs ranging from 1 to 10 mm. in diameter. Several tumor metastases as large as 9 mm. in diameter were found under the endocardium of the left ventricle of the heart. There were a few small nodules in the medulla of the left suprarenal gland and a large mass 5 by 4 by 3 cm. in the head of the pancreas, which markedly compressed the duct. There was a second mass 3 cm. in diameter in the tail of the pancreas. A small tumor metastasis 1 cm. in diameter was found in the body of the left testis, and another 8 cm. from the distal end of the left ulna involved the medial tissues of the bone for a length of 6 cm. and extended into the soft parts between the ulna and radius to form a mass 2 cm. wide and 4 cm. thick.

While the examination of other parts of the body, especially the osseous system and the head, was desirable, these procedures were not undertaken because of the restrictions imposed by relatives in consenting to the post-mortem examination.
Histology

Left lobe of the thyroid gland removed surgically: This pyriform mass 6.5 cm. long and 4.5 by 4 cm., weighed 55.8 grams. The external surface had a fibrous capsule except one side, 4 by 4 cm., which was rough and granular as though torn from a closely adherent structure. The four broad surfaces made by cutting twice through the long dimension of the mass were chiefly tough, opaque, white, lobulated tissues marked by a number of slender yellow lines like a filigree. The edges were slightly scalloped, and along one side was a narrow margin of pink and white, finely lobulated thyroid tissue 6 mm. wide. The histologic preparations of the thyroid were those of a gland markedly infiltrated by a complex growth of tumor tissue, in which only small focal aggregates of acinar structures had survived. These acini were medium and small, they had a low cuboidal or a flattened epithelial lining, and usually the lumen contained a dense mass of colloid. Together they formed only a small part of the tissues in the histologic preparations.

The complex infiltrated tumor tissues, because of the marked variations in the proportion and character of the cellular units and the stroma comprising them, differed in minute detail in almost every square millimeter examined. The tumor tissues consisted of: (1) many undifferentiated cells, 10 to 12 microns in diameter, with a scanty acidophilic cytoplasm and a large oval or indented vesicular nucleus containing chromatin granules arranged on a fine nuclear reticulum with wide
meshes (Fig. 1); (2) large (180 by 10 microns) and small (50 by 10 microns) spindle-shaped cells also with an acidophilic cytoplasm and one or several vesicular nuclei aggregated or distributed at intervals (Figs. 2 and 3); and (3) multinucleated fused-cell aggregates resembling giant cells and also varying markedly in size (25 to 170 microns in maximum diameter) and shape (Fig. 4). The large spindle cells in sections stained with phosphotungstic acid-hematoxylin had the purple staining qualities of myoglia cells and in them were longitudinal fibrils, many with the alternating light and dark bands of embryonic skeletal muscle fibers (Fig. 3). Some of the large fused-cell aggregates in the sections stained by this method had a thin capsular or ectoplasmic membrane with the

![Fig. 2. Photomicrograph Showing the Spindle-shaped Cells. × 212](image)

orange-red quality of collagen connective tissue or this mixed with the purple component. Closely arranged on the inside of this capsule were flattened cell-like structures resembling the lining of acini (Fig. 5). The central portions, not separated from the cell-like elements and corresponding to the lumen of an acinus, contained a granular purple substance with several nuclei. Other structures of this kind had many nuclei much less regularly arranged, and in the cytoplasm were large vacuoles and even hyaline inclusions staining like the colloid of the thyroid acini. The conclusion that some of these multinucleated masses were abortive acinar structures of the thyroid gland was confused by the possibility that they were foreign-body giant cells formed about inert colloid or hyaline substances of necrotic thyroid tissues. For this
FIG. 3. Photomicrograph of a Spindle-shaped Cell with the Cross Striation of Skeletal Muscle Fibers. × 1650

FIG. 4. Photomicrograph showing Abundance of Fused-cell Aggregates in Portions of Primary Tumor and Metastases. × 212
reason the study of these fused-cell aggregates in the lymph node metastases is simpler.

_Tissues of left axilla removed surgically:_ The irregular mass, 11.5 by 6.5 by 3.5 cm., consisted of fibrous and fat tissues and markedly enlarged lymph nodes, the latter comprising about four-fifths of the bulk. The lymph nodes were discrete; the largest was 4 cm. in diameter, and the surfaces made by cutting were opaque, firm, white tissue with small regions of necrosis. Another mass of lymph node tissues 3.5 by 3 by 1.7 cm. resembled in essential details those first mentioned. The lymph node structures were entirely replaced by a growth of fibrous and tumor tissues. Those portions with tumor had thick septums of collagen connective tissue forming the boundaries of alveolar masses of tumor cells. These alveolar units varied in size to as much as 1 mm. in diameter, and they contained many compactly arranged undifferentiated cells of the variety designated (1) in the description of the thyroid gland, supported by a scanty fibrous stroma. Along the edges of these alveolar masses, in their septal walls, or traversing them at different angles, were spindle cells staining as myoglia, some with cross striations. Fused-cell aggre-

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**Fig. 5. Photomicrograph showing the arrangement of the nuclei along the periphery of the fused-cell aggregates, which, with other details, suggest an attempted differentiation into acini of the thyroid gland. × 850**
gates resembling giant cells occurred in different places and without regularity. A large one had a maximum diameter of 170 microns. The nuclei in this irregular mass were distributed without order in the central and peripheral portions. Many of these cell masses, however, were oval, had a narrow ectoplasmic membrane which contrasted with the central granular portions, and just within the membrane were nuclei in close peripheral arrangement, discontinuously scattered, or distributed in the cytoplasm in aggregates without regular order. The diameter of many of these cells was 80 to 100 microns, of others in the undifferentiated tissue it was 20 to 25 microns and these had only 1 to 4 nuclei. Others formed a gradual transition series to the large forms mentioned, and varied markedly in size and in the number of their nuclei.

The tissues of chief interest among those selected for histologic study during the post-mortem examination were from the region of the thyroid gland, and those with tumor metastases, namely: the heart, lungs, lymph nodes (cervical, mesenteric, periaortic, cecal, peribronchial), bone marrow, left testis, left forearm, skin, pancreas, and peritoneum. The tissues of the thyroid gland were in all essentials like those removed surgically by Dr. Meyers, and a repetition of description is, therefore, unnecessary. The tumor tissues in all of the metastatic growths consisted of undifferentiated cells, spindle cells, and fused-cell aggregates resembling giant

![Fig. 6. Spindle Cell in a Small Subperitoneal Metastasis. × 3200](image-url)
cells, in varying proportions. The small metastases, and even some of
the larger, were chiefly masses of the undifferentiated cells, but careful
search invariably demonstrated at least a few of the other two cellular
elements. Sections of the mesenteric lymph nodes, abdominal periaortic
lymph nodes, cecal lymph nodes, and peritoneal metastases were stained
with phosphotungstic acid-hematoxylin, and all contained spindle cells
varying in length and having longitudinal fibrils with cross striations like
embryonal skeletal muscle fibers. These spindle and band-like cells in
certain parts of the lymph nodes were interwoven loosely in all directions.
The repetition of the minute details of skeletal muscle fibers was remark­
able in some of these metastases, for in a peritoneal metastasis there were
spindle cells with fine transverse dark lines in the light bands—histologic
structures corresponding to Krause’s membranes (Fig. 6).

The microscopic examination of tissues from the esophagus, sub­
maxillary salivary glands, gall bladder, seminal vesicles, suprarenal
glands, prostate, stomach, diaphragm, splenic artery, ureters, urinary
bladder, and colon demonstrated no noteworthy changes. There were
marked myeloid tissue infiltrations along the sinusoids of the spleen and
liver. These masses of cells in the spleen included nucleated red blood
cells and large myelocytes with oxidase granules.

Tissues of the primary tumor of the thyroid gland and those of the
metastases in the left axilla removed surgically, and metastases obtained,
during the post-mortem examination, from along the spine and para­
bronchial lymph nodes, were fixed in absolute alcohol and stained for
glycogen. Many of the small undifferentiated cells and the spindle cells
contained an abundance of glycogen granules. The fused-cell aggregates,
as a rule, had none, although several were found with a few granules
distributed in the marginal portions of the cytoplasm, chiefly in tissues
with necrosis.

Comment

The large spindle cells with the cross striations of skeletal
muscle fibers in the primary neoplasm of the thyroid gland and
in the metastases of many parts of the body distinguish this
tumor from other malignant growths of the thyroid so far de­
dcribed. These cells suggest that the primary growth belongs to
the group of malignant mixed cell tumors of the thyroid and
whether designated as mixed tumors, carcinosarcomas, or sarco­
carcinomas, they have components derived from epithelium and
mesothelium. The mesoblastic component of the tumor here
reported is skeletal muscle. The existence of an epithelial com­
ponent in the tumor tissues is not as securely demonstrated
because the only structures suggesting acinar derivation are the
huge fused-cell aggregates resembling giant cells. The possibility
that these are other abortive structures of skeletal muscle origin
cannot be denied. However, some of the fused-cell aggregates
had a marked resemblance to thyroid acini and in the cytoplasm were globular masses of a hyaline substance as much as 10 to 12 microns in diameter that contrasted sharply and, in sections stained by the Van Gieson method, had a yellow to light brown color. A specific stain would be helpful in identifying such substances as thyroid colloid but such a stain, universally accepted, has not been devised, according to Wegelin and others (Abrikossoff). The absence of glycogen granules does not favor the contention that these cell masses are derivatives of muscle cells. A comparison was made between the tissues of this thyroid tumor and those of a malignant rhabdomyoma of the leg (Hirsch), and, while in the latter a few multinucleated cells were found resembling closely those of the thyroid tumor, these cells were not as large or as abundant in the muscle tumor as in the tumor of the thyroid gland.

**Summary**

A malignant tumor of the thyroid gland and its metastases in many of the visceral tissues of the body contained embryonal skeletal muscle fibers, undifferentiated cells, and large fused-cell aggregates. Some of the fused-cell aggregates contained hyaline masses with the staining qualities of thyroid colloid. These cell masses, however, were not identified conclusively as abortive thyroid acini, although some resembled such structures closely.

**References**


Hirsch, E. F.: Malignant rhabdomyoma of the left leg, Arch. Path. 8: 9, 1929.


