Rhabdomyoma of the Ovary

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Tumors of striated muscle are sufficiently rare to make the observation of a new and characteristic case worthy of record. The rhabdomyoma which is the subject of the present discussion is of special interest because of the peculiar forms assumed by the myogenic cells and the wide variations of structure in the tumor.

At the present time a detailed discussion of the literature of this neoplasm is unnecessary; but the facts which are of more direct bearing on the present case may be mentioned. Benenati's list of 65 cases was published in 1903; and the cases reported since then do not show any material change in the relative frequency of this tumor in the various parts of the body. They may be divided according to the regions in which they occur. Rhabdomyoma is found most often in the genitourinary tract. There are 39 cases occurring in this region: kidney, 13; testis, 9; uterus, 6; pelvis of the kidney, 3; vagina, 3; bladder, 3; ovary or uterus, 1; ovary, 2. The tumor of the ovary described by Virchow in 1850 was a papillary cystic rhabdomyosarcoma, some of the papillae being formed of striated muscle. A second rhabdomyoma of the ovary was reported by Vignard. It was similar to the tumor about to be described, the greater part being striated muscular tissue with cystic degeneration at one extremity.

Wolfensberger noted the frequency of this tumor in the neck and adjoining regions, which stand second to the genitourinary tract with 9 cases. These localities are: orbit, 2; temporal bone, nose, tongue, parotid, mandible, esophagus, and mediastinum. Four examples are found posterior to the pelvis. They were in the lumbar region, hip, ischial tuberosity, and anus.
Homologous rhabdomyomas are found with greatest frequency in the heart, where 8 cases are recorded. Recently Wolbach has added an instructive case to the list. The remaining 5 examples were found in the following regions: pectoralis major, breast, shoulder, elbow, and thigh.

Muller has recently published a case in which rhabdomyosarcoma followed successive fractures of the femur. In his case the tumor probably arose from previously normal adult voluntary striated muscle cells. Such tumors, while probably not infrequent, are rarely reported, and belong to a group entirely different from the ordinary heterologous or teratomatous rhabdomyoma.

Clinically, rhabdomyomas are tumors of moderately rapid growth. Most of the tumors are well encapsulated and form no metastases; however, there are others with infiltration of surrounding tissues and recurrence after removal (Billroth, 2 cases; Buhl, Kaschewarowa) and some which formed metastases (Wolfensberger, Eberth, Benenati). Burgess has reported a case in which there were multiple metastases throughout the body.

Cohnheim's theory of embryonal rests has been accepted by many authors as accounting for the genesis of this tumor, especially of the heterologous rhabdomyomas. Ribbert has suggested as the origin of his renal tumor the development of striated muscle from the smooth muscle present in the pelvis of the kidney. His arguments do not seem to be convincing.

Benenati gives five possible derivations for rhabdomyoma testis. It may arise from smooth or striated muscle derived from the cremasteric muscle or from the gubernaculum; he finally concludes that the new growth arises from an embryonal rest. In 1904, Ribbert came to the conclusion that rhabdomyoma testis is a one-sided development of a teratoma. In the present communication I hope to extend this interpretation to rhabdomyoma of the ovary.

The genesis of teratoma has been variously explained. Verneuil in 1855 agreed with other writers in finding the origin of this tumor in a twin inclusion. Theories which found the source of tridermal neoplasms in polar bodies and isolated blas-
Fig. 1. Gross Section of Tumor

Note capsule and thin strands of connective tissue surrounding the individual spheroidal masses which make up the tumor.

Fig. 2. Low Power Field, Including the Cell Shown in Greater Detail in Figure 5

The giant cells are surrounded by myxomatous tissue. In large portions of the neoplasm the latter element is found exclusive of any other.
tomeres have given way to one which is based on the parthenogenetic development of the sex-cell. At the present time the last mentioned theory has the greatest number of adherents.

The results of experiments performed by Stockard have led me to believe that the twin inclusion theory will best explain the origin of this neoplasm. In the following I shall endeavor to prove that this theory is applicable not only to rhabdomyoma of the ovary, but to most rhabdomyomas in common with many simple tumors occurring inferiorly, either in front or behind the pelvic zones, in the genitourinary tract, or superiorly, in the neck region.

Present case. October, 1918, Edith M., one and a half years of age was found to have a mass in the abdomen reaching half way to the umbilicus. In shape and size it seemed to resemble a kidney with the long diameter horizontal. It was freely movable. There were no subjective symptoms. At the time of the operation nine months later, the mass appeared to fill the whole abdomen up to the umbilicus. Early in February, 1919, the child begun to vomit to such an extent as to cause the mother to give consent to operation. At that time a yellowish discoloration appeared on the skin about the umbilicus.

Operation, performed February 9, 1919, disclosed a well encapsulated tumor arising apparently from the region of the left ovary, filling the pelvis, with a narrower upper portion lying under the inferior surface of the liver. The capsule was attached to the anterior abdominal wall posterior to the umbilicus. The entire new growth was removed. In the process of removing the tumor the capsule was broken so that some of the myxomatous tissue fell into the abdominal cavity. The child died of abdominal recurrence, May 31, 1919.

Gross anatomy. The tumor is covered by a thin, movable capsule and consists of two parts, a lower, hard, spherical mass, 11 cm. in diameter, and an upper myxomatous portion, 4 cm. in diameter. It weighs 26 ounces. The surface is smooth and presents various rounded protuberances. On section of the larger part, the capsule is seen to run inward from the surface in thin strands throughout the tumor, giving the impression that it was the covering of an ever increasing growth. The tumor is made up of rounded masses, 3 cm. to a few millimeters in diameter, suggesting that it grew by the appearance of new parts, as well as by the increase in size of the older portions. On section the myxomatous division was found to contain a cavity.
Fig. 3. Giant Cell with Extension of Fibrillated Process in Muscle Fiber Formation

Adjoining are muscle fibers showing to some degree longitudinal and cross striation.

Fig. 4. Giant Cell with Well-Formed Fibrils Arranged without Definite Order

There are four nuclei situated at one end of the cell
Structure. Several main histological features deserve description. Perhaps the most striking are the giant cells. These cells have an acidophile cytoplasm in which usually there are concentric striae, most prominent at the periphery, while the perinuclear cytoplasm is granular. The nucleus or nuclei are round or broadly oval, sometimes containing 1 to 3 nucleoli. In other cells one or more centrosomes, as shown in figure 6, give evidence of active mitosis.

Muscle fibers. There are areas in the tumor composed of long cells with the characteristics of muscle fibers. The nuclei are oval and usually situated in the median axis. The peripheral cytoplasm is fibrillated, but only rarely can any cross striations be made out. Some of the fibers branch.

Myxomatous tissue. In several parts star-shaped cells with nuclei the size of those seen in the muscle fibers, and fibrils extending radially from them, can be seen separating the muscle fibers, showing that they developed alongside each other. In other places, they are the only element seen in large areas, giving the tumor a distinctly myxomatous appearance.

Histogenesis. The normal embryology of muscle may be taken as a guide to the anaplastic process. Striated fibers arise from myoblasts which elongate and by repeated mitotic division of their nuclei form a syncytium. The nuclei are surrounded by granular cytoplasm in which fibrils differentiate peripherally. The myofibrils became striated. The fibers increase in size and the nuclei migrate to the periphery. Heart muscle undergoes a similar development; but the nuclei remain centrally situated, sarcolemma never develops, and the individual syncytia are in connection with each other. Assuming that the tumor arose in a cell or group of similar cells we might expect to be able to follow the development till we arrive at the picture given in the histological description. Examining the three elements of the tumor it is possible to discern such an unfolding.

Giant cells. The giant cells as a group show a fundamental error in development; they have failed to elongate.

1. There are giant cells which show the extension of a process in an abortive development of muscle fiber (fig. 3).

2. There are giant cells which never elongated, while in other respects, they went through a more or less normal and complete development (fig. 5).

3. There are others which show increasing anaplasia until we come to some in which the fibrils lack definite order (fig. 4).
FIG. 5. THIS CELL DID NOT ELONGATE, BUT IN OTHER RESPECTS IT WENT THROUGH A COMPLETE DIFFERENTIATION

The fibrils and cross striae are shown as concentric and radial striae

FIG. 6. "SPIDER CELL" IN WHICH THE CYTOPLASM BETWEEN THE PERIPHERY AND THE NUCLEI HAS DEGENERATED AND BEEN ABSORBED

The perinuclear cytoplasm contains five centrosomes. This cell occurs only in cardiac rhabdomyoma.

I am indebted to Mr. William Dunn for the photographs.

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4. Lastly, there is a group of cells, some of which resemble the "spider-cells," first described by Cesaris-Demel in a remarkable tumor, a rhabdomyoma of the heart (fig. 6). Others lie in spaces which Wolbach showed to be intracellular. Seiffert concluded that these spaces were formed within the peripheral differentiated portion of the cell by the degeneration and disappearance of the greater part of the remainder of the cytoplasm. The histogenesis of the "spider-cells" is similarly explained.

The fact that this type of cell has been found exclusively in rhabdomyoma of the heart, and the fact that I have found branching in some of the fibers, have led me to conclude that the present tumor arose from heart muscle. Katsurada, among others, reported heart muscle in dermoid cysts. It should be added that while sarcolemma is occasionally developed in rhabdomyomas, it is never found in those of the heart. Also, here as in heart muscle, the perinuclear cytoplasm remains undifferentiated. Some writers have described branching in other rhabdomyomas. This may indicate that in an anaplastic process such forms may be evolved, or that these other neoplasms had an origin similar to the one now being described.

The second element of the tumor need not long detain us. The muscle fibers are descendants of cells which developed more normally than those heretofore mentioned.

There are many cells which show intermediate stages of development between the muscle fibers and myxoma cells. The genesis of the myxoma is explained as follows: it occurred in the most rapidly growing portion of the tumor, and, as is well known, parallel with an increasing rapidity in the multiplication of cells there is a corresponding loss in differentiation.

In this laboratory there are three other rhabdomyomas with a mucous element very similar to the one described. The literature affords other cases in which myxoma complicated an otherwise pure rhabdomyoma (Billroth, Kaschewarowa, Targett). The possibility thus arises that with the preponderance of myxomatous tissue a rhabdomyoma may be misinterpreted as a pure myxoma.
In some parts of the tumor surrounded by myxomatous tissue, the nuclei disappear, leaving areas of pure fibrils. These areas of fibrils raise the question of the possibility of the multiplication of fibrils without the corresponding multiplication of the myxoma cells. An analogous condition seems to obtain in neurocytoma, in which a similar picture of excessive fibrils may appear. It does not seem possible for the multiplication of fibrils to take place without the corresponding division of nuclei, but the overgrowth of fibrils of the individual cells is quite possible. A similar overgrowth of cytoplasmic derivatives is seen in the formation of epithelial horn.

Origin of the tumor. 1. Having shown that all the elements may be derived from myogenic cells, the next question to be considered is the origin of the group of cells from which the tumor arose. In considering this heterologous neoplasm we may leave a metaplastic origin out of the question. This leaves two possibilities: the tumor arose (a) from an embryonal rest; or (b) as a one-sided teratoma.

We may safely eliminate the former possibility. In general, nothing is known about embryonal muscle rests in the ovary. In particular, the organ is not situated near striped muscle so as to make such a rest possible. This conclusion becomes more evident since we are dealing with cardiac muscle.

It is an accepted fact that one element of a teratoma may outgrow the others (Pick and Walthard) and that the neoplasm may be represented by a single tissue. In the case of rhabdomyoma this conclusion gains added strength when we remember that striated muscle sometimes identified as cardiac, is often found in teratomas. It is interesting to note that Cornil thought the rhabdomyoma described by Vignard, the only case in the literature similar to the present one, was a fetal inclusion.

Additional support is found in the occurrence of similar tumors in an analogous organ. Rhabdomyoma testis is admittedly of teratomatous origin.

2. Since the teratomatous origin is the only one which will explain the rhabdomyoma it is necessary to determine in what manner the teratoma arose, and again there are two possibilities; it arose either from a sex cell or from a twin inclusion.
In the ovary, where there are totipotent sex cells, it may seem unnecessary to seek further for the origin of the teratoma. The commonly accepted explanation is the parthenogenetic development of this cell. This viewpoint is open to criticism because mammalian ova, with the exception of one series reported by L. Loeb, have never been observed to develop parthenogenetically and then continue a separate existence. Loeb, himself, claims little vitality for these ova, while Bandler and Wendeler quote other investigators to the effect that ova which undergo such a development invariably end in complete degeneration.

On the other hand, the twin inclusion theory has a basis in experiments recently performed by Stockard. By slowing the rate of development of fish embryos at the time when the primary bud should arise, two or more buds may develop simultaneously. The degrees of doubleness of the resulting individual is determined by the distance between the two buds on the blastodisc. At 180°, that is diametrically opposite each other, two complete individuals are formed.

When one bud gets the start of the other by any advantage it obtains a supremacy which allows it to develop into a perfect individual. The component arising from the inferior bud is suppressed and interfered with so that it develops abnormally. The twins are attached anteriorly in the head and neck region, or posteriorly, the great majority of them in the latter situation. There are all degrees of this inhibition of the second twin until it is reduced to a mere fragment of included tissue. The point made by Stockard is that human monsters have been born which show exactly the same relation to each other, as above described. Monsters attached superiorly on the head, neck, or upper thorax, or inferiorly near the sacrum, or anteriorly in the ventral region, can be traced in an unbroken series until the inhibited twin is represented by a teratoma or dermoid.

On the basis of these experiments it is possible to explain the presence and frequency of rhabdomyomas in the regions given in the first part of the paper, that is, 9 superiorly in the neck region, 43 inferiorly in the pelvic region.
No facts have been brought forth to disprove the twin inclusion theory. However, there are two questions which need further discussion. The first is the great frequency of teratomas in the sex glands; and the second, the occurrence of chorioma in males and in females at such a time as to shut out the possibility of impregnation. These phenomena can be explained by the twin inclusion theory.

Bonnet remarked the fact, in defending the theory of the origin of teratoma from an independent blastomere, that if a blastomere should separate from the remainder of the blastula, the organ to which it would be most likely to attach is the mesonephros.

For a long time the mesonephros is the largest organ in the abdominal cavity. It is the most vascular. Later the mesonephros survives as functional and vestigial parts of the genital system; in the male, the efferent ducts, the paradidymis, epididymis and vas; in the female the paroöphoron, parovarium, and Gartner's ducts.

If the twin were attached to the mesonephros, we should expect to find it adherent in the testis to the mesonephric tubules which join those of the sex gland. This is actually the case, for Ewing in his paper on teratoma testis points out that almost invariably the neoplasm arises in the neighborhood of the rete. We can explain those which occur in the scrotum external to the tunica albuginea by the accidental attachment to other portions of the mesonephros. Bandler has made an attempt to explain teratoma as a development of the paroöphoron. We now see that while it does arise from this region it is not a development from this organ, but is rather attached to it.

The position of teratoma is explained by the organogenesis of the sex glands in which the mesonephros plays such a prominent part. This accounts for most teratomas attached anterior to the pelvis. It explains the 39 rhabdomyomomas found in the genitourinary system. The other four, being situated posteriorly, were not able to become adherent to the mesonephros. From these facts arises the thought that many simple tumors of the ovary may be of teratomatous origin. Ewing has come to
the conclusion that practically all common tumors of the testis are of similar origin.

In taking up the question of chorioma, we may again turn to an observed fact. Up to the present time nobody has been able to cause the spermatozoa of any species to develop into an embryo. How then can we explain chorioma testis except as an early inhibited twin with the predominance of this single chori-onic tissue?

Boestrom reported a case of chorioma with multiple metastases throughout the body in which the testicles were normal. Djewitski recorded a case of chorioma of the bladder in a virgin, seventy-five years old. Surely rather late for the partheno-genetic development of an ovum, but not against the growth of a long repressed twin. The facts of extragenital chorioma can be explained best as a twin inclusion. The relations between the two components is such that with the growth of one there is an inhibition of the other. The rate of development of the host after birth is much retarded, and the repressed component is given the required opportunity to grow. This explains why the majority of teratomas begin their growth in early life rather than during the longer adult period. Senile atrophy of the host gives the parasite a last chance for development.

Causal genesis. The frequency of teratoma testis after trauma is well known. This may not only directly precipitate the rapid growth, but indirectly, by lowering the vitality of the organ, give the long repressed twin inclusion the temporary advantage. The real causal genesis lies in the potential energy for growth constantly waiting a chance for expression. Further, that the growth should be autonomous is the only possibility in tissues which have been so disorganized. This may be capable of experimental verification.

To sum up the points of the theory of the twin inclusion: It is based on observed facts and therefore can give a true casual genesis. It explains the position and frequency of teratomas, in the sex glands as well as elsewhere in the body, obviating the necessity for multiple explanations for teratomas. The theory holds for all one-sided teratomas.
The possibility of new evidence in favor of any other explanation for the frequency of teratomas in the sex glands will not disprove the twin inclusion theory, but will be complementary to it. Likewise the theory holds independently of the method of the formation of the twin.

According to the theory of twin inclusion, the complete sequence of events is as follows: an ovum is fertilized; through some unfavorable condition the rate of development is slowed; two primary embryonic buds are formed on the blastodisc, one having the advantage over the other. The favored bud develops into a perfect individual, during which process the smaller bud is inhibited and disorganized. The latter, being united to the more vigorous component at its ventral region, becomes adherent to the mesonephros; hence, later it forms a part of the ovary. With the birth of the child and its consequent diminished rate of development, the inhibited twin is given a new opportunity to grow. Through its previous disorganization it is not capable of orderly development. The heart muscle grows more rapidly and succeeds in crowding out the other elements. The growth gains in momentum, and myxoma cells are formed which have no resemblance to the earlier muscle cells.

**SUMMARY**

The case described is one of rhabdomyoma of the ovary in an infant.

Three elements arose from one tissue by (a) histogenesis more or less normal; (b) anaplastic development; (c) degenerative changes. Although only one tissue, cardiac muscle, is present, the tumor is of teratomatous origin. Many simple tumors of the ovary are probably of similar origin. Many tumors of the head, neck, thorax, and genitourinary and posterior pelvic regions are of teratomatous origin. This group includes the great majority of heterologous and some of the homologous neoplasms.

Teratoma is a twin inclusion. A group of cells is found in this tumor which appears only in rhabdomyoma of the heart.
Therefore, the present tumor is a rhabdomyoma of the heart of a twin inclusion. Fibrils may be produced in such overabundance as to lose connection with their nuclei and seem to be multiplying independently. Myxoma may be secondary to rhabdomyoma.

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