MIXED MESODERMAL TUMORS OF THE UTERUS AND VAGINA

WITH REPORT OF SIX CASES

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The heterotopic mesodermal tissue tumors of the uterus and vagina constitute a remarkable group of bizarre and polymorphic neoplasms. The variable tissue composition of these tumors has given rise to a complex nomenclature. McFarland (1) tabulated a list of 116 terms that have been used to designate neoplasms which, on the basis of histogenesis and composition, may reasonably be grouped in one class. The term "botryoid sarcoma" is a purely descriptive one which is often applied to tumors of the vagina. In many instances the recognition of a dominant tissue element, or the presence in the tumor of a distinctive type of tissue, has resulted in the use of some such term as "myxoma," "myxosarcoma," "chondroma," "osteochondroma," "rhabdomyoma," or "lipoma." The designation "mixed mesodermal tumor" is frequently applied to those tumors which clearly exhibit the formation of various mesodermal tissue elements. In an effort to overcome the limitations of nomenclature and to permit abandonment of the idea that such tumors must be botryoid or mixed tumors, or even necessarily malignant, McFarland advocates the use of the term "dysontogenetic tumor" to designate this entire class of neoplasms developing in the urogenital system.

The theory of neoplastic metaplasia is now generally discredited, since it is difficult to accept the idea that fibrous tissue or smooth muscle can be redifferentiated into striated muscle. Wilms' (2) modification of Cohnheim's theory is more acceptable. It presumes the displacement of myotome and sclerotome elements in the early formation and downward growth of the wolffian ducts. It assumes further the inclusion of these misplaced tissue elements in the müllerian ducts when the latter pass under the wolffian ducts to become fused in the midline to form the uterus and vagina. The heterotopic cells remain dormant for a variable period until some growth stimulus causes them to proliferate.

Nicholson (3) explains the failure of these tumors to develop along the course of the wolffian duct remnants by attributing to these indifferent cells a migratory activity which carries them to other locations in the developing müllerian system. It is difficult, however, to accept such a specific migration theory, since only one case is recorded in which the neoplasm developed in the outer portion of the lateral wall of the corpus uteri.

Analysis of the assembled case reports shows that the tumors of this group are mucosal in position, and in the majority of cases are situated on the posterior or anterior surface of the endometrium, or on the posterior or anterior lip of the cervix. The complete absence of such mesodermal tumors along the course of the fallopian tubes or in the broad ligaments indicates that the genesis
of these neoplasms is definitely related to the embryological process of organoid fusion in the caudal portion of the mullerian ducts. Additional support for a dysontogenetic origin is offered by the fact that similar tumors develop in the base of the urinary bladder, which is also a site of embryonic organoid tissue fusion and tissue amalgamation.

It is possible that displacement of myotome and sclerotome elements is necessary to permit the formation of cartilage, bone, and striated muscle in these tumors.

The simplest explanation of the histogenesis of mesodermal tumors accepts the principle of the persistence of primitive mesenchyma or indifferent cells which retain pluripotential capacity for differentiation into varied mesodermal tissues. These tumors may therefore on occasion be simple in tissue structure and represent a unilateral type of differentiation. They may be benign, as in the case of lipoma of the uterus. More frequently they are complex in tissue composition and are malignant in behavior.

Parity has no influence in the development of mesodermal tumors. Of the vaginal tumors, 60 per cent develop in the first two years of life. Meikle (4) states that 30 per cent of the corpus tumors and 60 per cent of the cervical tumors occur in nulliparae.

There is no adequate explanation for the varied age incidence of these tumors in the different parts of the generative tract. The average age incidence of the corpus tumors is fifty-five years and of cervical tumors thirty-one years, while the vaginal tumors develop under twenty-two years of age with 60 per cent occurring under two years.

The symptomatology is essentially identical with that of uterine carcinoma or myoma.

Mixed mesodermal tumors possess a marked capacity for local recurrence, for extension and metastasis to the vagina, parametria, broad ligaments, and peritoneum. Remote metastasis is uncommon, the chief sites being the lungs, mediastinum, and bones. Fourteen examples of remote metastasis are recorded in a total of 447 cases.

The prognosis is uniformly bad. The average duration of life after surgical removal is about one year. Hartfall (5) reported a case with a five-year survival. In a case recorded by Frick (6) the patient, a child of two and a half years, was living and well two years after the second removal of a vaginal tumor. The second patient in the series here reported is alive two years after surgical removal of the primary cervical polyp. Intensive deep x-ray therapy with intervening hysterectomy was resorted to in this instance after recurrence of the polyp.

The mortality rate for the entire group of tumors reported in the literature is over 95 per cent. Whatever course of treatment has been instituted the results have been uniformly bad. Local removal is inadequate and recurrence is rapid. Frequently it appears that the surgical trauma and stimuli incident to repair enhance the malignant character of the growth. Meikle (4) states that local removal of a large cervical polyp is justified to relieve the patient of irritating vaginal discharge, and as a prelude to complete hysterectomy by the abdominal route. This preliminary procedure tends to lessen the risk of peritoneal infection or implantation of malignant cells.
Prompt radical surgery in these cases is predicated upon the early recognition of the true nature of the primary polyp. It is noteworthy that in but one of the six cases herein reported were the mesoblastic nature and malignant character of the primary polyp diagnosed. It is frequently necessary that multiple areas of these growths be examined to detect various mesodermal tissue elements. At times some of these tissue elements may be present in minimal amounts. Rhabdomyoblasts may be overlooked, or these embryonic muscle cells may be considered as an expression of the polymorphous cell nature of the tumor. An additional handicap to accurate interpretation is the failure to recognize myxomatous tissue as a definitely embryonic tumor element. A factor which lessens the possibility of early diagnosis is the observation that these polyps frequently acquire appreciable size before symptoms are sufficiently severe to cause the patient to seek medical examination.

**Fig. 1. Case I: Recurrent Microcystic Endometrial Polyp Producing Hyaline Cartilage in Its Dependent Part**

The uterine canal was uniformly dilated to the size of a three months gravid uterus.

A group of six heterotopic mesodermal tissue tumors is reported. The group includes one tumor which was primary in the lower vagina, four which involved the cervix, and one having its origin in the body of the uterus. The salient features of these neoplasms are illustrated with the view of stressing the occurrence and significance of one tissue component common to all, namely, embryonic myxomatous tissue. Botryoid tumors acquire their gross appearance largely because of the dominance and rapidity of growth of myxomatous tissue in a submucous position in a spacious hollow viscus, such as the vagina.

**Case I:** A fifty-seven-year-old white female, the mother of ten children, had been bleeding from the vagina for three months. The menopause had occurred at the age of fifty. Examination revealed a polyp protruding from the external cervical os, attached high in the uterine cavity. When removed it measured 5 cm. in diameter and 7.5 cm. in length. A single cross-sectional area was examined microscopically. The structure was similar to that of the ordinary glandular endometrial polyp. The stroma was moderately hyperplastic.
The gland elements present were round and regular in contour. No evidence of malignancy was detected.

Two years later the patient again complained of vaginal bleeding, with lower abdominal pain and slight enlargement of the abdomen. Laparotomy revealed numerous pelvic adhesions and miliary malignant metastases in the peritoneum and omentum. The uterine body was enlarged to the size of a three months pregnancy. The ovaries were normal. Complete hysterectomy was performed, and the patient died of shock the following day. No autopsy was permitted.

The uterine canal was dilated by a large, soft, partially hemorrhagic polyp which had a narrow attachment site high in the upper postero-lateral endometrium. The mass was microcystic and contained an area of translucent cartilage in its dependent portion (Fig. 1). Microscopic examination showed a malignant polymorphous-cell sarcoma. Irregular nests of hyaline cartilage and some bone were distributed in a malignant stroma consisting for the most part of large spindle cells (Fig. 3). In scattered areas throughout the tumor were poorly defined groups of large cells which were round, polymorphous, and occasionally cylindrical in shape (Fig. 4). These cells had an abundant, deeply acidophilic cytoplasm sometimes showing faint fibrils and rows of granules which occasionally assumed a radiating pattern or were arranged in one or more concentric rings in the periphery of the cytoplasm, leaving a clear perinuclear zone. The cylindrical or ribbon-like cells showed faint cross-striation in hematoxylin-eosin preparations and heavy cross-striation after staining with iron-hematoxylin (Fig. 5). In areas these rhabdomyoblasts were grouped about glands. At times they were found in a myxomatous tissue. The peritoneal metastases were composed of cells of indifferent differentiation.

CASE II: A twenty-four-year-old colored female complained of vaginal discharge and passage of blood clots for two weeks. Her menstrual cycle had previously been normal. Examination revealed a soft polyp protruding from the external cervical os, attached high in the cervical canal. The polyp was excised and the attachment site cauterized with phenol. The mass measured 4 cm. in length by 1.5 cm. in width. It was soft and microcystic. The
FIG. 3. **CASE I: AREA OF HYALINE CARTILAGE IN POLYMORPHOUS-CELL SARCOSARCOMATOUS STROMA.**
**Hematoxylin-eosin. × 120**

FIG. 4. **CASE I. RHABDOMYOBLASTS: LARGE AND SMALL ROUND TO SPINDLE-SHAPED CELLS POSSESSING ABUNDANT EOSINOPHILIC GRANULAR AND OFTEN VACUOLATED CYTOPLASM.**
Nuclei are peripherally located and occasionally multiple. **Hematoxylin-eosin. × 120.**
FIG. 5. CASE I. STRIATED MUSCLE: CYLINDRICAL AND WAVY RIBBON-LIKE CELLS SHOWING VARIED DEGREES OF STRIATION DIFFERENTIATION. IRON-HEMATOXYLIN. × 1050

FIG. 6. CASE II: STRIATED MUSCLE IN VARIOUS STAGES OF DIFFERENTIATION IN A NEOPLASTIC STROMA OF MYXOMATOUS TISSUE

Note the round to wavy cylindrical cells with peripheral placement of nuclei, and abundant granular and vacuolated cytoplasm. Various stages of cell differentiation are shown. Hema-toxylin-eosin. × 600.
glandular elements were both cervical and lower endometrial in character. The neoplastic tissue had a distinctive periglandular arrangement and consisted of spindle and stellate cells in a myxomatous stroma. In some areas there was condensation of the stroma to form precartilaginous tissue. The polyp was considered to be benign in character.

Vaginal bleeding of the spotting type recurred eight months later, and became increasingly severe. Fifteen months after removal of the primary polyp a vaginal examination revealed a large, soft, cystic mass filling the vagina. Biopsy showed spindle-cell sarcoma. The polyp was excised and deep x-ray therapy was instituted with intervening hysterectomy. The patient is living without sign of local recurrence or metastasis two years after removal of the primary lesion and one year subsequent to hysterectomy. Examination of the recurrent polyp shows a tumor consisting in part of soft, myxomatous tissue beneath the cervical mucous membrane. The dominant type of neoplastic cell was spindle-shaped. Nests of

![Image](image-url)

**FIG. 7. CASE IV: CIRCUMSCRIBED ISLAND OF HYALINE CARTILAGE ADJACENT TO A DILATED CERVICAL GLAND**

Undifferentiated small round and spindle cells forming minute intraglandular polypoid projections; loose myxomatous tissue in the lower part of the field. Hematoxylin-eosin. × 90.

cartilage and bone were scattered irregularly through the tumor. In a few areas rhabdomyoblasts were differentiated in a myxomatous type of tissue (Fig. 6). The gland elements were normal to the part.

**CASE III:** A white child, two and one-half years old, complained of pain on urination. The mother noticed some redness of the vaginal introitus, and later a soft red growth developed on the hymen, which soon became thickened and somewhat polypoid. The vagina showed similar changes. The hymenal ring was excised. Microscopic examination revealed a rhabdomyomatous growth.

Vaginal recurrence was prompt, and three months later a mass was palpable in the pelvis. Laparotomy disclosed two retroperitoneal malignant metastases in the region of the iliac vessels. Microscopic examination revealed a highly malignant sarcoma. Deep x-ray therapy and radium inserted in the vagina had no effect upon the tumor. The abdomen became tremendously enlarged by the rapidly growing tumor, and the child died thirteen months after onset of symptoms. Autopsy was not permitted.
The original hymenal tumor consisted largely of striated muscle, some of which was well differentiated into interweaving fibers. The tumor consisted in part of rhabdomyoblasts, round, polymorphous or elongated cells possessing abundant deeply eosinophilic cytoplasm in which some tendency to form granular fibrils was noted. Immediately beneath the surface epithelium neoplastic myxomatous tissue tended to produce small polypoid projections. The pelvic metastases consisted of some loose fibrous tissue, spindle cells, and rhabdomyoblasts. No cartilage or bone was produced.

**Case IV:** A cervical polyp, believed to be a soft fibroma, was removed in a hospital out-patient department. The patient did not return to the clinic and no further information was recorded, so that the subsequent course is unknown. The polyp was somewhat nodular and contained cervical glands of normal structure. The distinctive microscopic features were nests of sharply circumscribed hyaline cartilage situated near cervical glands in a soft myxomatous tissue consisting of stellate cells (Fig. 7). Small groups of indifferent round and small spindle cells with hyperchromatic nuclei were irregularly scattered beneath the mucosa. Imperfectly differentiated rhabdomyoblasts were recognized deeper in the tumor. Cross-striation was faintly exhibited. These cells varied from round to polymorphous in shape, with an eosinophilic cytoplasm. The nuclei were sometimes centrally placed but often were eccentric. Iron-hematoxylin staining demonstrated beaded granules radiating in the cytoplasm; in a few cells definite coarse cross-striation was recognized (Fig. 8).

**Case V:** A fifty-seven-year-old white female complained of vaginal discharge and hemorrhage for several months. Examination revealed a large, degenerating cervical polyp which filled the vagina. A biopsy was taken, and microscopic examination showed a soft, myxomatous tumor which was interpreted as a soft fibroma. The polyp was removed and the base was cauterized.
Recurrence was prompt. X-ray therapy was then instituted without effect. The patient died five months after removal of the polyp with clinical evidence of abdominal metastasis. Autopsy was not permitted.

A single section was available from the tumor. It exhibits growth of embryonic, highly vascular, myxomatous tissue in which no cartilage or muscle elements could be found. It is possible that this tumor may have been a pure myxosarcoma, though it is highly probable that if multiple sections had been examined, a complex tumor would have been recognized. This case again illustrates the necessity for a complete examination of such polyps.

**Case VI:** A sixty-two-year-old white female complained of intermittent vaginal bleeding of several years' duration; bleeding finally became profuse and was associated with a foul-smelling vaginal discharge. A large sloughing cervical polyp filled the vagina and a firm irregular tumor occupied the lower abdomen. The polyp was excised and a diagnosis of adenomyoma was made.

One month later a biopsy of the cervix showed sarcoma. A panhysterectomy was performed and x-ray therapy was instituted. Twelve treatments, totalling 3,600 r, were given during a period of four weeks. Six months later a recurrence had developed in the rectovaginal septum. A second similar course of x-ray therapy was given and the rectovaginal mass was excised. A third course of irradiation was then given, this time totalling 1,800 r. Eight months later the patient returned with vaginal recurrence and a pelvic tumor. Roentgen examination of the chest showed lung metastasis. Irradiation, 2,400 r, directed toward this site of involvement was without effect. Death occurred two years after excision of the primary polyp. Autopsy showed metastases to the pelvis, peritoneum, and lung.

The primary cervical polyp exhibited abundant submucous myxomatous tissue and irregular areas of poorly developed hyaline cartilage undergoing ossification. In other areas crystalline calcium was deposited in fibroblastic tissue, suggesting an attempt to produce fibrous bone. No striated muscle was found. The metastatic tumors consisted of large spindle cells without myxomatous tissue, cartilage, bone, or muscle.

**Conclusions**

Six mesodermal tumors of the female generative system are reported. This group includes one tumor of the vagina, four of the cervix, and one of the body of the uterus. All of these tumors formed mucosal polyps. In each case the pathological diagnosis was benign polyp. The vaginal tumor in the infant was recognized as a rhabdomyoma, but the case was treated expectantly as a benign lesion. The malignant nature of these tumors was not appreciated until recurrence had developed.

Those cases where radiation therapy was instituted late in the course of the disease indicate the relative resistance of this class of tumors to irradiation therapy.

A review of the tissue sections from these cases reveals that all of them contained myxomatous tissue. In the absence of other evidence of mixed mesodermal tissues, it is our opinion that myxomatous tissue, which is an embryonic structure, should be accepted as strong presumptive evidence of the probable mixed mesodermal nature of these polyps and the malignant character of such a tumor should be appreciated.

The simplest explanation of the histogenesis of this group of neoplasms is based upon the inclusion and persistence in the müllerian organs of mesenchymal cells which retain a pluripotential capacity for differentiation into various mesodermal tissues.

These tumors may be simple in tissue structure. They may be benign, as in the case of the rare lipomas of the uterus. More frequently these tumors are of complex structure and malignant in behavior.
The recognition of the true nature of the primary polyp in these cases is important, since early complete hysterectomy associated with intensive irradiation appears to offer the greatest possibility for the control or eradication of mesodermal tumors.

References