A PAPILLARY MIXED TUMOR OF THE BODY OF THE UTERUS

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Mixed tumors of the uterus vary markedly in structure, and for that reason some confusion has arisen in the terms used in discussing these growths. Theoretically any tumor of the uterus containing at least one mesoblastic tissue foreign to those of the uterus belongs in this group. On the basis of such reasoning, lipomas, osteochondromas, and composite growths of carcinoma and sarcoma as reported by Jaffé (6), Schiffmann (15), and others, would be included. There seems to be no concise definition of the group. Perlstein (10), Ritter (13), and Gamper (3) discuss these growths as mixed mesodermal or mesenchymal tumors of the uterus. They include the occasional tumors with epithelium but exclude those that are benign. Halter (5) spoke of heterotopic mixed tumors, irrespective of embryonal origin or structural characteristics, while Jones (7) and Cox and Benischek (1) chose the descriptive term, "sarcoma botryoides." Others designate the tumors as rhabdomyosarcoma and chondromyxosarcoma. In none of the reports has much consideration been given to the mono-, bi- or tridermal composition of these bizarre tumors—factors concerned with origin—or has the dearth of epithelial derivatives been especially emphasized.

There is such a wide variety of mixed tumors, each individually different, that it is possible here to indicate only their more important features. Tumors of the uterus commonly referred to as "mixed" are of more complex structure and usually contain sarcoma-like tissues. Petersen (11) collected thirty fatty tumors of the uterus, but these generally are not considered complex enough to be included in the mixed group; they are seldom malignant and only occasionally contain striated muscle, cartilage, or embryonic myxomatous tissue. Other simple mesoblastic tissues, as the angiomas, and the more complex teratomas are excluded, as are the atypical growths of the cervix described by Geller (4), which contain only modified epithelium.

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Mixed tumors of the corpus vary in size, shape, and consistency. They are usually polypoid and of grape-like structure. The presence of vesicles is so common that Jones believed his tumor belonged to the "mixed" variety even though it contained only myxomatous tissue. He referred to the tumor reported by Plett (12) as similar except that it contained cartilage, which, in reality, was what stamped it as a "mixed" tumor. Others consider the vesicles as simple edematous tissue produced by vascular disturbances and not, strictly speaking, tumor growth, or the result of edema or mucoid degeneration in a sarcoma. It seems safe to say that while "botryoid" formations do occur in mixed tumors, they should not be regarded as diagnostic criteria without microscopic examination, since the vesicles may or may not contain heterologous tissues.

Of the 17 mesodermal mixed tumors of the body of the uterus reviewed in 1919 by Perlstein (10), to which he added one, 11 contained embryonal or adult striated muscle fibers and 5 smooth muscle, 8 myxomatous or loosely arranged edematous connective tissue, 8 cartilage, one fat, and all but 4 spindle, round, or polymorphous cells, or admixtures of these. In 10, the connective-tissue cells were described as sarcoma, one contained gland tissues, and in only two were there nests of epithelial cells as in a carcinoma. Of the 19 similar tumors of the cervix collected by Perlstein from reports in the literature, 6 contained embryonal or adult striated skeletal muscle and 2 smooth muscle, 11 myxomatous or edematous connective tissue, 13 cartilage, 2 glandular tissue, 2 fat, one bone, and 7 fibrous or elastic tissue. Twelve had strands or nests of spindle, round, or fusiform cells, and of these, 9 were considered sarcomas. The usual presence of the various mesodermal tissues and the dearth of epithelial derivatives are mentioned by Petersen (11) and by Shaw (16), although these authors did not limit their investigations to so-called mesodermal mixed tumors. Since Petersen's review in 1923, tumors of this general character have been reported by Wiener (18), Mann (8), Ritter (13), Fels (2), Gamper (3), Cox and Benischek (1), Halter (5), and van Akkeren (17).

The exact nature of the spongy connective tissue in these tumors is not definitely known. Ritter obtained a positive test for mucin with thionin. Others consider this stroma edematous connective tissue but most authors look upon it as myxomatous embryonic tissue because of the frequency of its occurrence and its
association with other immature elements, especially striated muscle. The cartilage, in various degrees of differentiation, is hyalin and is distributed in large or, more often, small islets surrounded by a more or less compact tissue described by some as perichondrium. All but three of the tumors reviewed by Perlstein (10) with spongy tissue also contained cartilage. This favors the embryonal character of both and suggests a possible origin of the cartilage, namely, from connective tissue. The loose connective tissue of the growths reviewed by Perlstein was in the substance of the tumors, differentiating it from that found only in vesicles at the periphery and described by Jones (7) as sarcoma botryoides. Striated skeletal muscle is significant in these tumors, since some contain no other heterologous mesenchymal tissues. Bone, which is rarely present, develops in the small islets of cartilage.

Shaw (16) excluded from the mixed group all tumors of the uterus that did not contain muscle or cartilage or both, thus contrasting them from the mixed tumors of the vagina (McLean and Wollstein, 9), which usually contain striated muscle but very rarely cartilage. Sage and Miller (14) reported as leiomyosarcoma a tumor with smooth muscle and spindle, polygonal, and giant cells. This was not considered "mixed" because it contained no striated muscle, fat, or cartilage. The mixed tumors described as containing sarcoma cells have compact masses of spindle, round, or atypical cells that merge gradually into myxomatous tissue or form collarettes of dense tissue about the islets of cartilage. The presence of epithelium with mesenchyme derivatives has received little attention, probably because it occurs so rarely. It was observed in only 4 of Perlstein's 37 tumors and in these the glandular structures (two cases) may have been endometrial inclusions.

Mixed tumors of the corpus occur most frequently during the menopause and those of the cervix in middle adult life, as contrasted with composite tumors of the vagina, which have been seen only in children. The corpus tumors reviewed by Shaw occurred between the ages of forty-nine and seventy-five years, those of the cervix between seventeen and fifty-three. There is apparently no association with multiparity. These tumors are extremely malignant. Patients rarely live longer than two years after the onset of symptoms. Metastases occur in about 50 per cent of the patients. They are late and seldom contain more than one kind of tissue. Occasionally a metastatic nodule consists of
tissue not recognized in the primary growth. These uterine tumors rapidly recur locally, and involve other pelvic tissues even after radical excision. As with other malignant tumors of the uterus, those of the corpus infiltrate surrounding structures later than do those of the cervix. The presence or absence of a given tissue component, or the amount, does not seem to be an index of the degree of malignancy. However, practically all tumors containing fat are benign; they seldom contain cartilage, and very rarely epithelium.

Case Report

M. M., a white woman, aged sixty-four years, a widow with one child living and well, entered St. Luke's Hospital for observation and diagnosis Nov. 4, 1928, because of pain in the lumbar region and left hip and a feeling of pressure in the left lower quadrant of the abdomen. Three years previously she had been treated for "catarrh of the uterus." Since that time her symptoms had become progressively worse, and she had suffered from urinary frequency and constipation which greatly accentuated the abdominal symptoms.

The patient was well nourished and not acutely ill. Physical examination demonstrated slight tenderness in the region of the urinary bladder and over the large bowel in the left lower quadrant of the abdomen. Bimanual examination of the uterus was not made. The urine showed an occasional leukocyte. The hemoglobin of the blood was 78 per cent and there were 3,950,000 erythrocytes and 9,300 leukocytes per c.mm. Respiration, pulse rate, and temperature were within normal limits. A roentgen examination of the large bowel demonstrated a marked spasticity of the distal portion of the colon and with this diagnosis the patient was discharged, Nov. 7, 1928.

She re-entered St. Luke's Hospital Sept. 10, 1930, complaining of bleeding from the vagina for three weeks and a sharp pain in the lower portion of the abdomen of one day's duration. Three weeks before, she had been treated for "catarrhal discharge," and the bleeding had begun when she removed a pack from the vagina. The blood was dark red, liquid and clotted, and had been of moderate quantity until the day preceding admission to the hospital, when it became profuse and was accompanied by pain in the lower portion of the abdomen. There had been no noteworthy complaints since leaving the hospital in 1928 but the patient had been given liver powder because of anemia. The physical findings at this time were essentially the same as at the previous examination. There were from 6 to 8 erythrocytes and 8 to 10 leukocytes per high power field and 10 mg. of albumin per 100 c.c. of urine (non-catheterized specimen). The hemoglobin of the blood was 84 per cent and there were 4,280,000 erythrocytes and 12,100 leukocytes per c.mm.

On Sept. 10, 1930, a pelvic examination demonstrated the uterus to be of premenopausal size but freely movable, and the cervix atrophic, smooth, and pale gray-purple. The cervical canal admitted dilators
with gentle pressure and was found to contain a little bloody fluid. Tissues were removed from the cavum of the uterus for microscopic examination and a report was made of "mixed tumor of the uterus."

Five days after the curettage the adnexa and uterus were removed. The postoperative course was uneventful and the patient was discharged from the hospital on Oct. 10, 1930, after having received four deep roentgen-ray treatments. When last examined (July 1931), she was in good general health and had lost no weight. At that time there was slight thickening of the pelvic wall tissues but no definite evidence of local recurrence or metastasis.

![Image](image_url)

**FIG. 1. POSTERIOR SURFACE AS SEEN AFTER BISECTING THE UTERUS AND TUMOR GROWTH IN THE FRONTAL PLANE**

**Gross Description of Tissues Removed:** The uterus, complete except for the vaginal portion of the cervix, was 75 mm. long and 50 by 32 mm. between the horns. The portion of cervix included was cone-shaped, 25 mm. long and 27 by 22 mm. wide. The left fallopian tube coiled on itself was 50 mm. long and 10 mm. in diameter proximally. The ostium was patent and easily admitted the blunt end of a probe into the proximal third of the tube. A shrunken left ovary measured 35 by 25 by 15 mm. On the right side, adherent to almost the entire length of the lateral wall of the uterus and continuous into it, was a smooth nodular mass measuring 60 mm. long and 35 mm. dorsoventrally. It extended out from the uterus as much as 35 mm. The peritoneum of the uterus was smooth and glistening except for a few places roughened by torn ends of fibrous tissue. The cervical canal at the level of amputation had diameters of 10 and 2 mm. At the lower end of the nodular mass adherent to the right side of the uterus, the tissues were torn in a place 10 mm. in diameter and to a depth equally great. The line of cleavage
here was not sharp. The nodular mass lay more on the dorsal than the ventral side, and the tube and ovarian tissues of this side were not identified.

After fixation in Kaiserling's solution the uterus was bisected in its frontal plane (Fig. 1), and the anterior surface made by cutting was used in completing the following description. In the cavum of the uterus was a mass of opaque gray tissue 38 by 34 mm., with one border 25 by 12 mm. and scattered pearly-white islets of elastic glistening tissue like cartilage, as large as 5 mm. This mass of tumor tissue extended into the cavum from the left lateral and fundic walls and into the cervical canal 5 mm. below the internal os. The islets of elastic tissue were more numerous toward the center of the mass away from the attachment. Where attached in the region of the left cornu, the tumor tissues blended with the myometrium and the walls were thinned to as little as 3 to 4 mm. The right lateral wall of the uterus was 7 mm. thick and in a small region 13 mm. above the internal os the myometrium contained numerous small masses of tough gray tissue. Opposite this, in the cavum, and attached to the wall near the internal os was a mass of tumor tissue 20 mm. in diameter in apposition with the main mass but apparently not continuous. Within the uterus, between its right lateral wall and the main tumor mass, was an irregular cleft 16 by 7 by 5 mm. corresponding to the deformed cavum. One surface of this was smooth, pink endometrial lining; the others were irregular, gray, opaque, and granular because of small papillary projections of pearly-white cartilaginous tissue.

The mass along the right side of the uterus, mentioned above, was firmly attached to the middle 30 mm. of the right wall, and there was no line of demarcation between the myometrium and tumor tissue comprising the mass. This nodule of tissue had a thin, fibrous capsule less than 1 mm. thick except laterally, where it was 9 mm. and was composed of fibrous tissue and fat (microscopically compressed ovarian tissue). Beneath the thickened portion of the capsule was a potential cleft-like space 10 mm. long and about 8 mm. deep, with a smooth, gray-brown lining. The nodule of tumor tissue was roughly divided into three parts by marginal indentations. The upper was 17 by 16 mm. and consisted of opaque gray-brown tissue; the central was 19 by 2 mm. and similar to the upper except for slight softening of the tissues at the center; the lower division, irregular in outline, 21 by 17 mm., was mottled gray and brown and was slightly softer in its inferior portion, which corresponded to the torn margin of the mass.

The tissues of the cervix were tough, gray, and fibrous, without noteworthy changes; included were 21 mm. of the cavum, with a diameter of 4 mm. Within the lumen of the canal there was a little gray-brown, gelatinous material, and the lining was gray-pink and smooth. The posterior surface made by bisecting the uterus and its attached nodular mass in the frontal plane was similar in all essentials to the anterior, except for slightly more disarrangement and fragmentation of the center of the mass in the cavum.

*Histology:* Sections for microscopic examination were made from various parts of the tumor, the uterine wall, the left fallopian tube, and
the nodular mass attached to the uterus on the right side. The tumor of the cavum was composed chiefly of low columnar cells on slender branched fibrous papillary stalks (Fig. 2). The stalks were continuous into and had the same histologic structure as the myometrium, and converged to form broad bands of dense fibrous tissue that blended with the wall in the left cornu. Scattered in the tissues, and increasing in size and frequency toward the cavum of the uterus, were oval and round islets of cartilage ranging in diameter from 0.1 to 3 mm. (Fig. 3). These consisted of round, spindle-shaped, and irregular stellate cells with large, deeply staining nuclei, and they blended with the cells of the stroma with little differentiation. Those toward the center of the larger islets were more regular in outline and many lay in lacunae well distributed in a slightly fibrillar, pale blue matrix (hematoxylin and eosin). The

smallest islets of cartilage and the peripheries of the larger ones, identified by serial sections, were irregularly arranged groups of spindle cells poorly differentiated from those of the fibrous stalks (Fig. 4).

Serial sections were made of one block in order to study the details of the cartilage masses. These tissues were distributed in club-shaped, spherical, or branching masses that arose from discrete foci scattered in the fibrous connective-tissue stalks. The narrow, compact epithelial papillae were in close apposition with the cartilage but nowhere compressed, and some of the islets were bordered by a single layer of columnar cells as if the stroma stalks had been expanded by the growth of a focal mass of cartilage. In the more compact tumor tissues several papillae, both stroma and epithelium, blended with a single islet of cartilage, and the columnar cell nuclei, as well as those of the stroma, merged with the cartilage cells.

The tissues of the tumor near the internal os of the cervix on the

Fig. 2. Loosely Arranged Branching Papillae with Narrow Fibrous Stalks Covered by Columnar Cells (Hematoxylin and Eosin) × 160
right side had a similar dense papillary structure, and the scanty fibrous stalks converged to one broad attachment with the myometrium like that in the left cornu. Dispersed in the compact papillary regions with scanty stalks or without stroma were small discrete islets of cartilage (Fig. 5). The matrix of these islets was more homogeneous than in the islets of the tumor in the fundus, and the cells were less compact and larger, and lay in large lacunae. The columnar cells about these masses were less regular and seemed to merge gradually into the cells of the cartilage.

The mass of tissue outside the uterus on the right side also had a papillary epithelial and to some extent tubular structure, but in the regions examined no islets of cartilage were found (Fig. 6). Near the center the tissues were necrotic. Outside of the tumor mass was a dense fibromuscular wall from 1 to 2 mm. thick, like that of a fallopian tube, and the stroma of the papillae merged with this everywhere without converging into a discernible base. The softer parts along the outer surface of the mass were fibrous tissue with many small blood vessels, fat tissues, large corpora albicantes, and other ovarian structures.

Sections stained with phosphotungstic acid-hematoxylin, safranin, Mallory's "methylene blue," and van Gieson's stain differentiated the tissue structures, and these were compared with sections of cartilage from the larynx and leg in a 73 mm. human fetus. The stroma of the papillae

**Fig. 3. Large Single Islet of Cartilage (Hematoxylin and Eosin) × 130**

The cells of the periphery are more compact and spindle-shaped and along the outside is columnar epithelium, as though the islet had originated in the stroma stalk.
The focal distribution and the differences in size and structure of the islets suggest that they originated at different times and in various centers of growth during the development of the tumor.

The matrix is homogeneous and the cells, in large lacunae, are less compact than in many other islets.
contained not only differentiating and mature collagenous connective-tissue fibers, but also long, narrow fibers of smooth muscle in about the same proportion as found in the myometrium. The staining reactions of the tumor cartilage and of the surrounding perichondrium, if this may be so designated, were identical with those of the cartilages from the fetus, and the cellular structure was similar, slightly more compact in the cartilage of the tumor. The large islets in the tumor tissue stained more nearly like mature cartilage, while the small masses stained like the collagenous fibers of the stroma. Phosphotungstic acid-hematoxylin stained the columnar cell nuclei deeply, and there were many cells in mitosis.

These portions are more compact and have less stroma than other regions of the tumor.

**Comment**

The predominating papillary structure with many isolated masses of cartilage in this tumor of the body of the uterus stamp the growth as a "mixed tumor." Most of the mixed tumors of the uterus so far reported contained mesoblastic derivatives only. An occasional growth has been reported as containing epithelium, which may have been an endometrial inclusion, but none of those reviewed contained as much of the epithelial tissues as the tumor.
here reported. (This statement does not apply to the tumors designated carcinosarcoma, which are growths usually of adult tissues.) Of the 50 mixed tumors of the uterus reported since 1900 and reviewed by Petersen in 1923 (11), only three contained epithelium of any kind. Petersen’s tumor, which made a fourth, was estimated to contain about one per cent of round and spindle-shaped cells arranged in alveoli. For this reason he considered the growth unusual. Cartilage and smooth muscle are the most common heterologous tissues found in mixed tumors of the uterus, but even these are present less frequently than edematous or myxomatous tissues. The presence of hyaline cartilage without myxomatous tissue is not in harmony with the idea that cartilage necessarily develops only from a loosely meshed embryonal fibrous tissue. The masses of cartilage in the tumor here reported have staining reactions similar to the cartilage of a small fetus and they seem to arise in the fibrous and smooth muscle stroma stalks, intimately associated with the columnar cells of the papillae. The absence of grape-like masses of edematous or myxomatous tissue refutes the idea that these are essential constituents of a mixed tumor of the uterus.

A completely satisfactory explanation of the origin of mixed tumors of the uterus has not been made, and only theoretical considerations have been offered, none of which is accepted generally. The presence of one or more heterologous mesoblastic tissues, usually immature, and the occasional presence of epithelial derivatives suggest that, for some reason, embryonic tissues were stimulated to growth. According to many authors, these tissues arise from fetal rests (Cohnheim’s theory). Wilms (19) in his monograph stated that embryonal germ cells are displaced along the Wolffian duct. These indifferent germ cells must be mesodermal in order to provide the myotome (striped muscle) and mesenchyme (cartilage, etc.) derivatives. It is possible that the tissues in the tumor here reported originated just above the internal os of the cervix from Gärtnert’s duct, or that the heterologous tissue of the fundus and the mass attached to the uterus arose from the anlage of one or both fallopian tubes (Müllerian ducts). The mass attached to the uterus was more compact than the tumor elsewhere and contained no cartilage, and the cartilage of the mass in the left cornu was more cellular and more fibrillar than that of the tumor on the right side just above the cervix. No anatomic connection was demonstrated between the two portions
of tumor within the cavum, and the mass attached to the uterus was on the side opposite the tumor of the fundus. The myometrium in places was thinned by the growth of tumor but nowhere was it penetrated. It may be that differentiation began simultaneously in more than one embryonal rest. Serial sections of one block and specific stains demonstrated that the cartilage originated in discrete foci of the fibromuscular stroma. The smallest islets and the periphery of the others had the staining qualities and the cellular structure of the fibrous stroma of the papillae. Toward the center of the large masses the tissues were more highly differentiated, and many of the cells were in lacunae. The recent idea that metaplasia is important in all mixed tumors may be significant. The many discrete masses of cartilage arising in widely separated places in the tumor suggest either multiple foci of cartilage cells widely scattered in the stroma from which the islets developed, or growth factors acting in the connective tissues in such a way that they focally differentiate into cartilage tissues. The latter mechanism seems plausible inasmuch as the islets of cartilage are not uniform in size and differ in their degree of differentiation.

**Summary**

A mixed tumor of the body of the uterus and adnexa is described, unusual in that it contained both epithelial and mesothelial derivatives. Narrow branched papillae with slender fibrous connective tissue stalks covered by columnar cells comprised most of the tumor. In the fibrous stalks were bundles of smooth muscle and masses of hyaline cartilage. Edematous or embryonal myxomatous tissue was not a constituent of this mixed tumor of the uterus. The cartilage tissues were distributed in multiple small focal masses which differed markedly in size and in degree of differentiation. Such variations in structure suggest the origin of cartilage islets from the connective-tissue stroma of the tumor.

**References**