SARCOMA BOTRYOIDES

Report of Two Cases and Discussion of Nomenclature

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"SARCOMA BOTRYOIDES" is a term that has come to include certain neoplasms of the lower genitourinary tract which occur predominantly in children. Although rare, sarcoma botryoides is the most common lower-urogenital sarcoma found in younger age groups. In boys it arises in the bladder, urethra, and prostate; and in girls in the bladder, cervix, and vaginal vault.

The word "botryoid," derived from a Greek term meaning "like a bunch of grapes," refers to the gross characteristics of the neoplasm: the formation of fleshy, polypoid or grapelike masses. However, the histopathologic findings in sarcomas with these gross characteristics vary. Many of these sarcomas are only indeterminately spindle-celled, and resemble embryonal connective tissue; others of the group contain heterologous mesenchymal elements that most often resemble immature striated muscle cells, and only occasionally resemble cartilage. Thus, on the basis of these histologic variations, these neoplasms have been classified by terms such as "embryonal sarcoma," "rhabdomyosarcoma," and "malignant mesenchymoma."

The problem of nomenclature and classification of the genitourinary sarcomas is not limited to those in the lower urogenital area or to those found in the very young age group. The Wilms's tumor or nephroblastoma of the kidney, the major renal neoplasm of childhood, also can be a heterologous mixture of tissue elements. In women, the malignant, mixed müllerian tumors of the uterus possess many elements usually considered to be of mesodermal origin, such as osteosarcoma, chondrosarcoma, or liposarcoma. The gross characteristics of these müllerian tumors are similar to those of the sarcoma botryoides occurring in the vagina or cervix of a young girl, in that the müllerian tumors often are polypoid and large; however the histopathologic characteristics of the two differ in that the müllerian tumors usually contain malignant epithelial components.

The purpose of this study is to present two cases of sarcoma botryoides that demonstrate most of the features of the polypoid neoplastic process affecting children.

REPORT OF CASES

Case 1

Clinical Features. The patient, an infant girl 17 months old, was seen because two months previously "red bodies" had been expelled from the vagina. The parents stated that the bodies were small, each about the size of a pea. They also had noted a slight amount of associated bloody vaginal discharge.

Physical examination revealed a well-nourished infant with positive findings limited to the genitalia. A polypoid, fleshy, pink mass protruded between the labia majora when they were separated and it apparently filled the vagina. The mass appeared to arise in the upper vaginal vault, but an accurate appraisal of the site of origin was precluded by the size of the neoplasm. The uterus was enlarged as determined by rectal examination. The roentgenograms of the chest and pelvis were normal; the laboratory findings were not significant.

In view of the extensive pelvic involvement, surgery was believed to be inadvisable, and therefore irradiation therapy utilizing both radium and roentgen ray was administered. However, the neoplasm resisted irradiation and the child died 18 months after the first symptoms had appeared.

Pathologic Features. The biopsy specimen consisted of several globoid, translucent, white nodules, ranging from 0.2 to 0.5 cm. in diameter, and arranged in a polypoid configuration.

Microscopic Description. In sections, the masses were composed of a loosely arranged tissue, the surface of which was covered by a thin layer of squamous epithelium (Fig. 1). In areas, small, cleared zones were evident immediately beneath the epithelium, but in others, long interlacing anastomosing cells were present, indistinguishable from mature skeletal muscle elements (Fig. 1a). Centrally in the masses there was a pleomorphic cellular pattern. The predominant cytologic element in the loosely arranged tissue was an elongate cell, at times of almost rectangular shape, at other times the cell was somewhat spindly with pink or red cytoplasm. Many of these cells contained coarse, longitudinal fibrils; some stained with hematoxylin and eosin showed cross striations intensified with the phosphotungstic-acid hematoxylin stain (Fig. 1b). Other cell types encountered included a fairly large and irregularly rounded cell with a homogeneous eosinophilic cytoplasm, and a small spindly form. The nuclei varied in size, but always were vesicular and contained prominent nucleoli; mitotic figures were present.

Case 2

Clinical Features. A 17 month old boy was admitted with a history of intermittent hematuria of three months' duration. The mother stated that initially she had observed drops of blood in his diaper, and tiny, round, pink masses in the urine. No difficulty in voiding had been noted. The infant was asymptomatic for six weeks and then he apparently developed some type of irritating discomfort; at that time the mother noted blood in his diapers on three successive occasions. The child, following the episode of pain, cried with each urination. Two days prior to admission, after straining hard, he passed a small red mass.

External physical examination was normal. Laboratory studies, including blood cell

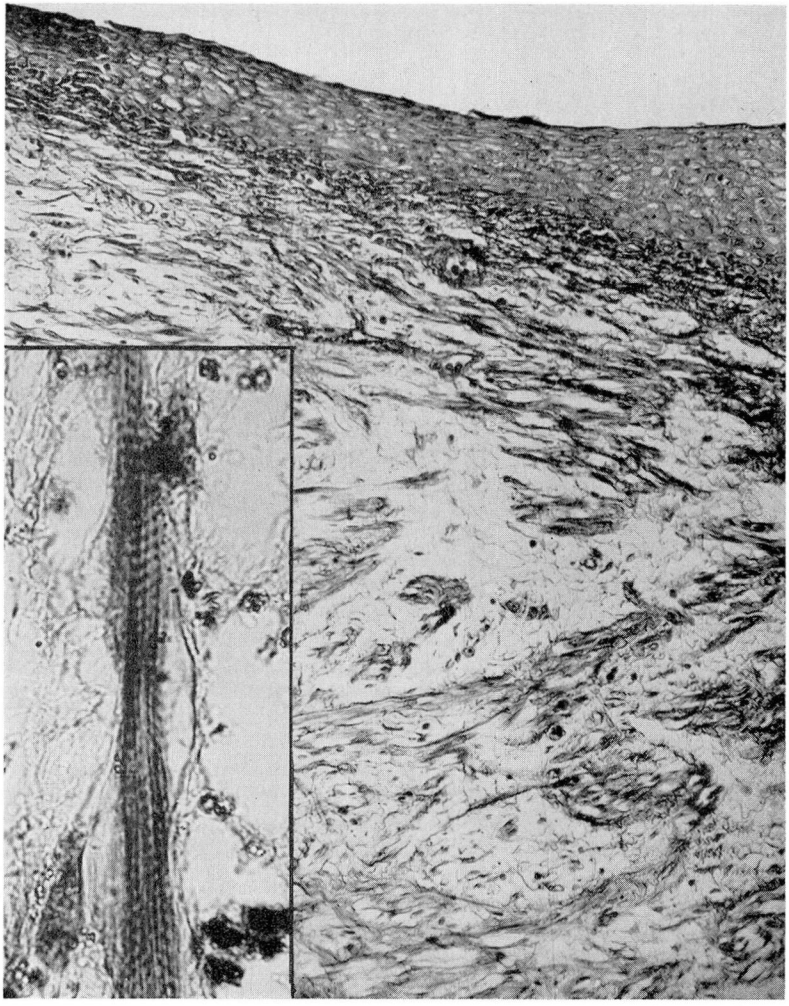

Fig. 1. (Case 1) **a.** Low-power magnification showing small interlacing bundles of elongate cells embedded in a myxomatous stroma. Phosphotungstic-acid hematoxylin stain, X 150. **b.** Prominent cross-striations in a neoplastic muscle cell. Phosphotungstic-acid hematoxylin, X 900.

counts, urinalyses and repeated blood urea tests, were within normal limits. Roentgenograms of the chest were normal.

Cystoscopy demonstrated numerous small polypoid structures within the prostatic urethra; cystograms demonstrated that the base of the bladder was elevated, but filling defects were not visualized in the bladder. The polypoid lesions were completely removed transurethrally, and external irradiation was administered to the urethra and to the base of the bladder both by suprapubic and by perineal ports. Although an adequate urinary stream was maintained and no evidence of a recurrence in the urethra was observed by

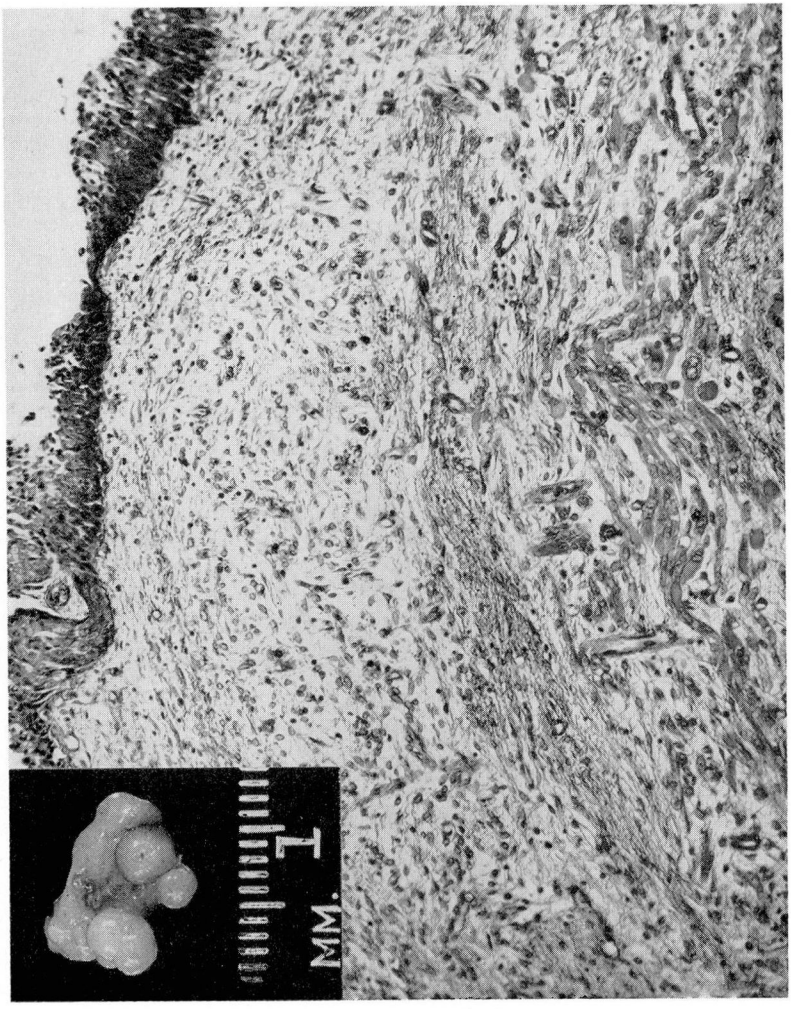

Fig. 2. (Case 2) **a.** Gross segment of neoplasm demonstrating the "botryoid" excrescences. **b.** Low-power magnification showing that the submucosal area is relatively acellular. A polymorphous cytology is present more deeply. Phosphotungstic-acid hematoxylin, X 150.

urethroscopy, examination five months later demonstrated a polypoid tumor in the bladder lateral to the left ureteral orifice. This small lesion was removed by transurethral resection, and a second course of roentgen therapy was administered. Eleven months from the date of initial treatment, the patient showed evidences of marked intrapelvic and pararectal extension of the tumor. No local recurrence was noted on cystoscopic examination.

Pathologic Features. The surgically ablated tissue consisted of several segments of tissue up to 1.5 by 1.0 by 0.4 cm., which were irregular in shape, white, and glistening. The external surface of one of these was covered with small white excrescences up to 0.3 cm. in diameter (Fig. 2a).

Microscopic Description. Sections of the globoid masses demonstrated them to be covered by a stratified squamous epithelium. The zone immediately beneath the epithelium was not uniformly hypocellular as is so commonly noted, but instead was composed in part of myxomatous-appearing tissue containing many small spindle cells, and others that had a more reticular appearance (Fig. 2b). Within this area occasionally were very small elongate blunted cells containing a few cross striations. The tissue was not homogeneous; however, occasional areas were relatively acellular. A biopsy of one of these acellular segments only did not suffice for making a definitive diagnosis. The histopathologic changes in the more central portions were spectacular. At first, there appeared to be a confused mass of many types of cells embedded in a myxomatous stroma; actually, certain morphologic patterns became apparent. Many of the cells consisted only of a round, small, vesicular nucleus with very sparse fibrillary cytoplasm. Other cells had essentially the same type of nucleus, but with a much more abundant eosinophilic cytoplasm containing longitudinal fibrils that seemed to flare terminally into separate minute processes. These cells were interspersed with cells of a round or oval form which had nuclei that were both centrally and occasionally eccentrically placed, and had the same type of abundant eosinophilic cytoplasm. This last type of cell has been described by others as being a specific type, although we believe it represents merely a cross section of the eosinophilic elongate form. The final type of cell seen was relatively small and often very elongate. It had much the same shape as the oxyphilic form and, in addition, commonly was multinucleate. The essential difference, however, was in the cytoplasm, which was pale, except for transverse, regularly placed condensations of material that stained brilliantly blue with the phosphotungstic acid-hematoxylin stain. None of the very large tadpole forms were seen which are so characteristic of rhabdomyosarcoma in neoplams of the extremities. The cross-striated cells in this particular tissue showed some tendency to occur in groups and small interlacing bundles. Mitotic figures were few in number.

COMMENT

Considerable medical literature has accumulated covering the general topic of mixed-mesodermal tumors. In 1911, McFarland[1] summarized the world literature on vaginal sarcomas, comprising 101 recorded cases, to which he added one case of his own. In compiling the series, he encountered a total of 119 different descriptive terms. Thirty-four of the cases that had been reported in the previous 57 years he accepted as examples of sarcoma botryoides.

A resurgence of interest concerning sarcomas of the lower urogenital tract has been evidenced by the recent literature. Mostofi and Morse,[2] and Ober and Edgcomb[3] divided the records of the cases filed in the Armed Forces Institute of Pathology. Mostofi and Morse[2] limited their study to ten examples of polypoid

rhabdomyosarcomas (sarcoma botryoides) found in the bladder, and Ober and Edgcomb[3] presented the overlapping study defined as "sarcoma botryoides in the female genitourinary tract," including three of the cases previously reported by Mostofi and Morse.[2] Sternberg, Clark and Smith[4] reported 21 cases under the term of "malignant mixed müllerian tumor" (mixed-mesodermal tumor of the uterus). However, two of these 21 cases occurred in children and lacked the neoplastic epithelial component seen in the tumors of women; these two should more properly be classified as "sarcoma botryoides."

The terminology used in diagnosing the lesions always has been a subject for discussion. Many of the terms have been based either on gross or on microscopic characteristics. If one uses the term based on the gross features, "sarcoma botryoides," the grapelike polypoid excrescences are the only features that must be seen for diagnosis. McFarland[5] in a later study was able to accumulate records of 74 vaginal tumors, 77 vesical neoplasms, and 48 prostatic growths, with such a gross characteristic, most occurring in patients less than 22 years of age. On the other hand, the terms "mixed mesodermal tumor" and "malignant mesenchymoma," although based on histopathologic findings, also are relatively indeterminate. Some of the polypoid lesions in children are not mixed in type so far as can be determined, but are composed of only spindle or stellate cells. A purist would consider all of the neoplasms of the uterus and renal parenchyma embryonically to be mesenchymomas. However, strict adherence to rigid histopathologic criteria may produce compartmented groups that closely resemble each other in their biologic behavior. If cross-striated cells are found in a tumor of the bladder, the neoplasm has been put in the category of the rhabdomyosarcomas of the bladder, a rare group in which less than 25 cases have been recorded. Nevertheless, there is a possibility that many tumors classified in the literature merely as "sarcoma botryoides" may have had such distinguishing cells which were not apparent because of their sparsity. McFarland[5] graphically describes the long search necessary at times to find the cells with cross striations. Because of the difficulty in histopathologic identification we believe that sarcomas of the bladder, prostate, and the lower female genital tract, which are closely related, are appropriately included in the term "sarcoma botryoides," that has come to be favored for this group of polypoid tumors found in young people.

The problems of pathogenesis have been widely discussed in many articles on this subject. The cited references contain brilliant discussions of the pathogenesis. The possibility of misplaced cell rests, variable relationships between stroma of the cervix and endometrium and epithelial components, and totopotentiality of neoplastic cells all in turn have been defended and doubted. We have relegated the debate to the background at the present time as being a philosophical problem.

Therapy either in the form of partial excision or of irradiation has been unsatisfactory. Early diagnosis and radical surgical removal of the tumor seems to offer the best hope for the patient's long survival. Long survivals occasionally have been reported in the relatively few cases that have been treated by this procedure. A course of such therapy has a sound basis and is favored, as the

neoplasms appear to be slow to metastasize. Only one of the ten cases reported by Mostofi and Morse[2] showed evidence of metastases; most of the deaths were associated either with inanition or with secondary urinary tract difficulties. It is possible that death occurred before metastases became evident; however, this biologic behavior is in sharp contrast to the widespread dissemination of the mixed uterine tumors of the older age group. Unfortunately, neither of these two cases presented were believed to be favorable for surgical treatment.

SUMMARY

Two cases of sarcoma botryoides have been reported occurring in children; one in an infant girl, involving the lower genital tract; the other in an infant boy, involving initially the prostatic urethra and later the bladder. Although histopathologically both neoplasms contained cross-striated cells, we have not subclassified them as "rhabdomyosarcomas," but have classified them with "sarcoma botryoides," favoring this term as including all such lesions found in children.

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