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Mixed Tumor of the Vagina
: A Case Report

We report a case of mixed tumor arising in the lower vaginal wall. The patient was a 20-yr-old nullipararous woman. The tumor was relatively well-defined with expansile margin, and showed solid sheets or fascicles of stromal-type spindle cells and ovoid epithelial cells with sparsely scattered nests of mature squamous epithelium and glands lined by mucinous epithelium. Cellular atypia was not conspicuous, however, mitosis was counted upto 6 per 10 high power fields. We examined this tumor immunohistochemically and ultrastructurally and reviewed the articles to identify the histogenesis. Positive reaction for vimenin and cytokeratin of stromal-type spindle cells and presence of desmosome-like structures and tonofilaments on electron microscopic examination suggested the epithelial origin of the stromal-type spindle cells.

Key Words : *Vagina; Mixed Tumor, Pleomorphic Adenoma*

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INTRODUCTION

Benign stromal tumor of the vagina occurs rarely, and include leiomyomas (1), rhabdomyomas (2), and others (3). Mixed tumor of the vagina is a very rare benign tumor described by Brown in 1953 (4). The benign "mixed epithelial tumor" of the vagina showed ductal structures and well differentiated squamous epithelium embedded in a less well differentiated stroma. However, its histogenesis is still not determined. We describe light and electron microscopic findings and immunohistochemistry of this rare tumor to elucidate the histogenesis of the tumor.

CASE REPORT

A 20-yr-old nulliparous woman presented with a painless, nontender vaginal mass. She had complained of a one-month history of itching sensation in perineum. Findings of the magnetic resonance imaging (MRI) of the pelvis revealed a 3.0 × 2.5 cm-sized ovoid mass arising from the posterior wall of lower one third of the vagina. The mass was well-circumscribed and showed homogeneous isodensity on T1 and T2-weighted image. No other gynecologic abnormalities were observed. The mass was excised with overlying skin.

The overlying skin was intact with neither discoloration nor ulceration. Cut surface showed well-demarcated, pale yellowish submucosal nodular mass with rubbery firm consistency (Fig. 1). Neither hemorrhage nor necrosis was seen. Microscopically, the mass was well defined, but unencapsulated with expansile margin (Fig. 2). The tumor was markedly cellular and composed predominantly of stromal-type spindle cells exhibiting small, round to oval to spindle-shaped nuclei with indistinct nucleoli and finely dispersed chromatin and scant, ill-defined cytoplasm. The stromal-type cells were tightly packed and often showed short fascicular arrangement (Fig. 3). Mitoses were counted up to 6 per 10 high-power fields in stromal-type cells. A few islands of mature squamous epithelium and small to medium-sized mucinous glandular structures were noted (Fig. 4). The glandular structures frequently showed squamous metaplasia. These epithelial cell nests smoothly blended with the adjacent stromal-type cells. Mitotic figures were rare in the epithelial cells. Various amounts of collagen fibers laydown with focal hyalinization was seen in the stroma.

On immunohistochemical study using formalin-fixed paraffin-embedded sections, positive reaction for cytokeratin was observed in stromal-type cells as well as epithelial component (Fig. 5A). Vimentin reactivity was noted only in stromal-type cells (Fig. 5B). The stromal-type cells were uniformly negative for smooth muscle actin, desmin, CD34, and S-100 protein. Electron microscopic examination revealed desmosome-like structures and scattered tonofilaments in the stromal-type spindle cells (Fig. 6), but basal lamina and pinocytotic vesicles suggestive of myoepithelial origin were not identified.

DISCUSSION

The term mixed tumor is usually used to designate a benign

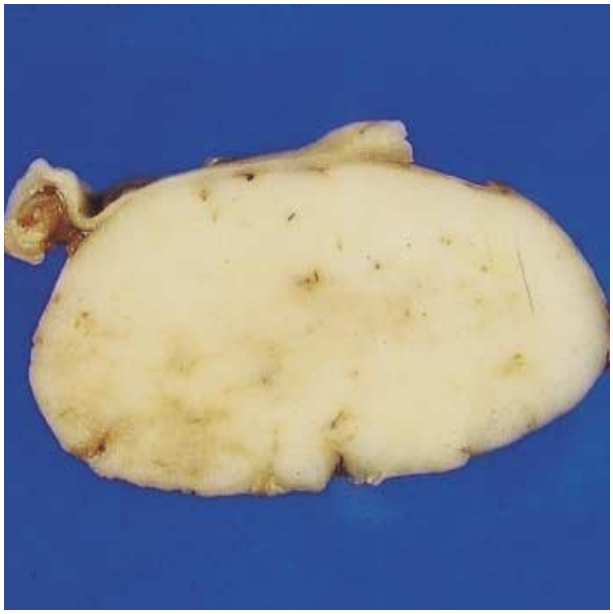

Fig. 1. Cut section reveals a well-circumscribed, pale yellow, and rubbery firm mass, measuring 3.0×2.5 cm. The overlying skin is intact.

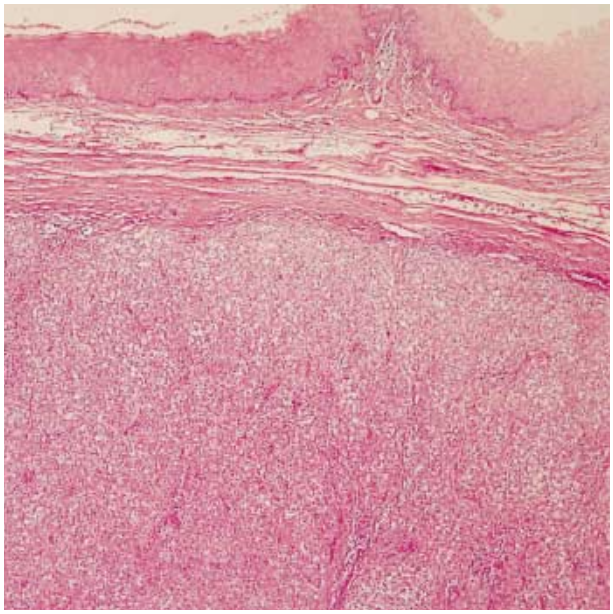

Fig. 2. Mixed tumor is typically well-defined with pushing margin and separated from the overlying epithelium (H&E, ×40).

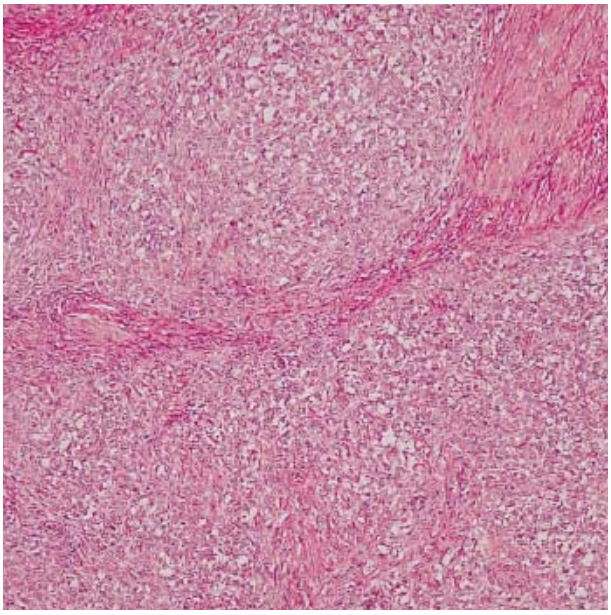

Fig. 3. The stromal-type cells are tightly packed often with short fascicular arrangement (H&E, ×100).

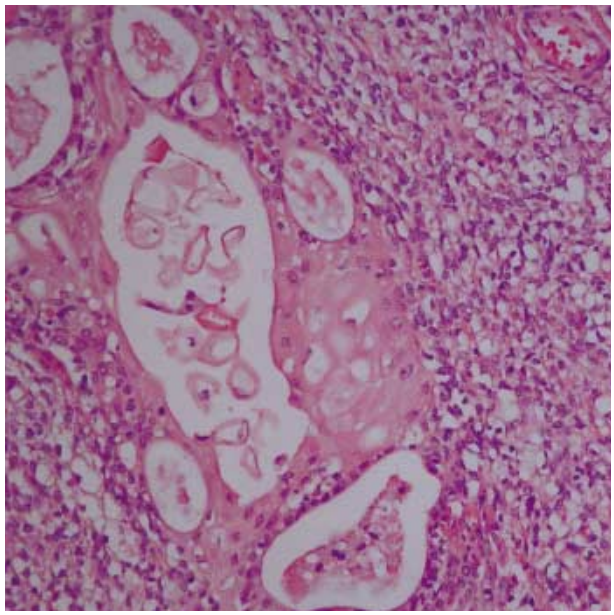

Fig. 4. The glandular component showing squamous metaplasia is embedded in stromal-type spindle cells (H&E, ×200).

neoplasm composed of two distinctive cell types: ductal epithelial cells and myoepithelial cells. The mixed tumor is common in salivary glands, and occurs also in the breast (5), mediastinum (6), trachea (7) and vulva (8). And an origin from myoepithelial cells is the common denominator for the mixed tumors (5-8).

However, the histogenesis of vaginal mixed tumor is debatable. Most of the speculation has focused on a possible embryonic remnant as a source for this unique neoplasm. The embryologic development of the vagina is not still completely understood. Since the vagina is thought to have a dual origin from the fused mullerian ducts and the urogenital sinus (13), both of these embryonic units should be considered in attempting to assign a cell or cells of origin to tumors in this location.

Buntine et al. (9) suggested ectopic müllerian tissue origin and reported two cases of benign müllerian mixed tumors. But the location of this neoplasm in the lowermost portion of the

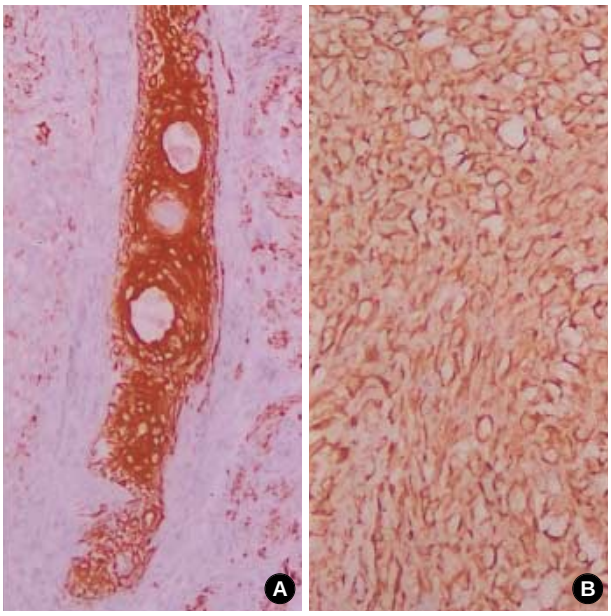

Fig. 5. (A) Immunohistochemical staining for cytokeratin reveals positive reaction in stromal-type cells as well as epithelial components (LSAB, ×100). (B) Vimentin reactivity is observed in stromal-type tumor cells (LSAB, ×200).

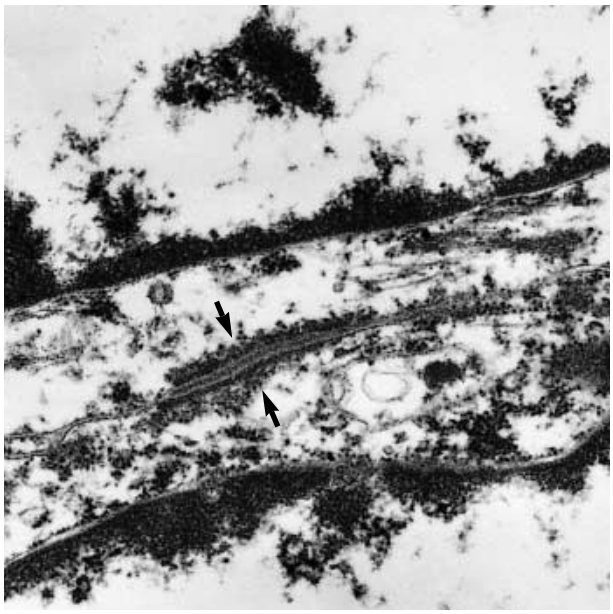

Fig. 6. Electron microscopic examination reveals desmosome-like structures (arrow) and tonofilaments in stromal-type spindle cells (×15,000).

vagina provides evidence against such an origin because müllerian epithelial remnants are least frequently encountered in the lower vagina (10). Actually, vaginal adenosis of müllerian derivation involves predominantly the upper third of the vagina. Watanabe et al. (11) suggested paravestibular gland origin of vaginal mixed tumor, and the paravestibular gland is a derivative of urogenital sinus and is lined by mucinous epithelium resembling that encountered in the tumors reported. However paravestibular glands and tumors have a vestibular location, whereas the vaginal mixed tumors presented as vaginal masses just above the level of hymen.

In addition, the myoepithelial nature of the tumor cells was reported by Watanabe et al. (11) based on ultrastructural and immunohistochemical studies, and the term "pleomorphic adenoma" was suggested. However, no cartilagenous component and negative reaction for S-100 protein and smooth muscle actin. Kawauchi et al. (15) suggested that myoepithelial differentiation of the tumor cells because they showed an immunohistochemical coexpression of cytokeratin and α-smooth-muscle actin and basal lamina and bundles of microfilaments with dense bodies on electron microscopic examination.

However, Sirota et al. (10) showed that the stromal-type cells had ultrastructural evidence of epithelial origin rather than stromal origin; close apposition, cell junctions, and basement membranes. Furthermore, some of the stromal-type cells close to the squamous epithelium contained prominent desmosomes and sparse bundles of tonofilaments.

Branton and Tavassoli (12) studied 10 cases of vaginal mixed tumor immunohistochemically, and nine of them showed positive reaction for cytokeratin, but all were negative for S-100 protein. Two cases of them displayed unequivocal morphologic evidence of epithelial differentiation on electron microscopic examination. They proposed the term "vaginal spindle cell epithelioma (VSCE)" to replace the designation of "mixed tumor" for these neoplasms. And they suggested ultimate origin of the tumor cells to be the urogenital sinus-derived epithelium depending on the preponderance of these neoplasms in or near the hymenal ring, the likelihood of an epithelial migration during vaginal embryogenesis, and the strong immunohistochemical and ultrastructural evidences for an epithelial origin. Fukunaga et al. (14) suggested that this neoplasm is probably originates from the remnant of vestibular gland. In our case, the cytokeratin-positive reaction of spindle cells and desmosome-like structures and tonofilaments on electron microscopic examination were compatible with those of Branton and Tavassoli (12) and Fukunaga et al. (14).

The interrelation of squamous, mucinous, indifferent-appearing epithelial cells and small stromal-type cells is associated with reticulin and collagen deposition. The squamous nests were encountered as neoplastic component because no communication with overlying skin was observed in most cases (10), and the squamous epithelium within the tumors was regarded as a result of metaplasia of the mucinous-glandular epithelial component. There is even less doubt about the neoplastic nature of the mucinous-glandular epithelial component, because neither adenosis nor any other source of glandular epithelium was identified. Some of the squamous cell nests smoothly blended with the adjacent stromal-type cells, which

Table 1. Summary of pathologic findings of mixed tumor of the vagina

Case No. (Ref.)	Size (cm)	Location	Mitosis
1. Brown et al.	5.0	Posterior vaginal wall just above hymen	rare
2. Buntine et al.	?	Vaginal vault	?
3. Sirota et al.(Case 1)	1.5	Hymenal ring	rare to absent
4. Sirota et al.(Case 2)	2.5	Hymenal ring	rare to absent
5. Sirota et al.(Case 3)	3.5	Hymenal ring, posterior vaginal wall	3/10 high-power fields
6. Sirota et al.(Case 4)	3.2	Hymenal ring, lateral vaginal wall	rare to absent
7. Sirota et al.(Case 5)	3.0	Anterior one-third of vagina	6/10 high-power fields
8. Sirota et al.(Case 6)	2.5	Hymenal ring, lateral vaginal wall	rare to absent
9. Sirota et al.(Case 7)	5.0	Posterior vaginal wall	rare to absent
10. Sirota et al.(Case 8)	2.0	Posterior vaginal wall	rare to absent
11. Fukugana et al.	2.5	Just above the hymenal ring, posterior wall of the lower vagina	absent
12. Nakashima et al.	1.5	Posterior vaginal wall	?
13. Kawauchi et al.	2.0	Posterior vaginal wall	?
14. The present case	3.0	Posterior vaginal wall, lower one-third	6/10 high-power fields

suggested that both the squamous and stromal-type cells may have arisen from a single multipotential cell (10).

Mixed tumor of the vagina is a benign neoplasm, and almost all reported cases are small, well-circumscribed and show few mitotic activities and little cellular pleomorphism (Table 1). However, mitoses were counted up to 6 per 10 high-power fields in our case even though there were no abnormal forms. Sirota et al. (10) also reported two cases exhibiting 3 and 6 mitoses per 10 high power fields, respectively, and the mitotic count had no prognostic significance. Mixed tumor should be differentiated from other tumorous lesions, e. g., aggressive angiomyxoma, solitary fibrous tumor, malignant mixed tumor and malignant tumor of the vagina resembling synovial sarcoma. Aggressive angiomyxoma and solitary fibrous tumor are usually ill-defined and less cellular than a mixed tumor of the vagina and contain no epithelial component. Although malignant mixed tumor and malignant tumor of the vagina resembling synovial sarcoma show epithelial and mesenchymal components, they occur in the upper part of the vagina and can show cellular atypia, frequent mitosis, and the absence of squamous epithelium. Fukunaga et al. (14) reported one case of vaginal mixed tumor with diploid DNA content and low S-phase fraction. This flow cytometric result seems to support a favorable clinical course for vaginal mixed tumor.

Most of the reported cases have been treated by simple excision. There was no report of metastasis, but three cases recurred. In the recurrent cases, no unique features other than apparent incomplete excision were noted. Thus complete excision and careful follow-up are recommended.

In conclusion, vaginal mixed tumor is a benign neoplasm originated from the epithelial cells of the remnant of vestibular gland and should not be confused with mixed tumor at other anatomic location. Familiarity with this rare tumors by gynecologists and pathologists is essential in avoiding misdiagnosis.

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