Spindle Cell Epithelioma of the Vagina Shows Immunohistochemical Staining Supporting Its Origin From a Primitive/Progenitor Cell Population

Henry Skelton, MD; COL Kathleen J. Smith, MC, USA

Spindle cell epitheliomas of the vagina (SCEVs) coexpress epithelial and mesenchymal markers and were first described as a “mixed tumors of the vagina.” However, unlike mixed tumors of other organs, which are believed to originate from myoepithelial cells, SCEVs neither immunohistochemically nor ultrastructurally show features of myoepithelial cells. The present expanded battery of immunohistochemical stains is presented on this rare tumor, including cytokeratin AE1/AE3, CK7, CK20, S100 protein, epithelial membrane antigen, α-smooth muscle actin, desmin, CD34, CD99, Bcl-2, vimentin, estrogen and progesterone receptors, and Ki-67. There was minimal expression of α-smooth muscle actin and negative staining with S100 protein, with coexpression of cytokeratins and vimentin and expression of estrogen and progesterone receptors, as previously reported in SCEVs. In addition, diffuse expression of CD34, CD99, and Bcl-2 immunohistochemical stains was found, which has not previously been reported. The coexpression of CD34, CD99, and Bcl-2 in SCEVs is consistent with its origin from a primitive/progenitor cell population.

(Arch Pathol Lab Med. 2001;125:547±550)

Spindle cell epitheliomas of the vagina (SCEVs) or “mixed tumors of the vagina” have some important differences from mixed tumors that arise in other areas, such as skin, salivary glands, breast, mediastinum, and trachea.1,3 All the latter tumors appear to arise from myoepithelial cells.2,5 However, an origin of myoepithelial cells was questioned in the largest review of SCEVs by Branton and Tavassoli.1 They pointed out that SCEVs are well circumscribed but not encapsulated and are characterized by proliferation of spindle cells admixed with clusters of cells with an epithelioid appearance and sometimes with squamous differentiation.1 In addition, SCEVs express both cytokeratin and vimentin and ultrastructurally show tonofilaments not only within recognizable aggregates of squamous cells but also within the spindle cell population.1 However, α-smooth muscle actin expression occurs mainly in the supportive stromal myofibroblastic cell and not in the tumor cells.1,4,5 This finding and lack of expression of S100 protein, another marker of myoepithelial cells, suggest that the cell of origin is not a myoepithelial cell.4

An additional case of a SCEV with a broader spectrum of immunohistochemical stains is presented that supports the origin of these tumors from a progenitor cell population.

REPORT OF A CASE

The patient was a 32-year-old woman who had not seen a physician for at least 7 years. She presented with a complaint of a mass in the vagina. She reported no pain or other symptoms. She had no prior history of tumor or gynecologic problems. During a gynecologic examination, a circumscribed firm nodular mass was found in the lower posterior vaginal wall. The lesion was surgically removed and submitted for pathologic examination. Six months after excision, the site was healed with no evidence of recurrence.

Histopathologic Findings

The biopsy specimen measured approximately 2 × 4 cm in greatest dimensions and appeared completely excised on the sections examined. Biopsy sections showed a well-circumscribed but not encapsulated tumor (Figure 1). The margins were expansile and located within a few millimeters of the overlying epithelium (Figure 2). The tumor was composed of a spindle cell population, with some more epithelioid cells, but no component that showed definitive epithelial features or squamous differentiation. The spindle cells were small, with sparse, faintly granular cytoplasm and poorly defined cell borders (Figures 1 and 2). The nuclei were dark, slightly vesicular, and ovoid and had fine chromatin. In some areas the spindle cells showed no pattern, whereas in other areas the cells formed cords and had a more epithelioid appearance (Figure 2). In some areas, there was hyaline matrix material between tumor cells (Figure 2). Small vessels were seen throughout the tumor, some of them branched.

Immunohistochemical Stains

The tumor expressed vimentin (BioGenex, San Ramon, Calif), CD34 (QBEND 10, BioGenex), CD99 (Signet, Dedham, Mass), and Bcl-2 (Dako, Carpinteria, Calif) diffusely (Figures 3 through
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Department of Dermatology, National Naval Medical Center, Bethesda, MD

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Figure 1. Biopsy specimen showing a well-circumscribed but not encapsulated tumor with numerous small vessels throughout, some branched. There are spindle cells and more epithelioid cells. The cells were small, with sparse, faintly granular cytoplasm and poorly defined cell borders. Nuclei are dark, slightly vesicular, and ovoid and have fine chromatin. In some areas there is no pattern, whereas in other areas the cells formed cords and are more epithelioid in appearance. In some areas, there is prominent hyaline matrix material between tumor cells (hematoxylin-eosin, original magnification ×100).

Figure 2. Higher-power view of the biopsy specimen shown in Figure 1 (hematoxylin-eosin, original magnification ×200).

Figure 3. Immunohistochemical staining for CD34 showing diffuse staining of tumor cells (original magnification ×100).

Figure 4. Immunohistochemical staining for CD99 showing diffuse staining of tumor cells (original magnification ×200).

Figure 5. Immunohistochemical staining for bcl-2 showing diffuse staining of tumor cells (original magnification ×200).

Figure 6. Immunohistochemical staining for CK7 showing positive staining in some of the tumor cells (original magnification ×200).
smooth muscle actin and/or S100 protein. In addition, tin and cytokeratin but, at least in areas, coexpress expressed mainly in progenitor cells and long-lived cells.

Bcl-2 has a restricted distribution and is believed to be a marker of mesenchymal origin. Although they were first described in the pleura, they have since been described arising in other serosal surfaces and many other sites. Morphologically, SFTs are well-circumscribed but not encapsulated tumors composed of bland spindle-shaped cells with several architectural appearances, including a storiform pattern, fascicles of spindle cells with a wavy, neural appearance, a patternless pattern, abundant myxoid matrix in areas, densely cellular fascicles of spindle cells with a herringbone pattern, and SFTs with atypical multinucleated giant cells admixed with the spindle cell proliferation. Mitoses and areas of necrosis are not identified except in the densely cellular variants, where there may be some nuclear atypia and scattered mitotic figures. The SFTs are characterized by prominent vascularity, often with branching vessels as seen in hemangiopericytomas and SVEs. Although scant collagen may be seen in SFTs, more advanced degrees of collagenization with spindle cells separated by strands of ropelike collagen may be seen. Although this collagenized pattern is distinctive, it may be mistaken for the eosinophilic matrix material seen in SVEs. In addition, SFTs show strong CD34 reactivity and CD99 expression, and they are negative for S100 protein, HMB-45, and α-smooth muscle actin, but they show no morphologic, immunohistochemical, or ultrastructural evidence of epithelial derivation. Similarly, hemangiopericytomas and schwannomas may show diffuse staining for CD34 but lack morphologic, immunohistochemical, and ultrastructural evidence of an epithelial origin. In addition, schwannomas express S100 protein and are encapsulated.

Mixed epithelial-mesenchymal tumors of female genital tract are rare. By definition, all these tumors contain intimately admixed epithelial and mesenchymal elements by standard light microscopic examination. They may occur as both benign (adenofibroma and adenomyoma variants, an intermediate variant [atypical polypoid adenomyoma]) and malignant variants (adenosarcoma, carcinosarcoma [malignant mixed mesodermal tumor, malignant mixed Mullerian tumor], and carcinofibroma). Unlike SVEs, mixed epithelial-mesenchymal tumors occur in the uterus as polypoid, noncircumscribed, usually solitary masses. Clinically, they present with vaginal bleeding. Adenofibromas show epithelium that is usually of proliferative endometrial type; however, a flattened single cell cuboidal cell can be seen admixed with a benign variably fibrous stroma. Adenomyomas are characterized by an intimate admixture of benign endometrial glands without architectural complexity and a stroma composed of smooth muscle and fibrous tissue. Adenosarcomas show an admixture of a benign epithelial component and a sarcomatous component, whereas carcinosarcomas are characterized by an admixture of malignant epithelial and mesenchymal elements, and carcinofibromas are composed of a malig-
nant epithelial component and benign fibrous component. The malignant components of these tumors show an aggressive infiltrative growth pattern and metastatic potential.

Rare malignant mixed tumors of the vagina do occur. They show a biphasic pattern of glands and spindle cells, which resemble synovial sarcoma. These tumors lack the circumscription seen in SCEV with more cytologic atypia and a higher mitotic rate. Malignant mixed tumors of the vagina have been proposed to arise from the Gartner ducts or related mesonephric rests.

The origin of SCEVs has been proposed to be from a possible embryonic remnant. Although the embryologic development of the vagina is controversial, the hymenal ring appears to be derived from the urogenital sinus. The greatest controversy exists on the relative contributions of the mullerian ducts and urogenital sinus to the development of the vagina. Some people believe that the proximal two thirds to four fifths of the vagina is derived from the mullerian ducts, whereas the urogenital sinus forms the remaining distal portion. Still others believe that the mullerian ducts descend to the level of the hymenal ring, fuse, and then are invaded distally by urogenital sinus tissue that ultimately forms vaginal epithelium.

The second theory suggests that foci of primordial vaginal epithelium may migrate and develop aberrantly, resulting in abnormal growths later in adult life. The expression of both epithelial and mesenchymal markers is well known with mullerian-derived tissue. Mullerian-derived tumors express cytokeratin AE1/AE3, vimentin, and CK7 with weak to minimal CK20 staining. Wolffian adnexal tumors, so-called female adnexal tumor of probable Wolffian origin, also show varying morphologic structures with solid (spindle cells), tubular, and retiform, and multicystic (spaces lined by cuboidal and attenuated cells) patterns. Wolffian adnexal tumors also coexpress vimentin and AE1/AE3 and have been shown to express CK7 with minimal expression of CK20.

Since urothelial epithelium expresses both CK7 and CK20 and the tumor we examined showed only CK7 staining, this may favor a Mullerian or possible Wolffian origin. Ki-67 expression showed only a small percentage of the cells were cycling, and to date none of these tumors have metastasized. Complete surgical excision is considered curative.

Most mixed tumors demonstrate an orderly sequence of transformation or metaplasia from an epithelial to a mesenchymal phenotype and in many cases show the development of relatively mature epithelial and/or mesenchymal elements. The SCEVs on the other hand appear to arise from a primitive/progenitor cell that coexpresses CD34, CD99, Bcl-2, cytokeratin, and vimentin and shows little or no mature epithelial or mesenchymal components.

References