Clinical Experience With Conservative Surgery for Vaginal Endodermal Sinus Tumor

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Two cases of vaginal endodermal sinus tumor (EST), a rare pediatric malignancy, were managed with conservative surgery followed by adjuvant chemotherapy. The first case involved a 9-month-old girl with EST of the vagina, who was treated with a partial vaginectomy and VAC regimen (vincristine, actinomycin D, cyclophosphamide) during a 2-year period. The serum alpha-fetoprotein (AFP) level returned to normal after excision of the tumor, and it remained normal throughout the treatment period. There was no evidence of disease 30 months after diagnosis. The second case involved an 8-month-old girl with EST of the vagina, who was treated with local excision of the mass through a vaginotomy. The VAC regimen was administered, but the serum AFP level remained elevated. A follow-up abdominopelvic computed tomography scan, taken 4 months after the operation, showed local recurrence of the tumor. The VAC regimen was then changed to a BEP regimen (bleomycin, etoposide, cisplatin). The serum AFP level returned to normal after 2 courses of the new regimen, and no tumor was visible on the follow-up magnetic resonance imaging study. For vaginal EST, primary conservative surgery and adjuvant chemotherapy are attractive measures to preserve both reproductive and sexual function. The extent of conservative surgery requires at least a partial vaginectomy. Simple tumor excision may not be adequate to achieve cure or to prevent local recurrence, even with adjuvant chemotherapy. The serum AFP level is useful for diagnosing and monitoring vaginal EST in the infant.

CASE REPORTS

Case 1

A previously healthy 9-month-old girl presented with gross hematuria of 2 weeks' duration. The physical examination results were unremarkable and the external genitalia appeared normal. Routine urinalysis showed hematuria and pyuria. Results of other laboratory studies at the time of admission were normal.

Combined digital rectal and vaginal examination with the patient under general endotracheal anesthesia showed a firm 3-cm mass in the posterior vaginal wall, 3 cm from the introitus. A vaginal biopsy specimen showed malignant cells (reported as clear-cell carcinoma) on the frozen section. The preoperative serum alpha-fetoprotein (AFP) level was 19,000 IU/mL (normal, 20 IU/mL). Abdominopelvic ultrasonography showed a 3.7- × 3.0-cm echogenic solid mass in the vagina. An abdominopelvic magnetic resonance imaging study showed a multilobulated solid mass confined to the distended vagina, with no evidence of distant metastasis (Fig 1).

After catheterization of the bladder, an exploratory laparotomy was performed through a Pfannenstiel incision. The upper vagina was filled with an obvious tumor mass. No tumor was seen penetrating the outer surface of the vaginal wall, nor did there appear to be any intraabdominal metastases. The rectum and bladder were separated from the vagina. The anterior vaginal wall was incised transversely. A 3-cm multinodular triable mass originating in the posterosilateral wall of the lower vagina was observed. Segmental resection of the lower vagina, including the tumor mass (partial vaginectomy), was performed with end-to-end anastomosis of the vagina. An abdominopelvic magnetic resonance imaging study showed a multinodular solid mass confined to the distended vagina, with no evidence of distant metastasis (Fig 1).

Histologically, glomeruloid bodies (Schiller-Duval bodies) were observed, characterized by papillae with a single central vessel.

INDEX WORDS: Endodermal sinus tumor, Schiller-Duval body, serum alpha-fetoprotein.
Fig 1. Preoperative sagittal MRI of case 1 shows a 4 × 3-cm multilobulated solid mass (M) confined to the distended vagina.

Microscopic examination showed PAS-positive hyaline globules (Fig 2). The immunohistochemical study was positive for AFP. The pathological diagnosis of EST was made.

The postoperative recovery was uneventful. The patient received 24 cycles of chemotherapy with a VAC regimen (vincristine, actinomycin D, cyclophosphamide) during a 2-year period. The serum AFP level decreased rapidly and remained normal (Fig 3). The patient is alive, without evidence of disease, 30 months after the initial diagnosis was made.

Case 2
An 8-month-old girl presented with bright red spotting on her diaper of 3 weeks’ duration. Her antenatal and subsequent medical history was unremarkable. The physical findings were normal except for a firm mass detected at a depth of 3 cm, palpable through the anterior rectal wall. The results of all routine laboratory studies at the time of admission were normal.

Pelvic ultrasonography showed a 2-cm homogeneous, hypoechoic, round, solid mass in the vagina. Abdominopelvic computed tomography showed a multilobulated solid mass confined to the vagina, without evidence of distant metastases (Fig 4). The preoperative serum AFP level was 848.1 IU/mL. The preoperative diagnosis was vaginal EST.

After catheterization of the bladder, an exploratory laparotomy was undertaken through a Pfannenstiel incision. No tumor was seen penetrating the outer surface of the vagina. There was no evidence of metastatic involvement. The anterior vaginal wall was incised transversely. A 2.5-cm multinodular friable mass arose from the posterolateral wall of the lower vagina. Simple tumor excision was performed, with preservation of the vaginal wall. The pathological diagnosis confirmed EST. After the operation, three courses of chemotherapy (VAC regimen) were administered, but the serum AFP levels did not return to normal and increased slowly. Abdominopelvic computed tomography performed 4 months postoperatively showed local recurrence of the tumor. The chemotherapy was changed to a BEP regimen (bleomycin, etoposide, cisplatin). The serum AFP level returned to normal after two cycles of the new regimen. Presently, 7 months after resection, the patient will receive the sixth cycle of the BEP regimen, and her serum AFP level remains normal.

DISCUSSION

EST is the most common malignant germ cell tumor in children. In females, EST usually is encountered in the ovary, either in the pure form or as a component of a mixed germ cell tumor. Infantile vaginal EST is a rare tumor that exhibits distinctive clinicopathologic features. The tumor develops exclusively in children under 3 years of age. The clinical presentation includes a history of vaginal discharge, usually bloody or blood-tinged. Vaginal examination (best performed with the patient under anesthesia) often shows a polypoid and friable lesion arising from the vagina or cervix. With this clinical presentation, it is not surprising that many cases of EST are misdiagnosed as sarcoma botryoides. As noted by Rezaiazadeh and Woodruff, the similarity between EST and clear cell carcinoma also contributes, pathologically, to the misdiagnosis of clear cell carcinoma. In our first case, the frozen section diagnosis was interpreted as clear cell carcinoma. The histological diagnosis of EST in both cases was based on the finding of Schiller-Duval bodies and the demonstration of AFP by immunohistochemical staining.

The usefulness of monitoring the serum AFP level in the management of patients who have EST or mixed germ cell tumors containing a component of EST has been well established. In case 1, the preoperative elevated AFP level returned to normal and remained there after excision of the tumor, without evidence of tumor recurrence 30 months after the diagnosis was established. In case 2, the
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Serum AFP level did not return to normal and became elevated when the tumor recurred. In patients suspected of having vaginal EST, an elevated serum AFP level may be a diagnostic tumor marker and also may be used to monitor the course of the disease (eg, recurrence).

As with other rare disorders, the ideal management of vaginal EST in infancy remains an enigma. There are too few cases available to permit a clear understanding of the natural history of this malignancy. Based on limited data, vaginal EST is both locally aggressive and capable of metastasizing via hematogenous and lymphatic pathways. Untreated patients have died within 2 to 4 months of presentation.8 Beller et al4 reviewed the literature in 1979 and collected 25 cases of vaginal EST. Young and Scully6 expanded the number of cases to 41 cases (seven additional cases from the available literature, 9 patients of their own). In their review6 of the 32 previously reported cases, 18 (56.25%) patients died of the disease despite radical surgical therapy. The prognosis and therapy of EST involving the vagina and other sites have changed significantly in recent years because of the advent of effective chemotherapeutic agents.3,4,8–11 Before 1965, local therapeutic modalities (surgery and/or irradiation) were employed exclusively, with universal failure.4 Radical surgery, ranging from vaginectomy to total pelvic exenteration, produces loss of sexual and reproductive function and possibly loss of the bladder and rectum. Long-term radiation effects to the pelvis include castration, abnormal growth of pelvic bones, aseptic necrosis of femoral heads, and destruction of bone marrow.12–14 Radiation also may be associated with a second primary malignancy in the irradiated field.

Vawter10 introduced the use of chemotherapy for EST in his report of two patients with recurrent and metastatic disease after surgery. Chemotherapy subsequently appeared as an integral part of most treatment regimens for EST used since 1970.9,11,15,16 Vaginal EST is responsive to a combination of cytotoxic agents. Among chemotherapeutic treatments, the VAC regimen is known to be the most useful for this tumor.5,6

Conservative surgery (local excision or partial vaginectomy) plus combination chemotherapy is recommended because it has improved prognosis, has acceptable complication rates, and preserves childbearing potential.5 The goal of conservative surgery is to eradicate local tumor cells and make subsequent chemotherapy more effective. Incomplete excision would leave the tumor in the vaginal wall and would result in local recurrence even with effective chemotherapy. In case 2, with local excision, the tumor recurred after 4 months even with the VAC regimen. The recurrent tumor was resistant to further VAC
treatment, necessitating more toxic agents (BEP) to control the disease. In case 1, partial vaginectomy was performed with a free resection margin.

In the treatment of vaginal EST, primary conservative surgery and adjuvant chemotherapy are highly attractive methods of preserving reproductive and sexual function. We believe that the extent of conservative surgery should require at least partial vaginectomy. Simple tumor excision may not achieve cure or prevent local recurrence even with effective chemotherapy. The serum AFP level is a useful marker for diagnosis and for monitoring the recurrence of vaginal EST in infants.

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REFERENCES

1. Teilum G: Endodermal sinus tumors of the ovary and testis: Comparative morphogenesis of the so-called mesonephroma ovarii (Schiller) and extraembryonic (yolk sac-allantonic) structures of the rat’s placenta. Cancer 12:1092-1105, 1959