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Michael L. Hicks
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Management of Advanced Endodermal Sinus Tumor of the Ovary with Preservation of Reproductive Function

Michael L. Hicks, MD,* Shari L. Maxwell, MD,‡ and Wooshin Kim, MD†

Endodermal sinus tumor of the ovary occurs primarily in children and young adults. This tumor is classified as a germ cell tumor which comprises approximately 5% of all ovarian tumors. In the past, patients with this highly malignant tumor had low survival. However, with the evolution of effective adjunctive chemotherapeutic regimens, specifically vincristine, actinomycin D, and cyclophosphamide, survival rates have improved. In an attempt to continuously improve survival rates, other combination chemotherapeutic regimens are currently under investigation.

Unlike epithelial ovarian malignancies, endodermal sinus tumor can be monitored by a specific tumor marker, alpha-fetoprotein (AFP). Serum levels of AFP can be followed from the preoperative period through the course of chemotherapy. When elevated, AFP has excellent predictability that persistent disease is present. Because this disease presents primarily in young females, preservation of reproductive function is of utmost importance. We report a case of advanced endodermal sinus tumor which was managed with conservative surgery only, followed by radical combination chemotherapy, resulting in preservation of normal reproductive function and total resolution of disease documented by second-look laparotomy. (Henry Ford Hosp Med J 1990;38:76-8)

Endodermal sinus tumor of the ovary is classified as an ovarian germ cell tumor. Germ cell tumors comprise approximately 5% of all malignant ovarian tumors. Endodermal sinus tumors occur primarily in children and young adults and are characterized by their highly malignant nature.

The tumor was initially described by Schiller (1) to be of mesonephric origin but was later shown by Teitum (2,3) to originate from extraembryonal germ cells. Histologic sections demonstrate papillary projections with a peripheral lining of neoplastic cells with associated blood vessels (Schiller-Duval body) (Fig 1).

In the past, early treatment modalities were unsuccessful because of the aggressive nature of these tumors. The prognosis was poor and survival rates low, ranging from 9% to 13% (4-6). To improve survival rates, several therapeutic regimens have been evaluated over the past decade and some have been incorporated in the management of patients with these tumors.

We report a case of advanced endodermal sinus tumor managed with conservative surgery followed by radical combination chemotherapy, resulting in preservation of normal reproductive function and total resolution of disease documented by second-look laparotomy.

Case Report

An 18-year-old, gravida 4 para 1/0/3/1, female presented with abdominal pain of one-month duration associated with nausea and vomiting. Her medical history was unremarkable. Physical examination revealed a palpable 16 cm abdominal mass with associated tenderness in both lower quadrants and voluntary guarding throughout the entire abdomen. Pelvic examination confirmed the mass to be centrally located, extending into the cul-de-sac, and solid in nature. Ultrasound findings showed a 13 X 10 cm solid mass extending into the cul-de-sac. No ascites were noted.

Exploratory laparotomy was performed, and 1,200 mL of ascitic fluid was removed from the abdominal cavity. Inspection of the pelvis revealed a 20 X 20 cm mass which was noted to be posterior to the uterus and extending into the cul-de-sac. The mass was contiguous with the right ovary and adherent to the sigmoid, colon, rectum, posterior uterine wall, and cecum. The left ovary and tube were normal. Intraabdominal biopsies sent for frozen section were consistent with ovarian malignancy. The patient underwent right salpingo-oophorectomy, omentectomy, lysis of adhesions, appendectomy, and paraaortic and pelvic lymph node biopsies, but tumor debulking was suboptimal. Pathology revealed endodermal sinus tumor with surgical staging consistent with stage IIIC disease. Postoperative recovery was unremarkable and the patient was discharged home on the fifth day.

Five days later, the patient was readmitted for initial chemotherapy induction which consisted of bleomycin, 20 U/m² intravenous weekly, etoposide (VP-16), 100 mg/m² intravenous daily for five days, and cisplatin, 20 mg/m² intravenous daily for five days (BEP regimen). All agents were repeated weekly for nine weeks. Maintenance chemotherapy, given after BEP induction, consisted of vincristine, 1.5 mg/m² (single dose not to exceed 2 mg) intravenous at two-week intervals for a total of six doses, and actinomycin D, 350 mg/m², and cyclophosphamide, 150 mg/m², intravenous daily for five days at four-week intervals for a total of three doses. Except for mild gastrointestinal and mucocutaneous toxicity, the patient tolerated the chemotherapy well.

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*Formerly Department of Obstetrics and Gynecology, Henry Ford Hospital. Currently Department of Gynecology Oncology, Roswell Park Memorial Institute, Buffalo, NY.
‡Department of Obstetrics and Gynecology, Henry Ford Hospital.
Address correspondence to Dr. Hicks, Department of Gynecology Oncology, Roswell Park Memorial Institute, 666 Elm Street, Buffalo, NY 14266.
The second-look laparotomy, performed after completion of the chemotherapy, was negative. The patient currently has normal menses and no clinical evidence of disease.

Discussion

The most common clinical findings with endodermal sinus tumor are abdominal pain, abdominal-pelvic mass, fever, and occasional vaginal bleeding. Complaints of pain are usually of less than one-week duration but can be acute in onset secondary to rupture or torsion of the ovarian tumor. The median age at presentation is approximately 19 years.

Intraoperative management principles are the same as with epithelial ovarian tumors. The surgeon’s goal is to achieve appropriate cytoreduction by removing the bulk of the tumor mass and to stage the disease adequately. Appropriate staging is accomplished by obtaining cytological washings of the peritoneal cavity, performing omentectomy, paraaortic and pelvic lymph node biopsies, and a detailed evaluation of the liver, diaphragmatic surface, and abdominal and pelvic peritoneum. Cytoreduction is essential to maximize tumor response to chemotherapy, whereas surgical staging allows the clinician to develop the prognosis.

In the two largest series analyzing the management of endodermal sinus tumor, both Gershenson et al (5) and Kurman and Norris (6) showed that surgery alone was not sufficient in improving patient survival. Reported mortality rates at 24 months were 75% and 82%, respectively. In an attempt to improve survival rates, radiation therapy was incorporated in the postoperative period but was shown to be ineffective with mortality rates of 100% in both series. Not until the use of combination chemotherapy with vincristine, actinomycin D, and cyclophosphamide (VAC) was there any significant impact on patient survival. In these two series, the survival rate with VAC was 72% (5) and 75% (6) at 120 months.

Although the use of adjunctive chemotherapy with the VAC regimen has been shown to improve survival, these rates were demonstrated primarily in earlier stages of the disease process (stages I and II). There have been reports of VAC failures in stages III and IV. This has stimulated the search for other management options in the treatment of advanced stages of endodermal sinus ovarian tumors. Alternative management regimens are currently being investigated in phase II clinical trials. The use of a different combination of chemotherapeutic agents has been suggested. Because vinblastine, bleomycin, and cis-platinum (VBP) have been shown to be effective in the treatment of testicular cancer (7), some propose that VBP may be more effective than VAC in advanced stages of endodermal sinus tumors and in cases where VAC has failed (8). Whether VBP will become the recommended first-line of chemotherapy or used for treatment salvage only is still under investigation. VBP is far more toxic than VAC, and cases of drug-related deaths from VBP have been reported.

The use of induction chemotherapy prior to maintenance chemotherapy has also been recommended and was used in the management of the present case. The purpose of this regimen is to elicit a more effective response against endodermal sinus tumor but with less toxicity. Etoposide (VP-16) is substituted for vinblastine and has been shown to reduce neurologic toxicity without compromising efficacy.

Because the disease presents primarily in young females, another problem the clinician must address is preservation of reproductive function. If the extent of disease appears to be only stage I at the time of initial laparotomy, unilateral salpingo-oophorectomy may be as effective as bilateral salpingo-oophorectomy with total abdominal hysterectomy (8). Slayton et al (8) reported that 21 of 30 patients resumed normal menses and that three patients became pregnant after VAC chemotherapy postoperatively. Gershenson et al (5) reported that after conservative surgery and VAC chemotherapy three patients subsequently had five normal pregnancies. With a more radical course of chemotherapy such as BEP induction followed by VAC in ad-
advanced disease states, conservative surgery can be done, allowing reproductive function to continue without compromising treatment.

The need for second-look laparotomy in patients with endodermal sinus tumor has not been formally established. These patients are followed during the postoperative and chemotherapeutic period by testing serum alpha-fetoprotein (AFP) levels. In our case, serum AFP levels were followed postoperatively and during the course of combination chemotherapy (Fig 2).

Several studies have demonstrated that patients with normal AFP levels after chemotherapy had no evidence of persistent disease at the time of second-look laparotomy (5,8,9). These data suggest that normal serum AFP levels may indicate no need for a second-look laparotomy. However, Curtain et al (10) recently reported two patients with normal serum AFP levels post-chemotherapy who had residual tumor noted during second-look laparotomy. Although there are only two reported cases of persistent disease following chemotherapy, there are some benefits of second-look laparotomy, including early detection of subclinical or persistent disease and documentation of complete versus partial response postchemotherapy.

When preservation of reproductive function is a major concern, we recommend that endodermal sinus tumor of the ovary be managed with conservative surgery followed by aggressive chemotherapy. AFP serum levels should be followed throughout the course of treatment. With this type of management, fertility can be preserved, survival improved, and identification of tumor response to treatment accurately monitored.

References


Fig 2—Relationship between AFP levels (tumor markers) before, during, and after BEP induction and VAC chemotherapy.