# Primary endodermal sinus tumor of the vulva in a 52-year-old woman with long-term survival: a case report

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**Summary**

A postmenopausal 52-year-old Japanese woman with a 5-month history of a right labial tumor was referred to the Department of Obstetrics and Gynecology. The resected tumor had been diagnosed as a primary endodermal sinus tumor of the vulva with pT2N0M0 in 2001. Six courses of adjuvant chemotherapy using bleomycin, etoposide and cisplatin were administered. The patient was free of recurrence or metastasis 67 months after the initial treatment.

## Introduction

Endodermal sinus tumors (ESTs) are extremely rare as extragonadal tumors. To date only nine cases of vulvar ESTs have been reported [1-4], with the first report in 1978. In general, such vulvar neoplasms, especially when the tumor size is greater than 5 cm or the inguinal lymph node is positive, are considered to possess an aggressive growth and a poor prognosis. The accumulation of such cases, including the present one, are shown in Table 1. All other cases, except for the present case, were under 30 years of age.

Extragonadal germ cell tumors are regarded as having a worse prognostic course than primary ovarian germ cell tumors. It is known that combination chemotherapy with vincristine, actinomycin and cyclophosphamide is partly benefical for primary ovarian germ cell tumors, but this regimen is not effective for ESTs which derive from the vulva [1, 2]. Recently, platinum-based chemotherapy (with bleomycin and etoposide or vinblastine) has become a standard treatment for disseminated ESTs [5].

We herein report a postmenopausal case of a primary EST of the vulva in which we describe the treatment course and long-term disease-free survival.

## Case Report

A postmenopausal 52-year-old Japanese woman, gravida two, para two, was referred to the Department of Obstetrics & Gynecology at Ibi General Hospital in May 2001 with a 5-month history of a right labial tumor. The tumor measured 3 cm in diameter and was localized in the right greater labium. The tumor was resected in June 2001. The resected tumor, measuring 3.5 x 3.0 x 3.0 cm, was pseudoencapsulated and had a yellowish-white color at the cut-surface. Microscopic findings included aggregations of polygonal epithelioid cells mixed with focal glandular and cystic areas (Figure 1A), and Schiller Duval bodies (Figure 1B). Immunohistochemically, the expression of a-fetoprotein (AFP) was confirmed in the tumor cells (Figure 1B). The tumor was diagnosed as an EST. The serum AFP level before tumor resection was 50.5 ng/dl (normal < 5 ng/dl). The patient was next referred to the Department of Obstetrics & Gynecology, Gifu University Hospital. No palpable inguinal lymphadenopathy was observed. A pelvic examination revealed no abnormalities, with the exception of the surgical vulvar wound. Her past medical or family history was not remarkable. She had not received any hormone therapy. To rule out the possibility of metastases from other primary tumors, a pelvic MRI, abdominal and thoracic CT, and whole body scintigraphy were performed, but all showed negative findings. The patient immediately underwent a modified radical vulvectomy around the previous surgical area with right inguinal lymphadnectomy in July 2001. The final postoperative diagnosis for this case was a primary EST of the vulva with pT2N0M0.

Six courses of adjuvant chemotherapy with 50 mg/m$^2$ IV of cisplatin on day 1, 80 mg/m$^2$ of etoposide twice on days 1 and 3, and 20 mg/m$^2$ of bleomycin on day 1 [body area: 1.33 m$^2$] were performed every three to four weeks from August 2001 to February 2002 [5]. No intolerable adverse effects were observed. Serum AFP levels remained under 5 ng/dl after the vulvectomy. The patient has demonstrated an uneventful course for 67 months from the initial treatment.

## Discussion

Extragonadal germ cell tumors are rare and most arise in the sacrococcygeal region of infants. The sites include the mediastium, intracranium, retroperitoneum and neck. Over 70% of these tumors develop in females, whereas about 50% occur in infants. The majority of extragonadal tumors in the external genital tract occur in the vagina or uterine cervix. Most cases tend to develop in infants or adolescents. The present case is considered to be the first case reported in a postmenopausal woman.

ESTs are recognized to arise from germ cells that become misplaced during embryogenesis. Such germ cells are suggested to migrate through the midline dorsal mesentery, thereafter proceeding to the developing gonadal ridge. However, the detailed mechanisms of such

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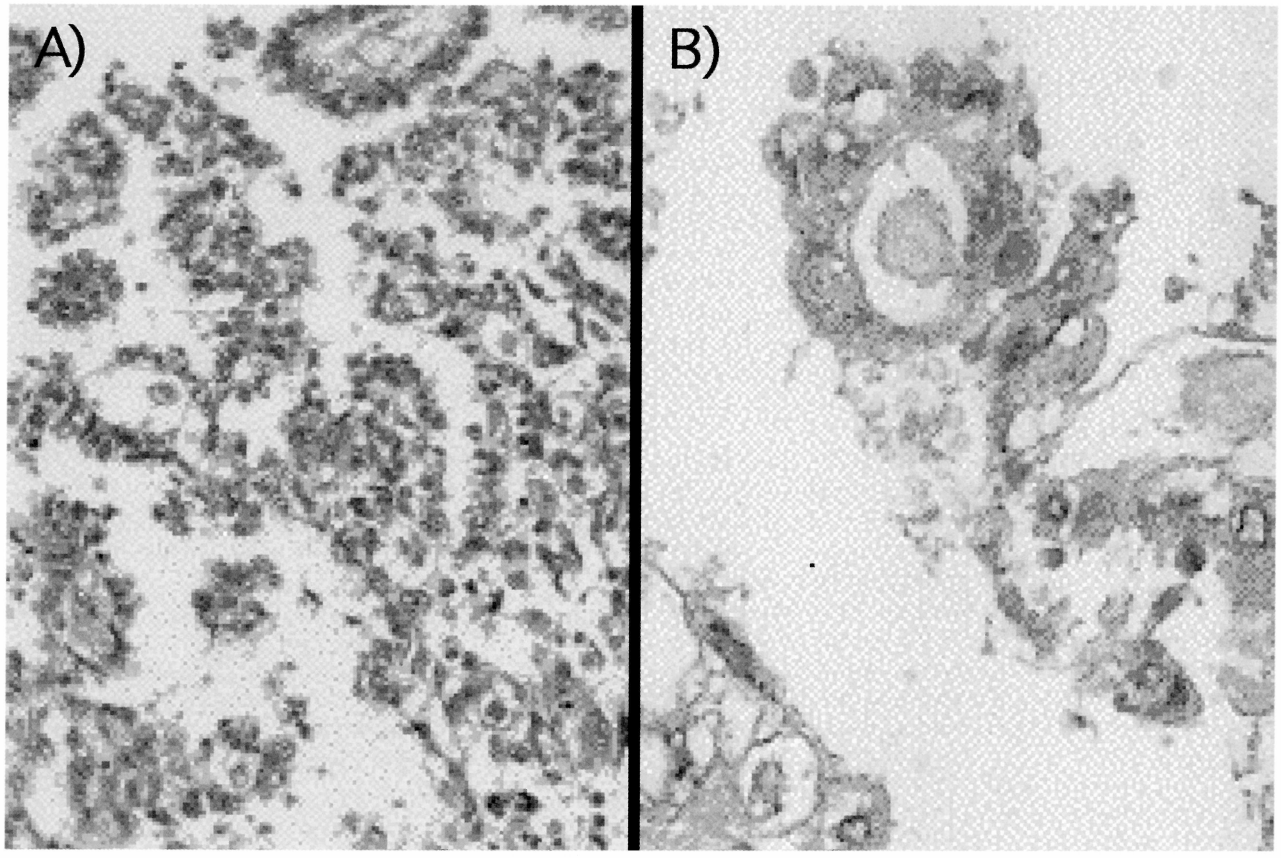


Figure 1. — Microscopic findings of the tumor. Aggregations of polygonal epithelioid cells mixed with focal glandular and cystic areas (Fig. 1A, H & E, x 350), and Schiller Duval bodies with positive immunohistochemical staining for AFP was positive (Fig. 1B, sABC x 350).

Table 1. — *Summary of the clinical information for patients with vulvar yolk sac tumors.*

| Cases | | Age | Size | AFP at Dx | Location | Inguinal lymph at Dx | Surgery | pTNM | Chemotherapy | Radiation therapy | Follow-up |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Ungerleider *et al.* | 15 | NA | WNL | Rt-labium | Negative | RV | T2N0M0 | VAC<br>VAD | <br>pelvis | LN(+) 12M<br>DOD, 23M |
| 2 | Castaldo *et al.* | 2 | 1.5 | WNL | clitolis | Negative | excision | T1N0M0 | no | no | NED 66M |
| 3 | Krishnamurthy & Sampet | 26 | 7 | WNL | Lt-labium | Negative | excision<br>re-excision and lt-groin | T2N0M0 | no<br>VA | no | local rec 6M<br>plueral<br>DOD 10M |
| 4 | Dudley *et al.* | 1 | 6 | NA | Rt-labium | meta (+) | RV, groin & lt-pelvic | T4N1M0 | C | pelvis & groin | DOD 3M |
| 5 | Penkar *et al.* | 25 | 10 | elevated | Rt-labium | not palpable | excision | NA | NA | NA | NA |
| 6 | Craighead and du Toit | 24 | 4 | NA | Lt-labium | not palpable | excision<br>excision | T2N0M0 | BEP | labium & groin | LN (+) 5M<br>NED 18M |
| 7 | Flanagan *et al.* | 18 | 5 | elevated | Rt-labium | negative | mod RV & rt-groin | T2N0M0 | BEP | no | NED 18M |
| 8 | Traen *et al.* | 19 | 3.4 | WNL | Rt-labium | negative | mod RV & rt-groin | T2N0M0 | EP x 3 | no | lung meta (*)<br>pleura (+) 20M |
| 9 | Khnuamornpong *et al.* | 30 | 3.5 | WNL | Rt-labium | meta(+) | excision | T2N1M0 | PVB<br>BEP | pelvis & groin | local rec 2M<br>NED 90M |
| 10 | present case | 52 | 3.5 | elevated | Rt-labium | negative | mod RV & pelvic, groin | T2N0M0 | BEP | no | NED 67M |

NA: data not available; AFP: serum alpha-fetoprotein; RV: radical vulvectomy; L: lymphadnectomy; V: vincristine; A: actinomycin; Ad: adriamycin; C: cyclophosphamide; P: cisplatin; M: methotrexate; E: etoposide; LN(+): ipsilateral inguinal lymph node metastasis; DOD: dead of disease; M: months.

misplacement are unclear. It is plausible that misplaced germ cells may travel along the gubernaculum and thereafter rest in the subcutaneous tissues of the vulva for a long-term period.

The appropriate therapy for vulvar ESTs remains to be determined due to the rarity. As for an adjuvant chemotherapy, a regimen of bleomycin, etoposide and cisplatin (BEP) has been proven to be benefical for the treatment of ESTs [2, 4, 5]. Surgical resection of the tumor as well as ipsilateral inguinal lymphadnectomy should be justified because inguinal lymph node metastasis is the first evidence of tumor spread outside the vulva in almost all cases (Table 1). As local recurrence can occur early in the course, even without inguinal symptoms, adjuvant radiation therapy may thus be needed [4].

Regarding the prognosis of vular ESTs, three of the available nine cases died within two years. Regarding the two cases with tumor size greater than 5 cm included in the three fatal cases, tumor size (> 5 cm) is thus considered to be one of the most variable prognostic factors. Even though most cases showed no elevation of serum AFP levels, the serum AFP level is nevertheless considered to be either a reliable diagnostic modality for follow-up or an early predictor of recurrence of EST, especially when an elevation is observed before surgery, as was seen in this case.

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