# A case of recurrent yolk sac tumor as spindle cell sarcoma of the abdominal wall

**M. Futagami, Y. Yokoyama, T. Shigeto, H. Mizunuma**

[1]*Department of Obstetrics and Gynecology, Hirosaki University Graduate School of Medicine, Hirosaki, Aomori (Japan)*

**Summary**

Few studies report on tissue morphology in recurrence of yolk sac tumor. The case of the recurrence of a yolk sac tumor as a spindle cell sarcoma of the abdominal wall is presented. A 27-year-old woman was referred to our hospital due to suspicion of an ovarian tumor. Right salpingo-oophorectomy, partial omentectomy, and extirpation of disseminated foci as fertility-preserving surgery was done since the intraoperative pathological diagnosis was yolk sac tumor. Final pathological examination showed a germ cell tumor of which yolk sac tumor formed the major component including a small area that appeared to be immature nerve tissue. Although residual tumor was not less than 1 cm, clinical complete remission was reached after the sixth course of BEP regimen. However, the recurrence of a yolk sac tumor as an unclassified spindle cell sarcoma of the abdominal wall was found about two years after the initial surgery. Thereafter, the patient expired due to progression of the intraperitoneal disseminated lesions. The mesenchyme-like component of the yolk sac tumor is characterized by spindle cells originating from epithelial elements, and is likely to give rise to a chemoresistant, diversely differentiated sarcoma. This report suggests that the sarcoma reported in the case here also arose when spindle cells of the mesenchyme-like component underwent sarcomatous change during or after chemotherapy, subsequently relapsed as a chemoresistant tumor, and metastasized.

*Key words:* Yolk sac tumor; Spindle cell sarcoma; Chemoresistance; Recurrence.

## Introduction

Yolk sac tumor is a type of malignant germ cell tumor common in young women. Although responsive to chemotherapy, recurrence is not uncommon. Few studies report on tissue morphology in cases of recurrence. This paper reports on the recurrence of a yolk sac tumor as a spindle cell sarcoma of the abdominal wall.

## Case Report

Our patient was a 27-year-old female with no history of pregnancy, 168 cm in height and weighing 94.8 kg. The patient was referred to our hospital due to suspicion of an ovarian tumor after consulting a local doctor in 2003 with lower abdominal pain as her chief complaint. Abdominal ultrasonography showed a mixed solid and cystic mass of 20 cm in its longest diameter. The patient was admitted to our facility with a fever of 39°C. She received antibiotic treatment and a detailed examination of the mass was performed. Serum AFP was high (24,694 ng/ml) and suggested the presence of a yolk sac tumor. With persisting pyrexia, progression of anemia (Hb 7.0 g/dl) and inflammatory findings (CRP 19.5 mg/dl), surgery was performed. Other biochemical tests showed no abnormalities. Tumor markers observed other than AFP were CA125 at 128 U/ml, CEA below 0.5 ng/ml, and CA19-9 at 26 U/ml. Magnetic resonance imaging revealed a large tumor reaching the umbilicus with marked contrast enhancement. A malignant tumor with large solid and small cystic components was suggested. The patient's uterus was of a normal size.

Operative findings were as follows. The tumor originated from the right ovary and consisted mostly of a solid component. Hemorrhage was observed from the tumor surface, and the tumor was adherent to the pelvic peritoneum and intestinal tract. Areas of dissemination of 2 cm in diameter and larger were found on the surface of the intestinal tract and the omentum. Because an intraoperative pathological diagnosis was of yolk sac tumor, only right salpingo-oophorectomy, partial omentectomy, and extirpation of disseminated foci were performed as fertility-preserving surgery in consideration of the patient's age and chemoresponsiveness of the histological tumor type. Residual tumor was not less than 1 cm. The resected tumor weighed 3.3 kg, was covered by a smooth capsule, and was solid, soft, and friable. The tumor was pale yellow to grayish white in color on cut section, and inhomogeneous with small and large cysts in the solid tissue. The cysts contained bloody content or viscous components (Figure 1). Pathological examination showed that cells with oval nuclei had proliferated into reticular and sac-like structures. Large numbers of hyaline globules were detected (Figure 2A). Some cells had formed as Schiller-Duval bodies (Figure 2B), positive for AFP on immunohistochemical staining. A yolk sac tumor was diagnosed based on these findings. The patient received six courses of BEP chemotherapy following surgery (D2; bleomycin 30 mg/body, D1 to D5; VP-16 100 mg/m$^2$ and CDDP 20 mg/m$^2$). Serum AFP returned to normal values for the first time after the completion of the fifth course, and computed tomography (CT) scanning showed no identifiable lesion after the sixth course.

In 2005 a mass was found just under the incision wound on the abdominal wall. On abdominal CT, a 9 cm mass was found on the abdominal wall just below the wound. Fine-needle aspiration cytology of the mass found no malignant cells and suggested a desmoid tumor. The abdominal wall mass was resected. Serum AFP was below 2 ng/ml, and no lesion was found other than the abdominal wall mass. The cut section of the resected tumor showed a pale yellow mass with clear margins and a cystic cavity at its center (Figure 3A). Postoperative

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Fig. 1

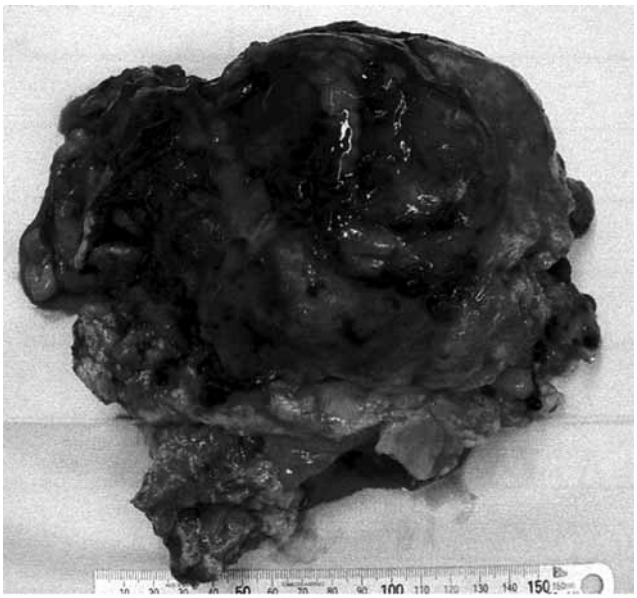

Figure 1. — Macroscopic finding of the primary tumor. The tumor was pale yellow to grayish white in color on cut section, and inhomogeneous with small and large cysts in the solid tissue.

Fig. 2

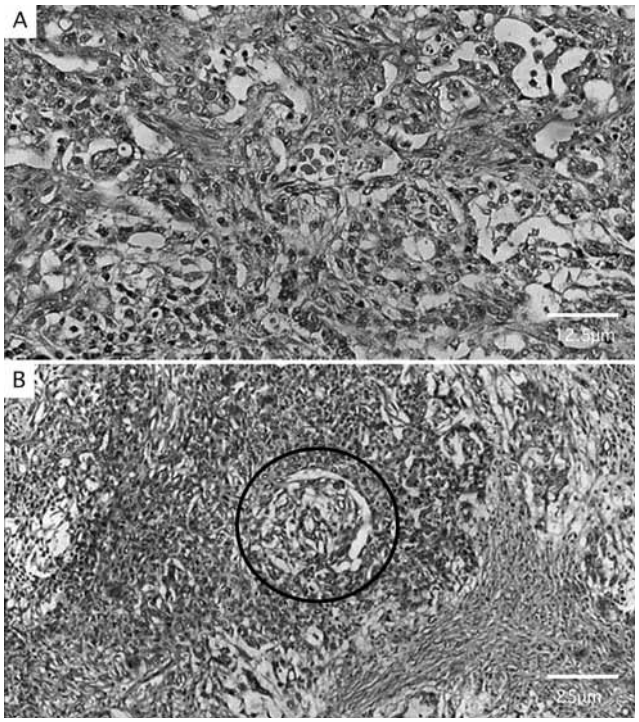


Figure 2. — Microscopic finding of the primary tumor. A, cells with oval nuclei had proliferated into reticular and sac-like structures. Large numbers of hyaline globules were detected. B, the inside of the black circle showed a Schiller-Duval body.

pathological examination confirmed the proliferation of oval or spindle-shaped tumor cells with a reticular structure, and a diagnosis of unclassified spindle cell sarcoma was given (Figure 3B). The tumor consisted of areas of high and low cell density, and a high mitotic count of 15/10 HPF. The tumor was negative for AFP and positive for vimentin on immunohistochemical staining. Reexamination of ovarian tissue specimens taken from the primary lesion found a small area that appeared to be immature nerve tissue (Figure 4). The tumor was considered to be a germ cell tumor of which yolk sac tumor formed the major component. The abdominal wall mass diagnosed as an unclassified spindle cell sarcoma was diagnosed to be a recurrent germ cell tumor. A central pathological review gave an identical diagnosis. BEP chemotherapy was performed after resection of the relapsed tumor, but during the early stages of treatment a 14 cm mass was found in the upper abdomen by CT. The tumor originated from the transverse mesocolon, and multiple disseminated lesions were found. The transverse colon including the mass was resected and anastomosis performed, and resection and anastomosis of the small intestine was also performed. Subsequent progression of the disseminated lesions resulted in patient death 30 months after initial treatment.

## Discussion

Cases of malignant germ cell tumor are reported to constitute 4-6% of malignant ovarian tumors [1]. Around 13% of these malignant germ cell tumors are estimated to be yolk sac tumors [2]. Yolk sac tumor is most common among young people in their teens and twenties [2]. Common symptoms of malignant germ cell tumors including yolk sac tumors are abdominal pain, pyrexia, abdominal distension, and genital bleeding [2]. Around 10% of yolk sac tumor diagnoses are given by emergency surgery for acute abdomen caused by capsule rupture, hemorrhage, and torsion of the pedicle [3]. The patient in this paper presented with abdominal pain and pyrexia, both symptoms frequently found in patients with disseminated yolk sac tumor. Unlike epithelial ovarian cancer, between 60-70% of yolk sac tumor patients are FIGO Stage I and II, 20 to 30% Stage III, and Stage IV patients are relatively rare [4]. Yolk sac tumor rarely occurs in both ovaries, as in the patient reported here with tumor of the right ovary only.

On gross examination the tumor was covered with a smooth capsule and was solid and soft. Patients with yolk sac tumor are known to have an increased AFP level, and in some cases show increased CA125 and LDH. Immunohistochemical staining for AFP is particularly useful for the histopathological diagnosis of yolk sac tumor. Yolk sac tumor cells are positive for cytokeratins, and in 50% of cases are PLAP-positive. Various histological subtypes exist (endodermal sinus pattern, polyveiscular vitelline pattern, hepatoid pattern, glandular pattern), with two or more subtypes often coexisting, and histological changes common place. There are reports that patients with three or four histological subtypes have better prognosis than those with only one or two subtypes [5, 6]. There are also reports of yolk sac tumor being difficult to differentiate from ovarian clear cell adenocarcinoma and endometrioid adenocarcinoma, both epithelial ovarian cancers, indicating caution for diagnosis [7, 8].

Malignant germ cell tumor patients are often young, with reports showing that fertility-preserving surgery has

Fig. 3

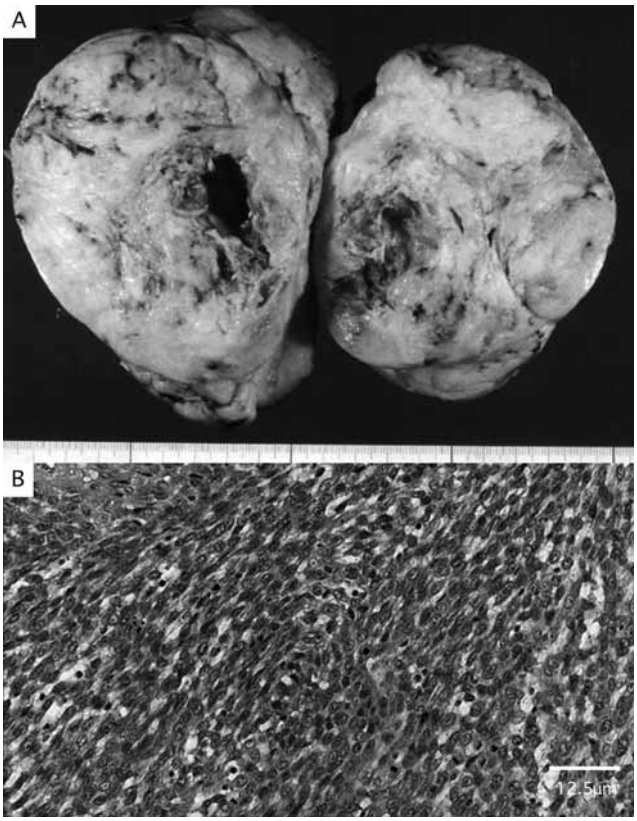


Figure 3. — Recurrent tumor of the abdominal wall. A, macroscopic finding of the recurrent tumor. The cut section of the resected tumor showed a pale yellow mass with clear margins and a cystic cavity at its center. B, microscopic finding of the recurrent tumor. The proliferation of oval or spindle-shaped tumor cells with a reticular structure, and a diagnosis of unclassified spindle cell sarcoma was given.

Fig. 4

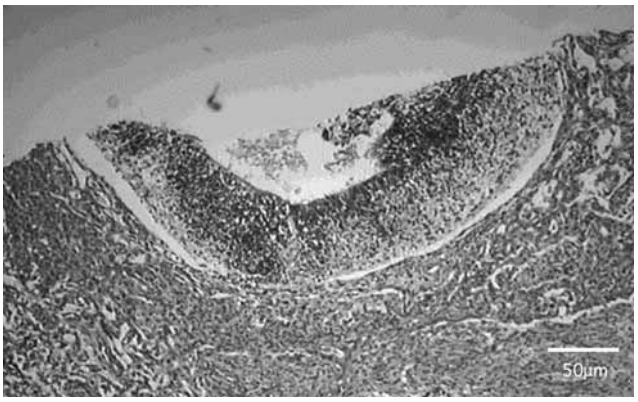


Figure 4. — Macroscopic finding of the primary tumor. A small area that appeared to be immature nerve tissue was found in the primary lesion.

no affect on prognosis [2, 9]. In cases that require fertility preservation a surgical procedure is chosen that will conserve ovarian function and fertility where possible. BEP, PVB, and VAC chemotherapies are common postoperative therapies [10-12]. Recent reports often advocate three-course BEP chemotherapy, but four courses are recommended in cases of residual tumor [4]. The patient reported here received six courses in total due to residual tumor and normalization of AFP occurring during the fifth course. Anticancer agents are known to cause ovarian dysfunction, though few reports show ovarian dysfunction arising from BEP, PVB, and VAC therapies [13]. The patient reported in this paper was first severely obese with irregular menstruation, with a regular menstruation cycle returning subsequently.

Nishio *et al*. [14] reported patients with malignant germ cell tumors who received fertility-preserving surgery immediately followed by chemotherapy had good prognosis regardless of clinical stage. However, patients with yolk sac tumors of the ovary often experience relapse or recurrence despite responding to chemotherapy, and are known to have poor prognosis [2]. Most recurrences are seen within two years of surgery, with recurrence in this paper seen about two years after the initial surgery. Clinical stage, tumor size, and residual tumor size are factors considered to influence prognosis in patients with yolk sac tumors [15, 16]. Volume of ascites fluid has also been counted as an important prognostic factor, and Kawai *et al*. [15] reported Stage I patients with no residual tumor or ascites, or with less than 1000 ml of ascites have good prognosis. Nawa *et al*. [16] have also reported a residual tumor size of 2 cm or less and ascites of less than 100 ml as prognostic factors for yolk sac tumor. There is a continuing disagreement as to whether a correlation exists between AFP values and prognosis for yolk sac tumor [15, 16].

Although many patients with recurrent yolk sac tumors exhibit increased AFP, and AFP is a useful aid for determining tumor recurrence [17], no increase in AFP was seen in the patient of this paper. On the significance of AFP, Baniel *et al*. [18] reported 28% of patients with recurrent yolk sac tumors of the testis were negative for AFP. Kommmoss *et al*. [19] reported one case of an endometrioid-like variant of yolk sac tumor recurring after 12 years that also showed no increase in AFP. Although AFP is often increased in recurrent tumors, it is important to note there are also patients negative for AFP who also recur, such as the patient reported here.

Almost no literature reports exist on the histomorphology of tumors in cases of recurrent yolk sac tumor of the ovary. Although the patient presented in this paper was a case of mixed germ cell tumor with major yolk sac tumor components, and as such may be inappropriate as a case of recurrent pure yolk sac tumor, pure yolk sac tumors are considered the exception. Other types of germ cell tumors are often mixed within yolk sac tumors, and patients where yolk sac tumor constitutes the major component of a large tumor are reported to have poor prognosis [20]. The patient reported here had a yolk sac tumor constituting the predominant component of a mixed germ cell

tumor of 20 cm in its longest diameter, and poor prognosis was expected. The patient showed no increase in AFP on recurrence of the tumor, and the recurrent tumor found just under the abdominal wall was a spindle cell sarcoma and quite different from the original yolk sac tumor. This at first led us to conclude the spindle cell sarcoma was not a recurrence. The mesenchyme-like component of yolk sac tumor has previously been characterized to be spindle cells originating from epithelial elements, and reported to give rise to a chemoresistant, diversely differentiated sarcoma [21]. This report suggests that the sarcoma reported in the case here also arose when spindle cells of the mesenchyme-like component underwent sarcomatous change during or after chemotherapy, subsequently relapsed as a chemoresistant tumor, and metastasized.

## Conclusion

Although yolk sac tumors respond to chemotherapy, the risk of recurrence necessitates caution. The female patient reported by this paper had a germ cell tumor with major yolk sac tumor components. Serum AFP originally considered to be useful for follow-up observation showed no increase even during recurrence. Although few reports exist on the histomorphology of recurrent yolk sac tumors, we found that tumors recurring after chemotherapy, such as the case reported here, show a sarcomatous morphology. Literature reviews of patient cases of yolk sac tumors reviewing therapies and outcomes exist, but the number of cases examined are small. Large numbers must be collected for further interpretation and analysis.

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Address reprint requests to:
Y. YOKOYAMA, M.D.
Department of Obstetrics and Gynecology
Hirosaki University Graduate School
of Medicine
5-Zaifu-cho, Hirosaki, Aomori
036-8562 (Japan)
e-mail: yokoyama@cc.hirosaki-u.ac.jp