Case Report

Ovarian Mucinous Carcinoma with Mural Carcinosarcomatous Components in a Prepubertal Girl

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A B S T R A C T

Background: Epithelial ovarian cancer development before menarche is extremely rare.
Case: We report a prepubertal girl who developed ovarian mucinous carcinoma with mural carcinosarcomatous components.
Summary and Conclusion: Magnetic resonance imaging showed a polycystic mass with solid components. The left adnexa was removed. Histological analysis revealed a mucinous tumor with mural carcinosarcomatous components. Three weeks later, ascites and peritoneal metastasis were detected. The patient received a combination therapy of paclitaxel with carboplatin. After 4 chemotherapy cycles the right adnexa, uterus, partial omentum, and pelvic peritoneum were removed. Four additional paclitaxel/carboplatin therapy cycles were administered. She remains free from recurrence after 29 months. To our knowledge, this is the first report of ovarian mucinous carcinoma with mural carcinosarcomatous components in a prepubertal girl.
Key Words: Ovarian mucinous carcinoma, Carcinosarcomatous components, Prepubertal girl

Introduction

Ovarian malignant epithelial tumors before menarche are extremely rare. Incidence rates of ovarian epithelial tumors have tended to increase with age, most of which occur after menarche. The development of epithelial tumors before menarche is uncommon and usually benign. We herein report a case of a 13-year-old prepubertal girl. To our knowledge, this is the first case report of an ovarian mucinous carcinoma with mural carcinosarcomatous components in a prepubertal girl.

Case

A 13-year-old prepubertal girl presented to Dokkyo Medical University Saitama Medical Center with a history of abdominal distention that had been worsening over the past 3 months, during which she had gained 7 kg. No notable medical history was present. However, her paternal grandfather died of gastric cancer at the age of 65 years, whereas her paternal grandmother died of pancreatic cancer at the age of 52 years. No family member had ovarian or breast cancer.

Her physical examination revealed a well-developed 13-year-old Japanese girl with a blood pressure of 103/75 mm Hg and a temperature of 37.8°C. No breast development or terminal pubic and axillary hair (Tanner stage I) were noted. Her abdomen was exceedingly distended. Ultrasonography showed a multilocular cystic tumor spanning from the pelvic cavity to the abdominal cavity, as well as ascites. The patient was admitted to our hospital on the same day because of the results of the detailed examination.

Magnetic resonance imaging (MRI) showed a $20 \times 12 \times 24$ cm polycystic mass with solid components in her left ovary (Fig. 1A-C). Massive ascites was also noted over the liver, along the bilateral paracolic gutters, and into the pelvis without peritoneal disseminations. No pelvic or para-aortic lymph node enlargement, as well as liver and lung masses, were identified after computed tomography (CT) imaging. On the image, the lesion was localized in her left ovary.

Her initial laboratory tests results were as follows: serum cancer antigen (CA) 125, 235 U/mL (normal <35 U/mL); serum CA 19-9, 1142 U/mL (normal <37 U/mL); serum carcinoembryonic antigen, 3.3 ng/mL; serum α-fetoprotein, 1.5 ng/mL; serum estradiol, 38.9 pg/mL; serum progesterone, 0.6 ng/m; serum luteinizing hormone, 2.7 mIU/mL; serum follicle-stimulating hormone, 3.7 mIU/mL; and serum prolactin, 3.8 ng/mL.

On the basis of imaging and laboratory tests, a presumed diagnosis of left ovarian mucinous carcinoma was established. On the third day of hospitalization, the patient underwent exploratory laparotomy with left salpingo-oophorectomy followed by biopsy of the peritoneum, particularly the pouch of Douglas. Serous light-yellow ascitic fluid (3580 mL) was obtained in the abdominal cavity (negative cytology). The tumor originated from the left ovary and ruptured spontaneously. The resected

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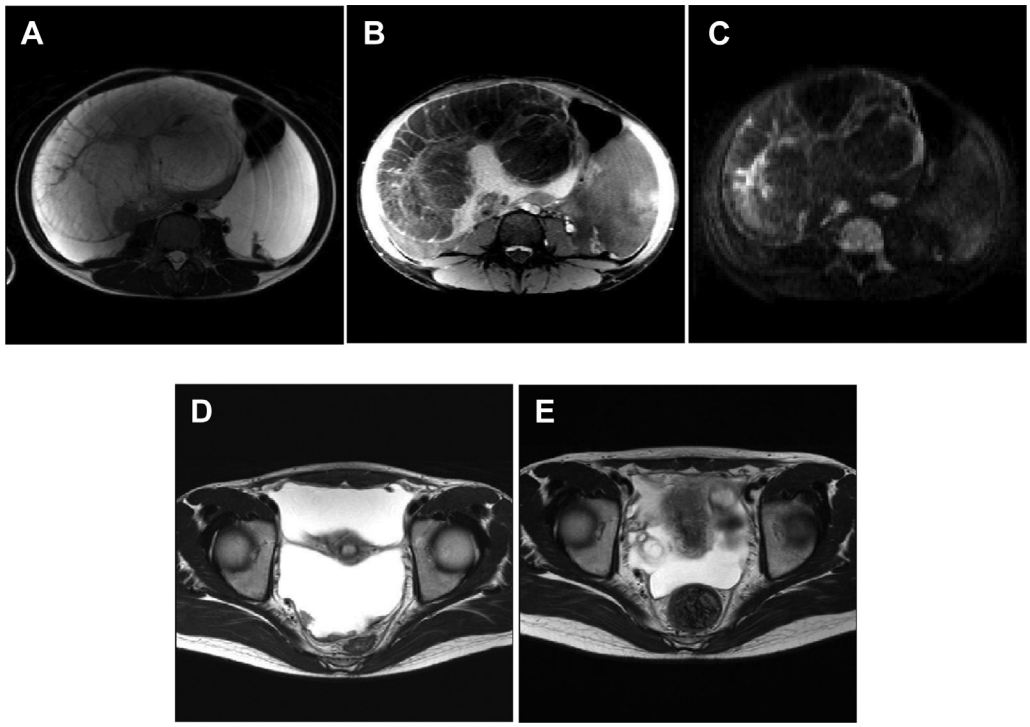

Fig. 1. Abdominal magnetic resonance imaging (MRI). (A) A 24 × 12 cm polycystic mass with solid components (arrows) in the left ovary and massive ascites were shown on preoperative T2-weighted MRI. (B) Solid components (arrows) in the left ovarian mass were enhanced using gadolinium-based contrast media on preoperative fat-saturated T1-weighted MRI. (C) Solid components (arrows) in the left ovarian mass showed a very strong signal intensity on preoperative diffusion-weighted MRI. (D) Peritoneal dissemination (arrows) in the pouch of Douglas and massive ascites were shown on T2-weighted MRI, which was taken 3 weeks after the initial surgery. (E) Peritoneal dissemination in the pouch of Douglas disappeared, and ascites decreased on T2-weighted MRI, which was taken after 4 cycles of adjuvant chemotherapy.

specimen showed a large mass measuring 20 × 21 × 13 cm and weighing 3600 g. No finding suggestive of metastasis to the greater omentum, mesentery, uterus, contralateral adnexa, retroperitoneal lymph nodes, or liver was noted. Thereafter, the patient was histologically diagnosed with stage IC2 ovarian mucinous carcinoma with mural carcinosarcomatous components (Fig. 2).

Initial laparotomy improved her abdominal distention partially; however, abdominal distention recurred 3 weeks after the initial surgery. Moreover, MRI showed peritoneal dissemination in the pouch of Douglas and ascites as well as no liver and lung masses 3 weeks after the initial surgery (Fig. 1D). CA-125 level decreased to 79 U/mL 1 week after the initial surgery, but it reincreased to 128 U/mL 3 weeks after the initial surgery. Because her disease was determined to be progressing rapidly, the patient subsequently received a combination chemotherapy of paclitaxel (175 mg/m^2) and carboplatin (area under the curve 5; TC) every 3 weeks. After 4 cycles of chemotherapy, MRI revealed disappearance of peritoneal dissemination and decreased ascites (Fig. 1E), CA-125 level decreased to 15 U/mL, and laparotomy was performed as interval debulking surgery (IDS). There were several nodules and dark reddish-brown lesions on the broad ligament and pelvic peritoneum, but there was no gross abnormality in the right ovary and greater omentum. As such, total abdominal hysterectomy (TAH), right salpingo-oophorectomy, partial omentectomy (OMTX), and excision of pelvic peritoneum were performed, consequently completing IDS with optimal cytoreduction (no macroscopic residual tumor). Histopathological diagnosis determined metastasis of the mucinous carcinoma to the right ovary, broad ligament, pelvic peritoneum, and greater omentum.

The patient received 4 more cycles of TC combination therapy after IDS and had been carefully followed-up. CA-125 level was measured every month until 2 years after the termination of chemotherapy and later every 3 months, and CT imaging was performed every 3 months after that. Accordingly, no finding suggestive of metastasis and recurrence has been detected 29 months after chemotherapy.

Summary and Conclusion

We herein report a case of a 13-year-old prepubertal girl who developed ovarian mucinous carcinoma with mural carcinosarcomatous components. Ovarian neoplasms are rare in children and adolescents, with an estimated incidence rate of 2.6 cases per 100,000 girls per year. Accordingly, the 2016 Annual Report of the Committee on Gynecologic Oncology, Japan Society of Obstetrics and Gynecology, revealed that among the 6761 patients with ovarian cancer and those aged 19 years or younger, 6 had ovarian mucinous carcinoma (0.09%), 4 had other epithelial serous ovarian cancers (0.06%), and 37 had malignant ovarian germ cell tumors (0.54%). Incidence rates of ovarian epithelial tumors have tended to increase with age, most of which occur after menarche. To our knowledge, there have been only 4 reported cases of ovarian mucinous carcinoma in premenarchal girls (Table 1),[1–4] with our patient being the fifth. Additionally, our patient showed no breast

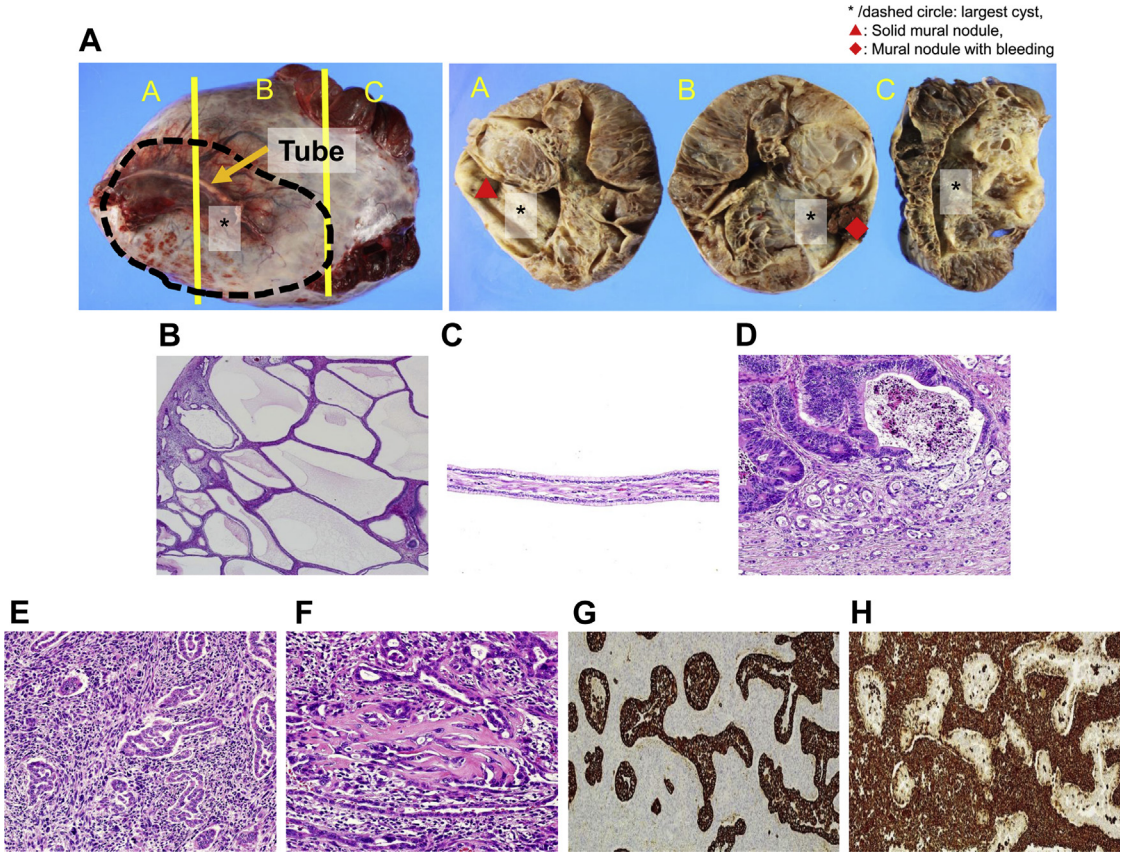

Fig. 2. Histological findings. (A) Macroscopic examination revealed a cut surface with multilocular cysts of various sizes and cysts filled with highly viscous fluid. Although most of the cysts had no solid components, the largest cyst contained solid mural nodules up to 25 × 12 mm, whereas some nodules showed hemorrhagic changes (arrows). (B) Microscopic examination revealed a multilocular mucinous cystic tumor. (C) The epithelium ranged from benign (D) to malignant with invasive carcinoma. (E) Several intramural nodules were composed of pleomorphic spindle cell sarcoma besides the aforementioned mucinous carcinoma. (F) Several sarcomatous nodules contained an eosinophilic matrix. (G) Immunohistochemical examination revealed that cytokeratin AE1/AE3 featured a carcinoma component (H) and vimentin was positive for a sarcomatous component. Estrogen recepter, progesterone recepter, p16, and CD10 were negative, whereas p53 was positive (data not shown). The fallopian tube was intact. Extensive exploration did not reveal a teratomatous component.

development or terminal pubic and axillary hair (Tanner stage I). Furthermore, the histopathological characteristics of the tumor in the present case consisted of mural nodules with carcinosarcomatous components. In 1979, Prat and Scully had first described sarcomas or sarcoma-like mural nodules occurring in association with mucinous epithelial neoplasia.[5] Although numerous cases of ovarian mucinous tumors composed of carcinomatous, sarcomatous, sarcoma-like, and anaplastic carcinoma mural nodules have been reported, only 3 cases of carcinosarcomatous mural nodules have been found in patients aged 29-35 years.[6–8] To the best of our knowledge, the present report is the first report of a case of ovarian mucinous carcinoma with mural carcinosarcomatous components in a prepubertal girl.

Table 1
Reported Cases of Ovarian Mucinous Carcinoma in Premenarchal Girls

Study	Age, years	Operative Treatment	FIGO stage	Additional Therapy	Outcome	Mural Nodule
Matsushita et al[1]	12	RSO	IA	None	No recurrence at 12 months from laparotomy	None
Morowitz et al[2]	N/A	N/A	N/A	N/A	N/A	N/A
Shankar et al[3]	11	LSO	N/A	4 cycles of etoposide, carboplatin, and bleomycin	Intrapelvic recurrent after 15 months from laparotomy • RSO and OMTX • Six cycles of cisplatin and paclitaxel • Died 24 months after first laparotomy	None
Hernandez et al[4]	10	LSO and biopsy of the right ovary and APX and OMTX	IA	12 cycles of melphalan	No recurrence for 22 months after chemotherapy	N/A
Present case	13	LSO	IC2	4 cycles of TC • RSO and TAH and OMTX • Four cycles of TC	No recurrence for 19 months after chemotherapy	Carcinosarcomatous components

APX, appendectomy; FIGO, The International Federation of Gynecology and Obstetrics; LSO, left salpingo-oophorectomy; N/A, not available; OMTX, omentectomy; RSO, right salpingo-oophorectomy; TAH, total hysterectomy; TC, paclitaxel and carboplatin.

Although the patient's disease progressed rapidly after initial laparotomy, combined treatment with TC and IDS was successful in controlling her disease. Currently, 3 cases of ovarian mucinous tumors with mural carcinosarcomatous components have been reported. A 35-year-old patient with a stage I ovarian mucinous borderline tumor with carcinosarcomatous mural nodules was followed up for 19 months after TAH, bilateral salpingo-oophorectomy, and OMTX, subsequently remaining free of disease without any adjuvant chemotherapy.[6] A 29-year-old patient with a stage IA ovarian mucinous borderline tumor with carcinosarcomatous mural nodule underwent left salpingo-oophorectomy, received 4 cycles of adjuvant chemotherapy with docetaxel and carboplatin, and presented 10 months after chemotherapy without recurrence.[7] Finally, a 30-year-old patient with stage IC1 ovarian mucinous carcinoma with carcinosarcomatous mural nodules underwent TAH, bilateral salpingo-oophorectomy, and OMTX, received 6 cycles of adjuvant chemotherapy with cyclophosphamide, actinomycin D, and cisplatin, and presented 5 years after the surgery without recurrence.[8] None of the patients with ovarian tumors with carcinosarcomatous components, as well as sarcoma-like mural nodules, have been reported to die of the disease. In contrast, most of the patients with mural nodules of anaplastic carcinoma have had a malignant, often rapid, clinical course. Remarkably few cases of ovarian mucinous tumors with mural carcinosarcomatous components have been published to warrant a conclusion regarding their good prognosis. In fact, our patient's disease had progressed rapidly after initial laparotomy. However, the combined treatment with TC and IDS had been successful in controlling her disease, suggesting that such an approach might be effective for patients with ovarian mucinous tumors with mural carcinosarcomatous components and for patients with ovarian cancer with common histological types. The patient underwent strict follow-up after the combined treatment as previously described, comprising clinical checkups, CA-125 evaluation, and CT scan because it was difficult to decide how often we should follow such cases. Nevertheless, more case studies are needed to establish a consensus regarding ovarian mucinous tumors with carcinosarcomatous mural nodules.

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