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CASE REPORT

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Mixed germ cell tumor of the ovary mimicking unruptured ectopic pregnancy presenting with unusually high serum alpha-fetoprotein level

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Abstract Malignant germ cell tumors of the ovary constitute fewer than 5% of all ovarian cancers. Malignant mixed germ cell tumors (MMGCTs) may secrete tumor markers including α-fetoprotein (AFP) and β-human chorionic gonadotropin (β-hCG) depending on the type of tumor cells. Because these tumors are almost always seen in the reproductive period, their differential diagnosis with β-hCG secreting ectopic pregnancy is of importance. The patient with MMGCT may present with abdominal pain, vaginal bleeding and pelvic mass similar to an ectopic pregnancy. Here, we present a case of MMGCT, which was referred to our clinic with the admission diagnosis of ectopic pregnancy. However, serum AFP level was exceedingly high (2,172 IU/ml), and transvaginal ultrasonography demonstrated an atypical solid mass 6 cm in diameter. As a result, a hormonally active germ cell tumor of the ovary needed to be considered in the differential diagnosis of ectopic pregnancy.

Keywords Beta-human chorionic gonadotropin · Ectopic pregnancy · Mixed germ cell tumor · Ovarian cancer · Alpha-fetoprotein

Introduction

Malignant ovarian germ cell tumors (MOGCTs) constitute fewer than 5% of all ovarian carcinomas in adults, while malignant mixed germ cell tumor (MMGCT) of the ovary is a fraction of the first mentioned and constitutes less than 1% of ovarian cancers [1]. Subtypes of germ cell tumors may occur in isolated or mixed forms. The MOGCTs secrete tumor markers useful in their diagnosis and follow up. In particular, MMGCTs with an endodermal sinus tumor component may secrete α-fetoprotein (AFP) [2, 3]. Similarly, tumors with a choriocarcinoma or dysgerminoma component may secrete β-human chorionic gonadotropin (β-hCG). Because of the mixed pattern, the endocrine activity of these tumors, especially the production of hCG, deserves attention, because this step is the diagnostic indicator specific for pregnancy.

Germ cell tumors may advance in size very quickly, and the patient presents with acute abdomen due to capsule distension, rupture, or torsion. Such clinical presentation associated with an increase in β-hCG in a fertile woman may be confused with ectopic pregnancy [4, 5]. We present a 25-year-old woman who was referred to our clinic with the diagnosis of ectopic pregnancy and who was later detected to have a mixed germ cell ovarian tumor.

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Case report

A 24-year-old woman, gravidity 2, parity 2, with abdominal pain and vaginal bleeding of 7 days' duration, was referred due to adnexal mass and positive pregnancy test. She had had amenorrhea for 6 weeks and was suspected to have an ectopic pregnancy. The patient used an intrauterine device for contraception and had no known systemic disease or history of drug use. Her family history was unremarkable. Gynecological examination revealed vaginal hemorrhage, adnexal tenderness, prominent on the left side, and a mass of 6–7 cm in size in the left adnexal area. Transvaginal ultrasonography demonstrated a 62 mm × 60 mm adnexal mass that had regular contours, composed mostly of solid parenchyma with partial hypoechogenic areas (Fig. 1). There was no free fluid in the abdomen.

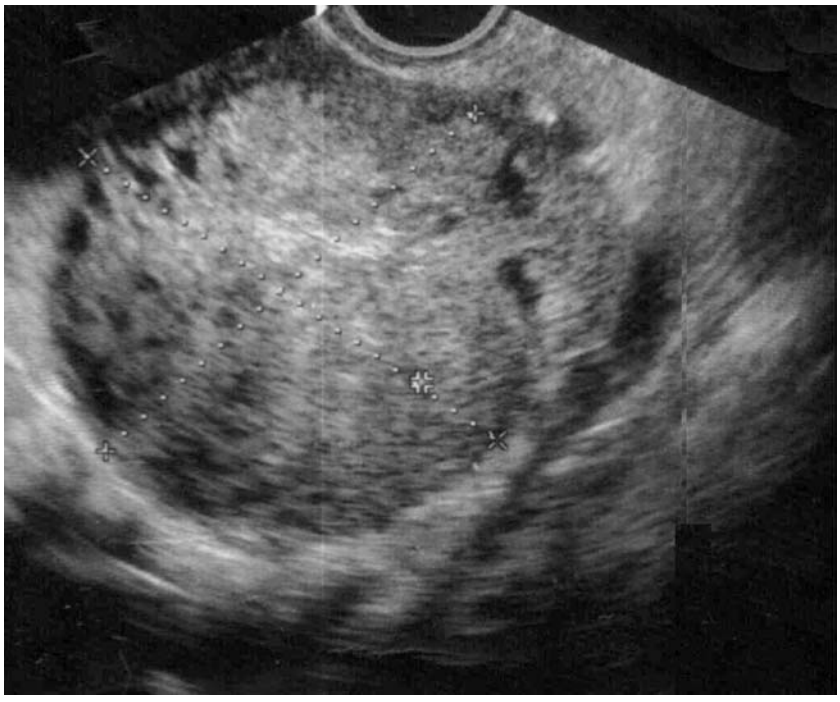

Fig. 1 Transvaginal ultrasound image of the mass

Computed tomography of the abdomen demonstrated a mass lesion of the left ovary with a size of 6 cm × 6 cm mostly of solid composition. Total blood count and results of serum chemistry panel and urine analysis were normal. Serum tumor marker results are given in Table 1. The AFP was unusually high for ectopic pregnancy. Explorative laparotomy was planned, with the preoperative diagnosis of pelvic mass.

At laparotomy the left ovarian mass, which was 6 cm × 7 cm in size, blue–purple in color, with regular contours and a fragile capsule, was resected and sent to be frozen and sectioned. When the frozen sections were examined, the tumor was diagnosed to be a MMGCT, with endodermal sinus tumor, dysgerminoma, choriocarcinoma and teratoma components invading the ovarian capsule. Unilateral oophorectomy with contralateral ovarian biopsy, followed by pelvic–para-aortic lymphadenectomy, omentectomy and random peritoneal biopsies, was performed.

The pathology of the tumor exhibited an infiltrating growth pattern. Areas of choriocarcinoma with cytotrophoblasts and syncytiotrophoblasts were present among areas of hemorrhage and necrosis (Fig. 2). Adjoining these areas were tumor cells with large vesicular nuclei, prominent nucleoli, large clear cytoplasm showing prominent cytoplasmic borders, and numerous mitoses separated by small islands of cells with thin fibrous bands and lymphocyte infiltration (Fig. 3). A few areas included teratoma components lined by squamous epithelium. Immunohistochemical staining with pankeratin revealed diffuse staining for yolk sac tumor focal positivity in dysgerminoma components. Staining for AFP was also positive in yolk sac components. All the tumoral components were negative for cluster designation 30 (CD 30). The final pathology diagnosis was MMGCT that included endodermal sinus tumor, dysgerminoma, choriocarcinoma and teratoma constituents. The tumor showed capsule invasion without any distant metastases, and hence, was labeled as stage Ic. A combined chemotherapy protocol with etoposide, bleomycin and cisplatin was initiated.

Table 1 Laboratory data (normal values within parentheses) (*CA* cancer antigen , *CEA* carcinoembryonic antigen)

Parameter	Value (normal range)
α-fetoprotein (IU/ml)	2,172 (0.5–5.5)
β-Human chorionic gonadotropin (U/l)	3,800
CA 125 (U/ml)	16.3 (< 35)
CA 19-9 (U/ml)	2.5 (< 18.4)
CA 15-3 (U/ml)	13.3 (< 38.4)
CEA (ng/ml)	0.68 (< 2.5)

Discussion

Malignant germ cell tumors are rare ovarian tumors originating from primitive germ cells and exhibit different subtypes (including dysgerminoma, endodermal sinus tumor, immature teratoma, choriocarcinoma and mixed germ cell tumors) [6]. Although most are unilateral, dysgerminomas may be present as occult tumors in the contralateral ovary in 10% of the cases [6]. The MMGCT may secrete tumor markers such as β-hCG and AFP. The differential diagnosis of β-hCG-secreting choriocarcinomas should always include ectopic pregnancies, which may present with a similar clinical picture

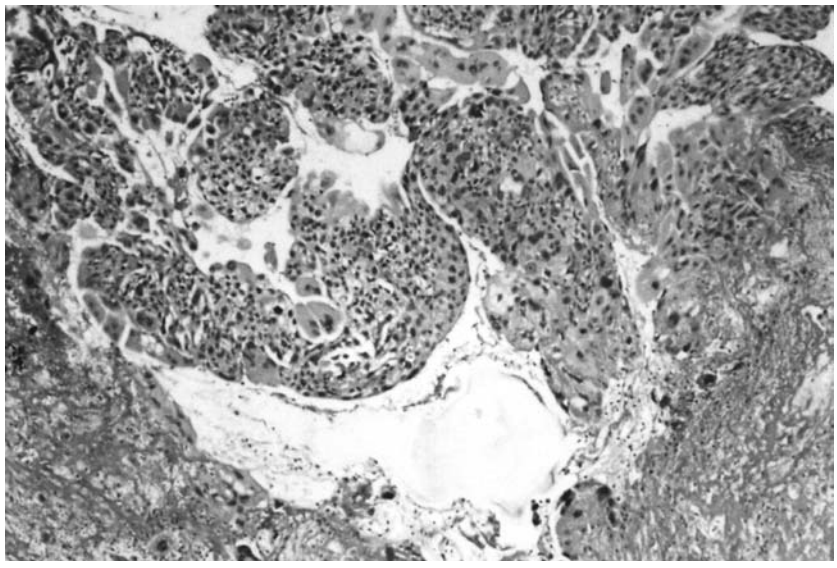

Fig. 2 Pathological appearance of tumor with foci of choriocarcinoma (H&E, x40)

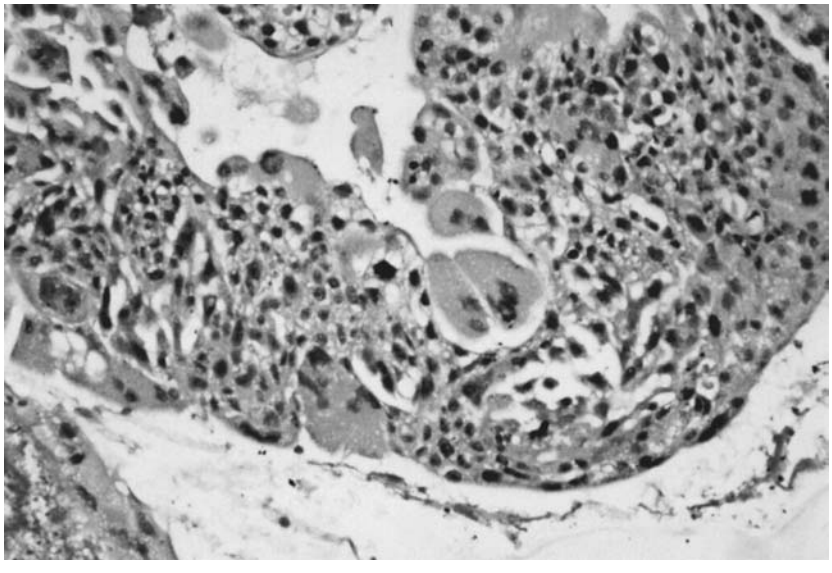

Fig. 3 High power (H&E, x100) view of tumor with trophoblastic predominance

[4]. As in our case, some cases are suggested to be ectopic pregnancies. Vaginal bleeding, positive pregnancy test results, empty corpus and hypoechogenic area on transvaginal ultrasonography might be the reason for the false interpretation of the whole diagnostic signs leading to the diagnosis of ectopic pregnancy.

In MMGCT patients who have plans for future conception, unilateral oophorectomy and preoperative or postoperative chemotherapy is the recommended treatment. In patients with a completed family and a high-grade tumor exhibiting extra-ovarian extension, cytoreduction is the treatment of choice. Because germ cell tumors are generally seen in younger women, preservation of fertility followed by chemotherapy carries great importance. Chemotherapy regimens composed of cisplatin, bleomycin and etoposide provide a success rate of 85–100% [1, 7]. Unilateral oophorectomy without interference with the contralateral ovary is recommended if future fertility is of concern but depends on the assumption that fertility might be decreased due to adhesions or diminished ovarian reserve secondary to the biopsy-taking procedure [1]. Chemotherapy is recommended before or after the surgery. Although a large number of chemotherapeutic protocols are available for the treatment of ovarian germ cell tumors, regimens composed of vinblastine, bleomycin and cisplatin (VBP) or bleomycin, etoposide and cisplatin (BEP) are most commonly preferred. Remission rates are reported to be over 90% with these regimens [7, 8]. Related studies have concluded that pure dysgerminoma or immature teratoma of stage Ia and grade I would benefit from surgery alone, without any requirement for chemotherapy [1].

Ectopic pregnancies most commonly present with delay in menstruation, vaginal hemorrhage, palpable

pelvic mass and abdominal pain. Because the use of intrauterine devices is more common in patients diagnosed with ectopic pregnancy, these clinical findings, accompanied by a mild elevation of serum β-hCG level, may lead to the diagnosis of ectopic pregnancy, as in our patient. However, the solid appearance of the mass on high-resolution ultrasonography and an accompanying elevation of AFP levels were supportive of our suspicion of a tumor of the ovary.

In conclusion, careful evaluation and appropriate therapeutic approach are essential considering that the 5-year-survival rates for ovarian germ cell tumors may rise up to 100% with proper treatment. Exclusion of pathologies such as ectopic pregnancy is of great importance in order to avoid incorrect surgical interventions conducted in insufficient and inappropriate conditions.

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