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CASE REPORT

Mixed Germ Cell Tumor of the Ovary with Sarcomatous Component

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Germ cell tumors constitute a very complicated group of tumors of the ovary and their histogenesis is not yet clarified. Besides their histological heterogeneity, sarcomatous areas have also been described. A right ovarian mass was found in a 23-year-old female, who was being treated in the hospital for miscarriage. Disseminated omental metastases were detected during abdominal laparotomy. Pathological examination of the dissected material revealed the tumor to be a mixed germ cell tumor (immature teratoma and dysgerminoma) with sarcomatous component. Areas resembling granulosa cell tumor were also encountered. This ovarian tumor with many different histopathological features is presented with a review of the literature. The importance of thorough sampling in determining the type and extent of the malignant components is also emphasized due to their direct relation with the prognosis. (Pathology Oncology Research Vol 7, No 1, 60–62, 2001)

Keywords: Ovary, germ cell, sarcoma

Introduction

Coexistence of a germ cell tumor with another malignant neoplasm such as a soft tissue sarcoma is rarely encountered. Only a few examples of rhabdomyosarcoma, angiosarcoma, chondrosarcoma, leiomyosarcoma and liposarcoma have been reported in combination with germ cell tumors.[2,10,12] The presence of non-germ cell malignancies within germ cell neoplasms have been classified as „teratoma with malignant transformation“ by the World Health Organisation (WHO).[5]

The admixture of dysgerminoma, teratoma and rhabdomyosarcoma encountered in the same neoplasm is presented as a rare example of the capacity of a germ cell tumor to undergo malignant transformation into somatic tissue, as well as differentiation into other germ cell components.

Clinical history

A 23-year-old female patient who was four months pregnant was admitted to hospital with symptoms of miscarriage. On abdominal examination, an approximately 10 cm firm mass in the right iliac fossa was palpated. Ultrasonography manifested a 10 cm mass related to the right ovary. Serum alpha-fetoprotein and human chorionic gonadotropin (HCG) levels were within normal limits, 5 ng/mL and 7 mU/mL respectively. Abdominal laparotomy revealed multiple metastases in the omentum and an ovarian mass. A right oopherectomy and omentectomy were performed. The patient was referred to Oncology where upon chemotherapy was commenced. Two cycles of chemotherapy regimen consisting of cisplatine (75 mg/m^2), ifosfamide (1×6 gr/m^2) and vinblastine (6 mg/m^2) with a three week interval wereplanned. Patient refused the therapy after the frist cycle and follow-up was not possible.

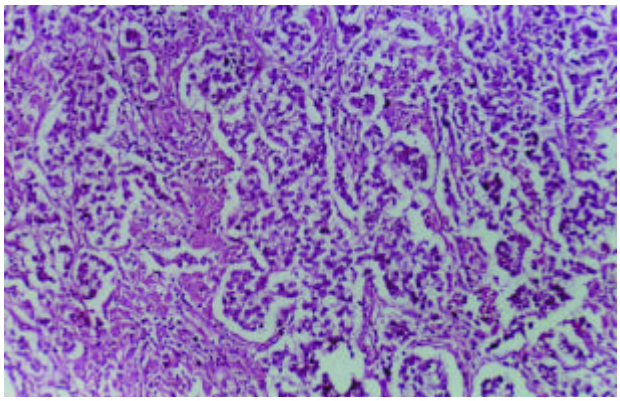

Figure 1. Areas representing dysgerminoma (HE, x125).

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Pathological Findings

The ovarian mass was 10 cm in diameter, well circumscribed, lobulated and solid. The cut surface of the tumor was fleshy grey in appearance, and a cystic area 4 cm in diameter was noted. The omentectomy material measured 8x6x2 cm; and was irregular, partly nodular and firm in texture. The histopathological examination of the ovarian mass showed a high degree of variation. There were well defined nests of tumor cells, separated by fibrous strands infiltrated by lymphocytes. The tumor cells were uniform, with large round vesicular nuclei and abundant cytoplasm. Granulomatous foci with multinuclear giant cells were also present.

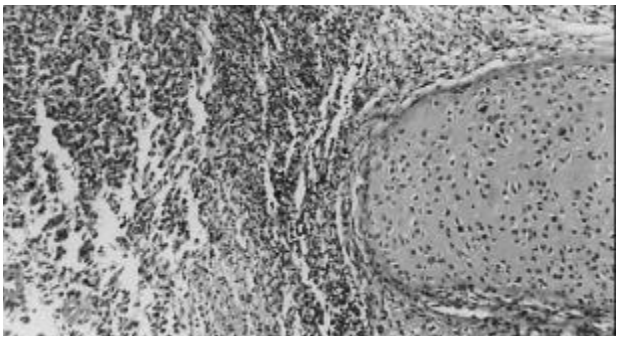

Figure 2. Mature cartilage tissue adjacent to undifferentiated tumor cells (HE, x125).

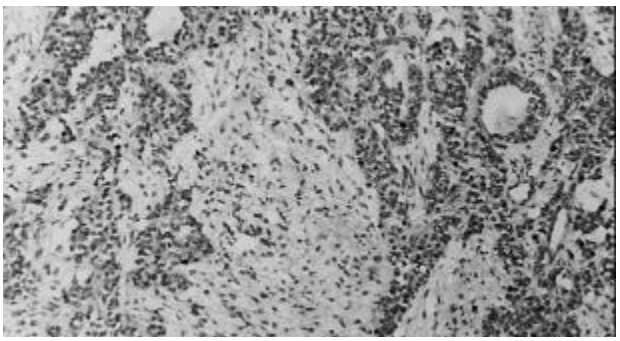

Figure 3. Areas resembling granulosa cell tumor (HE, x125).

These areas were diagnosed as dysgerminoma (*Figure 1*) Immunohistochemistry showed focally positive staining for placental alkaline phosphatase (Biogenes, 1/100 monoclonal) and negative staining for cytokeratins (Zymed, Clone AE1, AE3) and vimentin (Zymed, Clone V9). Multinuclear giant cells were negative for HCG (Biogenes, monoclonal, without dilution). In another area, mature cartilage tissue and a cystic cavity filled with keratin which was lined by epidermis were seen in keeping with the components of a mature teratoma (*Figure 2*). Some hypercellular areas composed of undifferentiated cells with hyperchromatic nuclei and scanty cytoplasm with immature connective tissue of myxoid appearance were noted. These areas were positive for vimentin and negative for cytokeratins and S100 (Zymed). Although there were immature teratomatous areas in the tumor, there were no immature neuroectodermal elements as verified by negative staining for chromogranin (Biogenes, 1/100 monoclonal) and synaptophysin (Signet 1/20). As well as these components of a germ cell tumor, a microfollicular pattern of growth resembling granulosa cell tumor was observed (*Figure 3*). However these areas did not stain for inhibin (Serotec). Adjacent to the tumor components mentioned previously there were areas composed of Iarge pleomorphic cells, some of which were spindle shaped, with excentric hyperchromatic nuclei and abundant eosinophilic cytoplasm (*Figure 4a*). Cross-striations in some of the cells were noted. In many areas, these pleomorphic cells were mixed with the non-differentiated areas. Similar sarcomatous infiltration was also observed in the omental material. The other components of the tumor were not encountered in the metastases. Immunohistochemistry of the sarcomatous areas were positive for desmin (Dako, Clone D 33), vimentin and myoglobin (Signet, Polyclonal, without dilution), confirming this element of the tumor as being consistent with rhabdomyosarcoma (*Figure 4b*).

With these histopathologic findings, the case was diagnosed as mixed germ cell tumor (dysgerminoma and immature teratoma) with sarcomatous differentiation. The patient was referred to Oncology where upon chemotherapy was commenced.

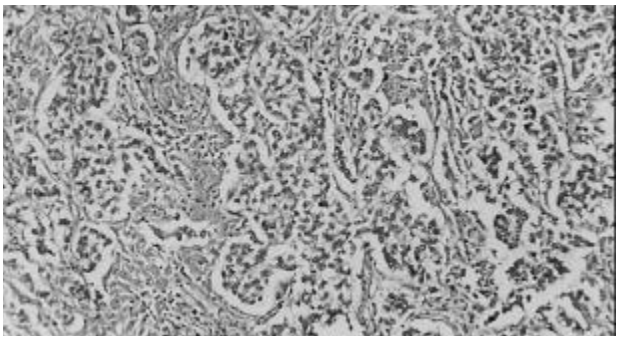

Figure 4a. Pleomorphic sarcomatous areas consistent with rhabdomyosarcoma (HE, x310).

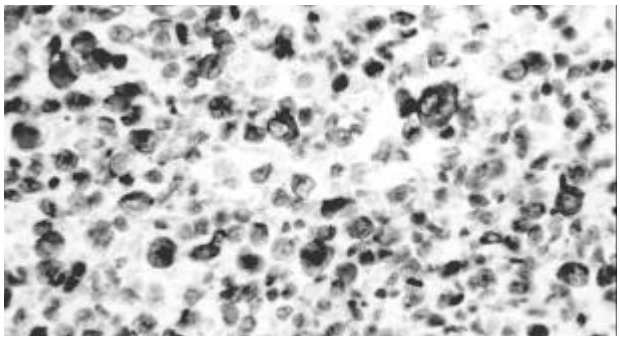

Figure 4b. These areas showing desmin positivity (x310).

Table 1. **Immunohistochemical results of different components of the tumor**

	CEA	*PLAP*	*HCG*	*AFP*	*Cytokeratin*	*Vimentin*	*S 100*	*NSE*	*Desmin*	*Myoglobin*	*Chromo-granin*	*Synapto-physin*
Disgerminoma	–	+	–	–								
Endodermal sinus tumor	–	–	–	+	+							
Immature teratoma	–	–	–	–	–	+	–	–	–	–	–	–
Sarcoma					–	+	–	–	+	+		

CEA: carcinoembryonic antigen, PLAP: placenta-like alkaline phosphatase, HCG: human chorionic gonadotropin, AFP: alpha-fetoprotein, NSE: neuron-specific enolase

Discussion

Germ cell tumors of the ovary show very labile and dynamic characteristics from the point of differentiation. About 8% of all malignant germ cell tumors of the ovary show more than one type of neoplasm.[4] Besides these histopathologically different neoplasms, they have the capacity to progress to a higher or lower grade of differentiation, change from malignant to benign behaviour or develop mature metastasis from an immature primary.[1,9,11]

In addition to the heterogeneity of these tumors, sarcomatous areas may rarely be observed in the primary tumor, in the metastasis, or in both of them.[1,13] The development of non-germ cell malignancies within germ cell neoplasms can be divided into two groups.[9] The first group consists of germ cell tumor components, in which the sarcomatous elements are considered to be derived from a malignant transformation within the mesenchymal component of the pre-existing teratoma. The second group includes a pure germ cell tumor, excluding teratoma, occurring in association with a sarcomatous component. It has been suggested that such sarcomas are derived from the monomorphic somatic differentiation of pluripotential tumor cells.[13] As our case contains components of a teratoma, it is likely that sarcomatous change has developed from malignant transformation of the mesenchymal component. With the help of immunohistochemistry, the differentiation proved to be rhabdomyoblastic.

Furthermore, sarcomatous transformation developing in patients treated with chemotherapy for germ cell tumors has also been reported.[7] Whether the differentiation occurs in the pluripotential germ cell component or as a malignant transformation in a pre-existing teratoma is controversial.[13]

Rare cases of mixed germ cell-sex cord stromal tumors have been reported.[3] Gonadoblastoma is a well defined entity in this group. We observed areas resembling granulosa cell tumor in our case. We could not accept a granulosa cell tumor component accompanying the tumor because of negative immunostaining for inhibin.[9,14] Also the patient was a phenotypically normal female with no abnormal hormonal manifestation.

Malignant potential of mixed germ-cell tumors is related to the extent of the malignant component, as well as the type and degree of tissue differentiation.[6] Sarcomatous areas comprise an extensive part of the primary tumor and metastasis in our case, indicating a poor prognosis. Thorough sampling of a mixed-germ cell tumor is essential in determining the type and extent of its malignant components, because these features are directly related to the prognosis.

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