Clinical Case Report

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Synchronous adrenocortical carcinoma and ovarian malignant mixed germ cell tumor

A case report and literature review

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Abstract

Rationale: Adrenocortical carcinoma (ACC) is an endocrine malignancy with poor prognosis, which commonly arises in a sporadic manner, but may also become a part of a familial syndrome. ACC rarely arises simultaneously with other malignant tumors.

Patient concerns: We report a case of a 29-year-old woman with ACC synchronously followed by an ovarian malignant mixed germ cell tumor. We describe the clinical, histopathological, and immunohistochemical findings and review the English literatures. So far, as we know, the patient presented here is the first case with synchronous malignant tumors of the adrenal gland and ovary.

Diagnoses: She was diagnosed with ovarian malignant mixed germ cell tumor with admixture of dysgerminoma and yolk sac tumor after ACC.

Interventions: The left adrenal tumor was resected laparoscopically on April 28, 2017. A total laparoscopic hysterectomy with unilateral (right) adnexectomy was performed on November 11, 2017.

Outcomes: Up to now, illness condition has not progressed. Patient is free of disease at 3 months of follow-up.

Lessons: This is the first report in English literature about coexistence of ACC with ovarian malignant mixed germ cell tumor and the sixteenth case that presents a synchronous tumor associated with a sporadic ACC. This case reminds us that a comprehensive examination of patients with ACC is necessary to identify a possible synchronous tumor.

Abbreviations: ACC = adrenocortical carcinoma, LS = Lynch syndrome.

Keywords: adrenocortical carcinoma, dysgerminoma, malignant mixed germ cell tumor, synchronous cancers, yolk sac tumor

1. Introduction

Adrenocortical carcinoma (ACC) is a rare malignancy, which accounts for only 0.02% of all reported cancers.[1] Most of ACC is sporadic. However, ACC may also be one of the manifestations of hereditary familial tumor syndrome including the Li-Fraumeni Syndrome, Beckwith-Wiedemann Syndrome, Gardner Syndrome, and Multiple Endocrine Neoplasia, type 1.[1] The risk of developing synchronous ACC with other malignant tumors is extremely rare. Here, we report a rare case of a young woman with ACC synchronously followed by an ovarian malignant mixed germ cell tumor.

2. Consent

The patient provided informed consent to collect data and images for publication. Ethical approval was not necessary in case of case report publication.

3. Case report

A 29-year-old woman was admitted to West China Hospital of Sichuan University in April 2017 because of an abdomen mass. A computed tomography scan of the abdomen and pelvis confirmed a left adrenal lump (Fig. 1A). Her previous medical history and her family history were unremarkable. The patient had no clinical symptoms associated with steroid excess. The adrenal tumor was excised by laparoscopy. Macroscopically, the tumor presented as a well-encapsulated mass which was measured 8.3 × 6.3 × 5.5 cm and weighed 110 g. The cut surface of the mass revealed a tan-grayish and focally golden appearance. Microscopically, the epithelioid tumor cells with eosinophilic cytoplasm and well-defined nucleoli were distributed in clusters and separated by fibrous septa (Fig. 1B). The vacuolated cells comprised less than 25% of the tumor. Expanded necrosis, a high mitotic rate (8 mitoses/50 HPF), and capsular invasion were also observed. The tumor met the Weiss criteria for malignancy. Immunohistochemically, the tumor cells were positive for Mart-1 (Fig. 1C), CR, Syn, p53 (Fig. 1D), HMB45, MLH1, MSH2,

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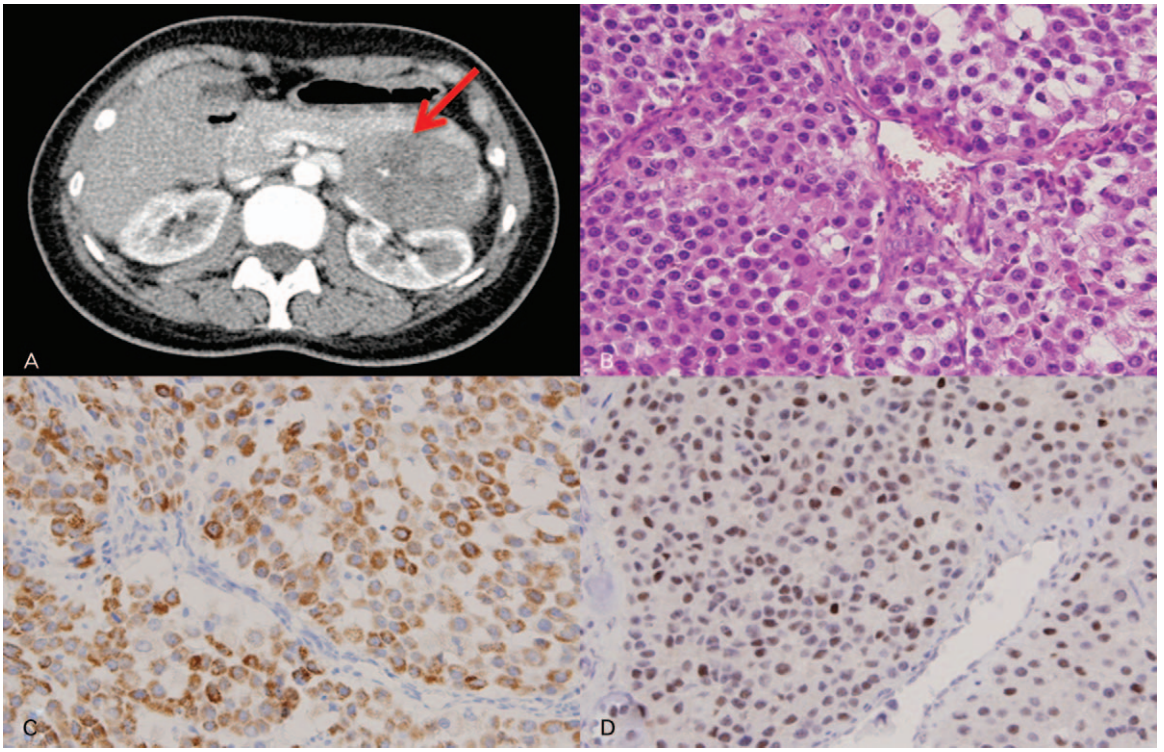

Figure 1. Adrenocortical carcinoma of the adrenal gland. A, Computed tomography scan showing mass of the left adrenal gland (red arrow). B, Microscopically, the clusters of tumor cells with eosinophilic cytoplasm and well-defined nucleoli (H&E ×200). C, Diffuse positivity for Mart-1 (×200). D, Nuclear positivity for p53 (×200).

MSH6, and PMS2. They were negative for P-CK, inhibin, CgA, and S100. The histopathologic diagnosis was an ACC. The patient did not receive follow-up chemotherapy.

However, computed tomography scan of the abdomen and pelvic demonstrated a cyctic and solid right ovarian mass in November 2017 (Fig. 2A). She was referred in our hospital for further treatment of the ovarian tumor. Preoperative serum level of alpha-fetoprotein (AFP) was 168.8 ng/mL (reference range <8.1 ng/mL), and the serum human choriogonadotropin (HCG), CA125 and CEA level were normal. The patient underwent

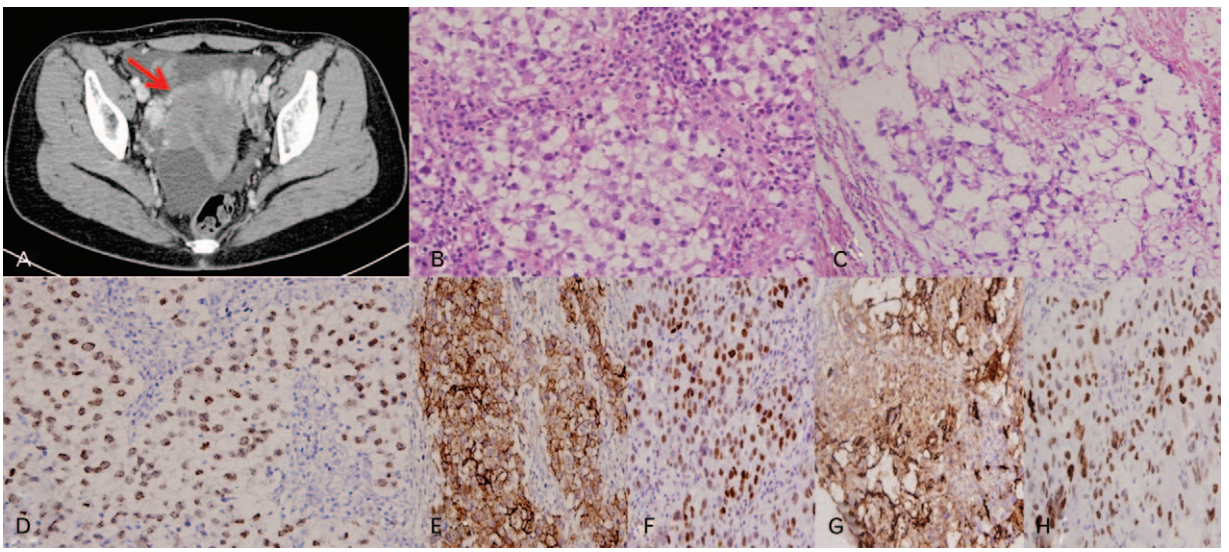

Figure 2. Malignant mixed germ cell tumor of the ovary. A, CT scan showing the right ovarian tumor (red arrow). B, Microscopically, the nests of tumor cells with eosinophilic or clear cytoplasm were separated by fibrous septa containing lymphocytes (H&E ×200). C, Papillary fibrovascular structures mantled by primitive tumor cells in myxoid stroma (H&E ×100). D, Nuclear positivity for Sall-4 (×200). E, Positivity for PLAP (×200). F, Positive staining for p53 in dysgerminoma (×200). G, Positivity for AFP (×200). H, Positive staining for p53 in yolk sac tumor (×200). AFP = alpha-fetoprotein, CT = computed tomography, PLAP = human placental alkaline pkosphatase.

unilateral adnexectomy. A smooth mass with well-defined margins, measuring 8.0×5.5×7.1 cm, was found to arise within the right ovary. The serum level of AFP was decreased to 36.7 ng/mL soon after tumor resection. Macroscopically, sectioning disclosed that tumor was solid and contained cystic area with focal hemorrhage and necrosis. Histologically, majority of the tumor (about 80%) composed sheets and nests of polygonal cells with abundant granular eosinophilic or clear cytoplasm (Fig. 2B). The tumor cells had uniformly medium-size nuclei with prominent nucleoli. Tumor cell nests were separated by fibrous septa containing lymphocytes. Some epithelioid histiocytes were also sprinkled among the tumor cells. Minority of the tumor (about 20%) consisted of loose and myxoid stroma that contained reticular, cribriform-tubular, and papillary fibrovascular structures mantled by primitive and atypical epithelial tumor cells (Fig. 2C). Mitotic figures were numerous. The nests and sheets of polygonal tumor cells showed diffusely positive immunoreactivity for spalt like transcription factor (SALL)4 (Fig. 2D), human placental alkaline pkosphatase (PLAP) (Fig. 2E), D2-40, p53 (Fig. 2F), MLH1, MSH2, MSH6, and PMS2. They were negative for EMA, AFP, HCG, CD30, Mart-1, CgA, and Syn. Other tumor cells with reticular, cribriform-tubular, and papillary fibrovascular patterns were strongly positive for SALL4, AFP (Fig. 2G), p53 (Fig. 2H), MLH1, MSH2, MSH6, and PMS2, while cells were completely negative for EMA, PLAP, D2-40, HCG, CD30, Mart-1,CgA, and Syn. The final pathological results indicated malignant mixed germ cell tumor with admixture of dysgerminoma (about 80%) and yolk sac tumor (about 20%). The patient received postoperative BEP protocol chemotherapy consisting of 3 cycles of bleomycin, etoposide, and cisplatinum. The patient was free of disease with a follow-up of 3 months.

4. Discussion

ACC is a rare malignant tumor, accounting annually for about 0.05% to 0.2% of all malignancies and the incidence is 1 to 2 per million/y.[2] Most ACC arise sporadically, but may also manifest as part of a familial syndrome. In our review of the English literatures, ACC had been reported to occur synchronously with testicular seminoma,[3] breast cancer,[4] rectal cancer,[4] osteosarcoma,[5] endometrioid adenocarcinoma,[1] and ovarian teratoma.[6] However, there has been no report about ACC with synchronous ovarian malignant mixed germ cell tumor. To our knowledge, this is the first report in the English literature about coexistence of ACC with ovarian malignant mixed germ cell tumor and the sixteenth case that presents a sporadic ACC associated with a synchronous tumor.[7]

Synchronous tumors of ACC appeared to develop independent of familial tumor syndromes. In the English literature, 3 patients showed a germline mutation of the p53 gene. One with simultaneous ACC and ganglioneuroblastoma possessed a single base substitution in codon 248,[8] the other one with synchronous rhabdomyosarcoma, osteosarcoma, and ACC showed a mutation at codon 273.[5] Another one with synchronous neuroblastoma and ACC had I162F germline p53 mutation.[9] Our case was also found to have diffuse nuclear positive staining for p53 at ACC and ovarian tumor, suggesting that p53 mutation may be one of the molecular events of the tumorigenesis.

Patient from a Lynch syndrome (LS) family with a germline mutation c.2063T>G (p.M688R) in the MSH2 gene can develop an ACC with the same MSH2 mutation, which indicated that ACC is probably due to the mismatch repair defect.[10] Raymond et al[11] found the prevalence of LS among patients with ACC is 3.2% and immunohistochemical (IHC) screening of all ACC tumors may be an effective strategy for identifying patients with LS. In our study, the ACC and ovarian tumor samples underwent IHC testing for mismatch repair proteins (MLH1, MSH2, MSH6, and PMS2), given the association of ACC with LS, but they showed positivity for all these markers.

In conclusion, no ovarian malignant mixed germ cell tumor-associated ACC had been reported before. This case suggested the importance of a comprehensive examination of patients with ACC to confirm a possible synchronous tumor.

Author contributions

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Supervision: Wei Wang.
Visualization: Min Feng.
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