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CASE REVIEW

Mesonephric-like Adenocarcinoma Arising from the Ovary: A Case Review and Treatment Considerations

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ABSTRACT

Mesonephric-like adenocarcinomas (MLAs) are a rare classification of pathologic cancers. These clinically high-grade cancers exhibit a distinct propensity for distant metastasis, notably in the lungs, often diagnosed at advanced stages (II–IV) according to The International Federation of Gynecology and Obstetrics (FIGO), and clinical course is unclear. A 62-year-old woman was diagnosed as a left ovarian tumor, magnetic resonance imaging (MRI) revealed a 68 mm nodule confined to the left ovary with no evidence of pelvic cavity invasion. After surgery, the patient was diagnosed with FIGO stage IIIA1(ii) mesonephric-like adenocarcinoma. Homologous recombination deficiency (HRD) status and breast cancer 1/2 (*BRCA1/2*) were negative. Postoperatively, the patient received six sessions of taxotere and cyclophosphamide (TC) chemotherapy as an adjuvant chemotherapy with no recurrent lesions. There are few reports that the positive rate of HRD score and the efficacy of poly adenosine diphosphate (ADP) - ribose polymerase inhibitors (PARPi) remain unclear. Adjuvant chemotherapy using carboplatin and paclitaxel after complete surgery has shown promising results with a low risk of recurrence. Further accumulation of cases and studies on regimens, including long-term prognosis and maintenance therapy are needed.

Keywords: Mesonephric-like adenocarcinoma, ovarian malignancy, pathological classification, prognosis, adjuvant chemotherapy.

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Introduction

Mesonephric-like adenocarcinomas (MLAs) are a rare classification of pathologic cancers, initially reported in 2016. These clinically high-grade cancers exhibit a distinct propensity for distant metastasis, notably in the lungs. This new variant of epithelial tumors has been included in the 5th edition of the World Health Organization's (WHO) recent 2020 classification of female genital cancers[1-3].

The term "like" is used because mesonephric-like adenocarcinoma (MLA) frequently occurs in the uterine body and ovaries without the presence of mesonephric remnants. It exhibits morphologic, immunophenotypic, and molecular features that overlap with mesonephric adenocarcinoma, which typically arises from normal or hyperplastic mesonephric remnants and is predominantly found in the lateral wall of the cervix. Thus, MLA shares similar characteristics with mesonephric adenocarcinoma and originates from mesonephric remnants.

MLA is often diagnosed at advanced stages (II–IV) according to the International Federation of Gynecology and Obstetrics (FIGO), with a tendency toward early recurrence and distant metastasis[3].

The pathological features of MLA included multiple structural patterns, such as tubular, glandular, pseudoendometrial, tubular, papillary, and full. Immunostaining demonstrated positive results for GATA binding protein 3 (GATA3), thyroid transcription factor 1 (TTF1), cluster of differentiation 10 (CD10), and paired box protein-8 (PAX8), but was negative for estrogen, other hormone receptors, and Wilms' Tumor Gene 1 (WT1). Additionally, wild type p53 was expressed. Other notable features included luminal eosinophilic colloidal material, dense or vesicular chromatin, inconspicuous nucleoli, nuclear densities, and an absence of squamous or mucous differentiation[4]. MLA represents an extremely rare ovarian malignancy, with only a limited number of case reports documented worldwide. Consequently, the clinical course, chemotherapy sensitivity, and efficacy of treatment for MLA remain unclear. In this report, we described a case of ovarian malignancy diagnosed as an MLA, including insights into the course of treatment.

Case

A 62-year-old woman (para 1-0-0-1) with bronchial asthma consulted a gynecologist who diagnosed her with a left ovarian tumor measuring approximately 6 cm. She visited our hospital for the first time a week later. Prior to this visit, she had not sought gynecological care for over 10 years.

Magnetic resonance imaging revealed a 68 mm nodule confined to the left ovary with no evidence of pelvic cavity invasion (Fig. 1). No other abnormal findings were observed on cervical and endometrial cytology. Blood tests showed an elevated cancer antigen 125 (CA125) level of 86 U/mL, while carcinoembryonic antigen (CEA) and cancer antigen 19-9 (CA19-9) levels were within the normal range. We decided that if the intraoperative rapid histological diagnosis indicated malignancy, we would perform a total abdominal hysterectomy, bilateral adnexectomy, pelvic lymph node dissection, para-aortic lymph node dissection, and oophorectomy.

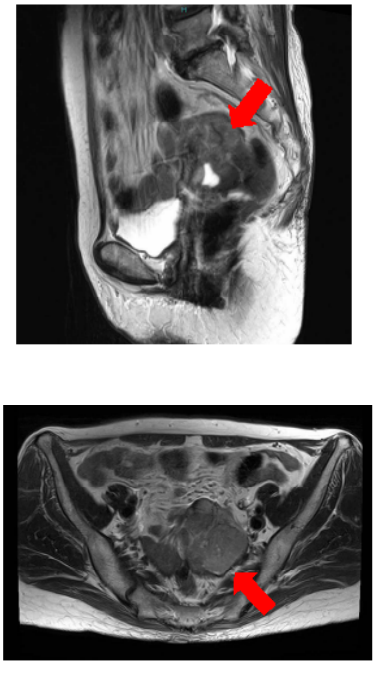

Fig. 1. Magnetic resonance imaging.
A substantial nodule is localized within the left ovary with no findings suggesting invasion into the pelvic cavity.

During the intraoperative examination, a minute amount of ascites was noted, and the left ovary appeared enlarged and swollen to the size of a clenched fist. However, the surface of the ovary was smooth without any signs of collapse. Additionally, a solitary enlargement of the para-aortic lymph node in the B1 region was observed.

Initially, left adnexectomy was performed, and a rapid pathological diagnosis confirmed the malignancy of the tumor. Consequently, a comprehensive surgical procedure, including total abdominal hysterectomy, bilateral adnexectomy, pelvic lymph node dissection, para-aortic lymph node dissection, and oophorectomy, was completed. The postoperative course was uneventful, and the patient was discharged on the seventh postoperative day. The intraoperative ascites cytology yielded a negative result. Moreover, the pathology of the left ovary revealed atypical cells forming glandular luminal structures, cribriform structures, and proliferative cells. The lumen exhibited an accumulation of highly acidic material, and necrotic lesions were also observed. Immunostaining results indicated a positive expression of PAX8 with CD10 observed on the luminal surface. The thyroid transcription factor-1 (TTF-1) showed weak to extensive positive staining, p53 expression was consistent with the wild-type status, and estrogen receptor (ER), progesterone receptor (PgR), Wilms' tumor protein (WT-1), GATA3, calretinin, and inhibin staining showed negative results. In addition, a solitary metastasis was identified in the B1 region of the para-aortic lymph nodes (Fig. 2 and 3). As a result, the patient was diagnosed with FIGO stage IIIA1(ii) mesonephric-like adenocarcinoma. Postoperatively, the patient received six sessions of carboplatin and paclitaxel (TC) chemotherapy (175 mg/m^2, AUC 6) as an adjuvant chemotherapy. As complication, the patient developed severe peripheral neuropathy. At present day, one year has passed since the initial surgery without recurrence and peripheral neuropathy is showing signs of mild improvement.

In addition, Myriad Mychoice Test® was performed for homologous recombination deficiency (HRD) search, Myriad HRD status was negative (patient genomic instabolity score was 1 point) and tumor mutation breast cancer 1 (BRCA1) / breast cancer 2 (BRCA2) status was negative.

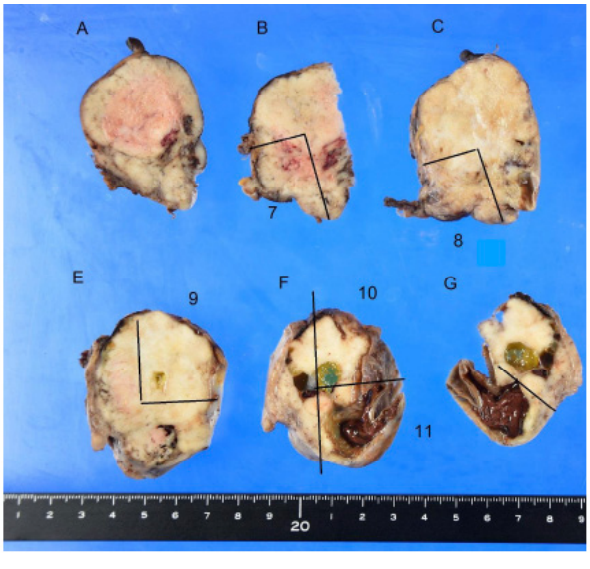

Fig. 2. The gross Findings.

Atypical cells form and proliferate in glandular luminal and cribriform structures. Within the lumen, there is an accumulation of acidophilic material. Necrosis is observed. Adjacent to this lesion are multiple cystic lesions. The cyst wall is mainly encapsulated by a single layer of epithelium, but shows partial papillary growths, some of which are contiguous with the above lesions.

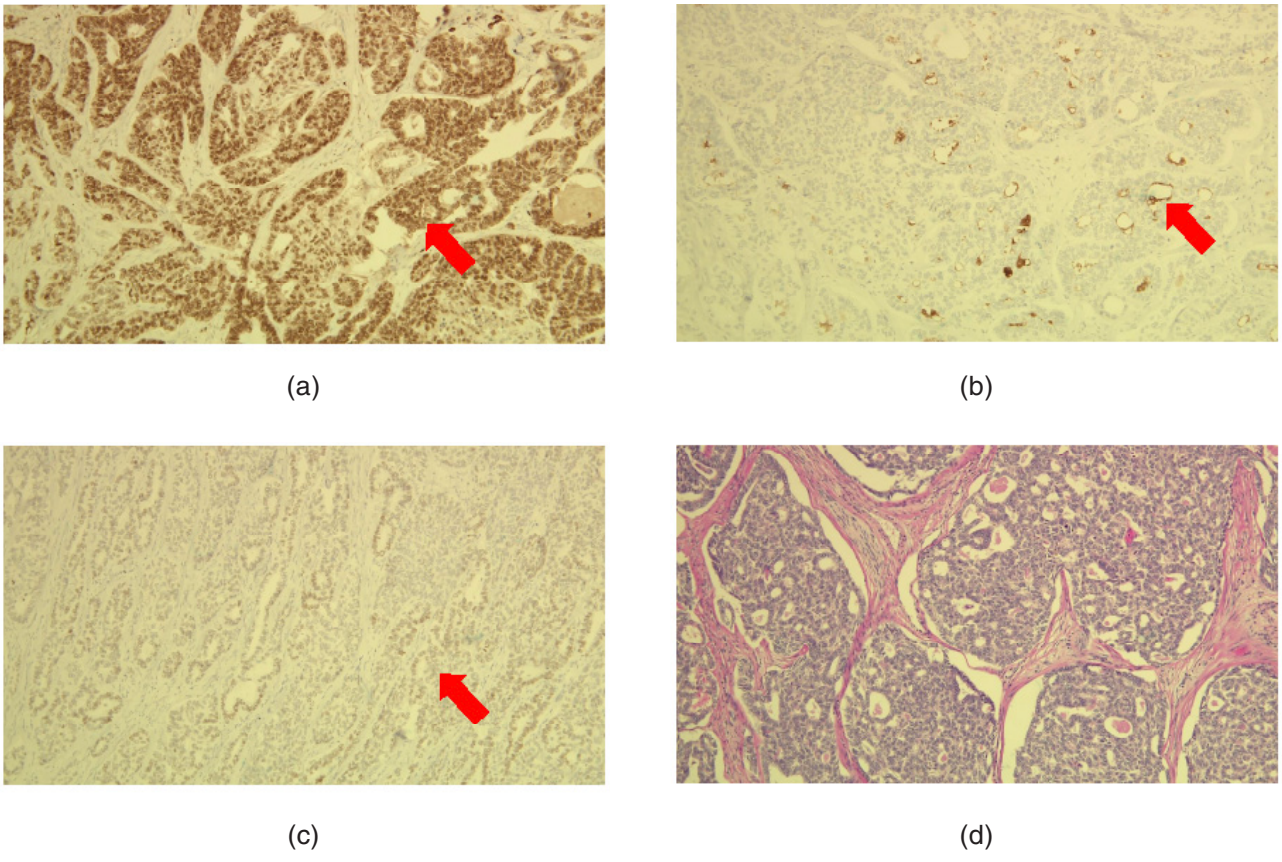

Fig. 3. Pathologic findings.
(a) PAX8 positive, (b) CD10 positive on luminal surface, (c) TTF-1 weakly to extensively positive, (d) hematoxylin and eosin stain

Discussion

Due to its recent addition to the WHO classification in 2020, there are limited available reports on MLA, which is a new pathological classification of ovarian malignancies. It arises from transdifferentiation of the mesonephric remnants of the parenchymal ovarian tissue or from benign or neoplastic Müllerian duct precursors. Furthermore, other genetic MLAs have been reported to have a very high frequency of Kirsten rat sarcoma viral oncogene homologue (KRAS) mutations, followed by Phosphatidylinositol 3-kinase catalytic subunit alpha (PIK3CA) mutations[5].

Clinically, MLA is often diagnosed at stages I–II in unilateral ovaries, although a considerable number of cases are detected at stages II–IV. Reports indicate that lung metastasis is the most common in advanced stages of ovarian cancer[6]. Furthermore, the tumor marker CA125 tends to increase as the advanced ovarian cancer progresses[7].

In terms of prognosis, MLA of ovarian origin has a worse prognosis compared with low-grade serous carcinoma and is similar to that of high-grade serous carcinoma (HGSC). Thus, MLA should be treated as a high-grade tumor, similar to high-grade serous carcinoma and clear cell carcinoma[4]. On the other hand, as a result that Myriad HRD Status was negative (patient genomic instability score was 1 point) and tumor mutation *BRCA1*/*BRCA2* Status was negative, compared to HGSC, chemotherapy including TC chemotherapy may be effective, while its efficacy against poly adenosine diphosphate (ADP) -ribose polymerase inhibitors is still unknown.

In a multicenter study by Jennifer, a 5-year

progression-free survival of 68% and overall survival of 71% were reported in 23 patients. The most common sites of recurrence were the lung (40%, 2/5) and omentum (40%, 2/5). However, many aspects of MLA remain unclear, and a larger study including the efficacy of post-therapy is warranted[6].

In a report on chemotherapy after surgical therapy, adjuvant chemotherapy was administered to four patients with stage IC-II tumors. Among the four patients, three had no recurrences based on available follow-up information. In contrast, patients with stage IA disease who did not receive adjuvant chemotherapy experienced multiple metastatic relapses approximately 13 months after surgery. Although the number of reports is limited, they suggest that sensitivity to chemotherapy may be favorable[7]. Conversely, Qiuhe et al recommended carboplatin and paclitaxel as the first-line chemotherapy of choice for MLA. However, they stated that the prognosis was poor[8].

There have been two reported cases of MLA arising from endometriosis[9] and one from a serous borderline tumor[10]. These findings suggested the potential involvement of precancerous lesions in the development of MLA. Although there was no history of MLA in our case, this possibility should be considered. However, it may be difficult to distinguish MLA from endometrial carcinoma pathologically, and morphological and immunohistochemical features should be examined. The diagnostic challenge associated with MLA may lead to diagnostic errors, potentially leading to the misclassification of patients as having low-grade neoplasms with a favorable prognosis, or vice versa[2]. Therefore, gynecologists and pathologists should actively consult and scrutinize these immunostains in the presence of clinically and pathologically non-specific conditions.

However, it is important to acknowledge the limitation of our current knowledge on MLA, as there is a scarcity of large case reports due to its rarity and novelty. The pathological diagnosis of MLA is often extremely challenging, carrying a potential risk of overlooked diagnoses.

Conclusion

Based on several case reports, adjuvant chemotherapy using a combination of two drugs, namely carboplatin and paclitaxel, after complete surgery has shown promising results with a low risk of recurrence. However, the positive rate of homologous recombination deficiency and the efficacy of poly ADP-ribose polymerase inhibitors remain unclear. Further accumulation of cases and studies on regimens, including long-term prognosis and maintenance therapy, are needed to enhance our understanding of MLA.

Potential conflicts of interest

The authors declare no conflicts of interest.

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