Current Problems in Cancer: Case Reports 17 (2025) 100[illegible]

Contents lists available at ScienceDirect

Current Problems in Cancer: Case Reports

journal homepage: www.elsevier.com/locate/cpccr

Mesonephric-like adenocarcinoma of the ovary: A rare case report and review of the literature

Maryam Hosseinirad [a,*], Elham Mirzaeian [a], Amirhossein Charejoo [b]

[a] Department of Pathology, Dr Shariati Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[b] School of medicine, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:
Ovary
Mesonephric-like adenocarcinoma
FIGO stage classification
Peritoneal dissemination

ABSTRACT

Mesonephric-like adenocarcinoma of the ovary is an exceedingly rare malignant tumor within the reproductive system, accounting for fewer than 1 % of all malignant tumors in women. Originating from remnants of the regressed Wolffian duct during embryonic development, its clinical manifestations are nonspecific, and its rarity often leads to delayed diagnosis, resulting in heightened morbidity and long-term recurrence. We discuss a case of 57-year-old woman with ovarian cysts that were incidentally found in abdominal and pelvic sonography and final diagnosis of mesonephric-like adenocarcinoma with peritoneal involvement and 2014 FIGO stage classification of stage IIIc which is extremely rare stage at presentation in this particular tumor. Diagnosis primarily relies on meticulous physical examination coupled with imaging, complemented by histological analysis and the marking of diagnostic immunohistochemical markers (positive for TTF1, GATA3, PAX8, and CD10 while uniformly negative for ER and PR). This study elucidates the clinical and pathophysiological attributes, diagnostic findings, and treatment strategies through the analysis of a subset of patients diagnosed with mesonephric-like adenocarcinoma in the ovary, followed by a comprehensive literature review.

Introduction

The embryonic period in men witnesses the mesonephric ducts as the genesis of vital components such as the epididymis, vas deferens, seminal vesicles, and the efferent duct of the testis ([illegible], 2023). Conversely, in women, these ducts regress, evolving into integral parts of the broad ligament and the lateral walls of the cervix and vagina. This phenomenon demonstrates the remarkable sexual dimorphism within the human reproductive system. However, these same components, though in the female reproductive system, occasionally undergo malignant transformation ([illegible] et al., 2021).

A distinctive manifestation of this transformation is mesonephric-like adenocarcinoma—a rare malignancy within the female reproductive system—constituting less than 1 % of all malignant tumors in women ([illegible] et al., 2020). Typically surfacing around the age of 60, this tumor is prevalent in the post-menopausal phase ([illegible] et al., 2022). Its origin resides in the mesonephric ducts, predominantly locating itself within the cervix and vagina. However, owing to the intricate complexities of its origin and pathophysiological behavior that are yet to be definitively delineated, it is called "mesonephric-like adenocarcinoma" ([illegible] et al., 2022).

Compounding the diagnostic challenges, the clinical features of this malignancy are non-specific, often presenting as abdominal-pelvic pain and discomfort. This nebulous symptomatology frequently leads to erroneous diagnoses of other reproductive ailments in women, subsequently causing diagnostic delays. It is most often found in the cervix and vagina, where embryological remnants are primarily located in the paravaginal region and deep cervical stroma ([illegible] et al., 2022). When this malignancy does manifest within the ovaries, it becomes an exceedingly uncommon occurrence, thereby amplifying the intricacies of accurate diagnosis. Mesonephric-like adenocarcinoma with classification of 2014 FIGO stage IIIC is an extremely rare presentation within the ovary, which is seen in our particular case ([illegible] et al., 2022). In this context, we endeavor to elucidate the clinical and pathophysiological intricacies, diagnostic findings, and treatment strategies through the examination of a subset of patients afflicted with mesonephric-like adenocarcinoma within the ovary, accompanied by a comprehensive review of pertinent literature.

Abbreviation: TTF1, Thyroid transcription factor-1; GATA3, GATA binding protein-3; PAX8, Paired-box gene-8; CD10, Neutral endopeptidase; ER, Estrogen receptor; PR, Progesterone receptor.

* Corresponding author.
E-mail addresses: [illegible] (M. Hosseinirad), [illegible] (E. Mirzaeian), [illegible] (A. Charejoo).

https://doi.org/10.1016/j.cpccr.2025.100[illegible]
Received 4 July 2024; Received in revised form 3 January 2025; Accepted 4 February 2025
Available online 8 February 2025

Case presentation

We present the case of a 57-year-old woman who initially displayed non-specific symptoms, including anemia and dysuria. The patient was referred to our medical center and underwent preliminary evaluations, which encompassed a comprehensive physical examination and the acquisition of routine laboratory tests, followed by thorough imaging assessments. Abdominal and pelvic ultrasonography incidentally identified cysts in both the right and left ovaries. Endometrial thickness was 2 mm. The patient was scheduled for a spiral computed tomography (CT) scan of the abdomen and pelvis (Fig. 1), revealing solid-cystic lesion within the right ovary and cystic lesion within the left ovary. The right ovarian lesion appears more solid, while the left ovarian cyst measures 50 × 31 mm in diameter, contains delicate septa, a mural nodule, and is accompanied by mild pelvic fluid. Additionally, the CT scan disclosed mesenteric and peritoneal nodules measuring up to 21 × 13 mm in diameter. Consequently, the patient underwent right-sided cystectomy and salpingo-oophorectomy. The excised specimen was promptly forwarded to the pathology department for immediate intraoperative frozen examination.

Based on the pathological analysis, a preliminary diagnosis of high-grade carcinoma was rendered. Given these findings, a comprehensive treatment plan was devised immediately after the frozen section, including total abdominal hysterectomy and left salpingo-oophorectomy (TAH-LSO), cystolysis, lymphadenectomy, appendectomy, and omentectomy. The obtained pathological specimens were dispatched to the pathology unit for further meticulous evaluation. Upon pathological examination of the TAH-LSO specimen, a solid-cystic lesion with a multi-nodular surface and a grayish-white appearance, measuring 60 × 48 × 40 mm, was identified within the left ovary. Additionally, gross examination of the omentum specimen revealed multiple nodular lesions with an average diameter of 25 mm, while the cytological assessment of peritoneal fluid robustly substantiated the malignancy diagnosis. Microscopic analysis of the left ovarian lesion unveiled invasive adenocarcinoma featuring diverse patterns, including tubular, glandular, ductal (with slit-like appearance), papillary, and solid structures, without the presence of squamous or mucinous differentiation (Figs. 2 and 3). In the immunohistochemistry study, the immunohistochemical markers TTF1, CD10, PAX8, and GATA3 exhibited positivity, whereas markers ER and PR exhibited adverse negativity (Fig. 4). This combination of findings conclusively affirmed the diagnosis of mesonephric-like adenocarcinoma. The dosage of the preoperative tumor markers are as follows: HE4 137/8 U/ml (increased), LDH 335 U/L (normal), CA19-9: 11 /95 U/ml (normal), CA125: 22/2 U/ml (Normal), CEA: 0/73 ng/ml (normal).

In this case, extensive involvement was noted in the surfaces of the left ovary and fallopian tube, as well as the right parametrium. Tumoral engagement was also discernible in the omentum and paraappendiceal soft tissue. The diagnostic assertions were reinforced through microscopic examination of permanent slides extracted from the right salpingo-oophorectomy specimen. Consequently, the proposed diagnosis aligned with pathological findings, culminating in the classification of 2018 FIGO stage IIIC for this particular case.

Our patient underwent 6 sessions of adjuvant chemotherapy with carboplatin plus paclitaxel with the combination of Bevacizumab after surgery for one year. She was recently followed up, and their condition is stable with no signs of tumor involvement on the CT scan.

Discussion

Mesonephric-like adenocarcinoma is an exceedingly rare malignant entity (D'Souza, 2023). The pathogenesis of MLAs is unclear, and it is still debated whether they are mesonephric (Wolffian) carcinomas originating in the endometrium/ovary, or endometrioid (Müllerian) carcinomas that closely resemble mesonephric carcinomas (Kolin et al., 2023).

While it predominantly arises within the uterine cervix, ovarian occurrences are even scarcer (Daniel et al., 2019).

Primary uterine mesonephric carcinomas are extremely rare, and the possibility of cervical origin should be excluded. The clinical data of this tumor in the uterus resemble those of other endometrial carcinomas, including symptoms such as vaginal bleeding. Adenocarcinoma of the uterine cervix, HPV-independent mesonephric type, is rare, representing less than 1 % of cervical adenocarcinoma cases. Symptoms include abnormal vaginal bleeding, abdominal pain, uterine prolapse, and dyspareunia. The prevalence of this tumor in the ovary is very low and typically presents with pelvic or abdominal pain. No epidemiological data on this uncommon tumor are available. Most cases occur in postmenopausal women (WHO Classification of Tumors 2020).

In general, Mesonephric-like adenocarcinomas are estimated to

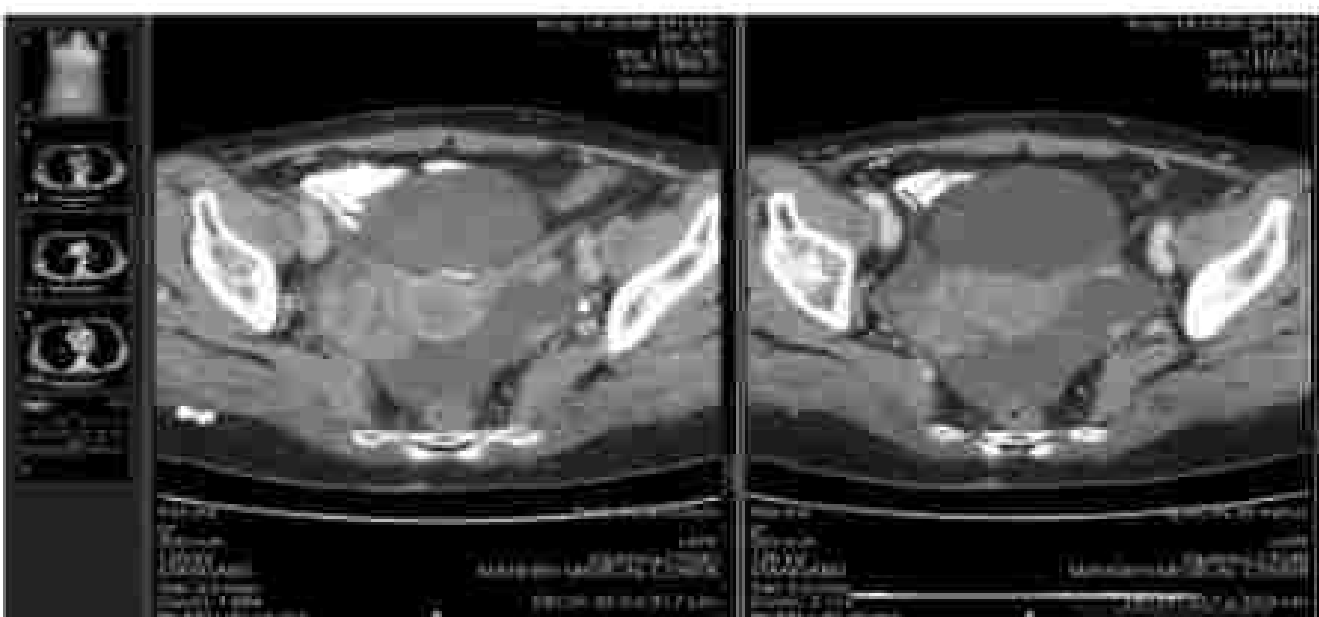

Fig. 1. Computed tomography feature of Mesonephric-like adenocarcinoma of the right and left ovaries.

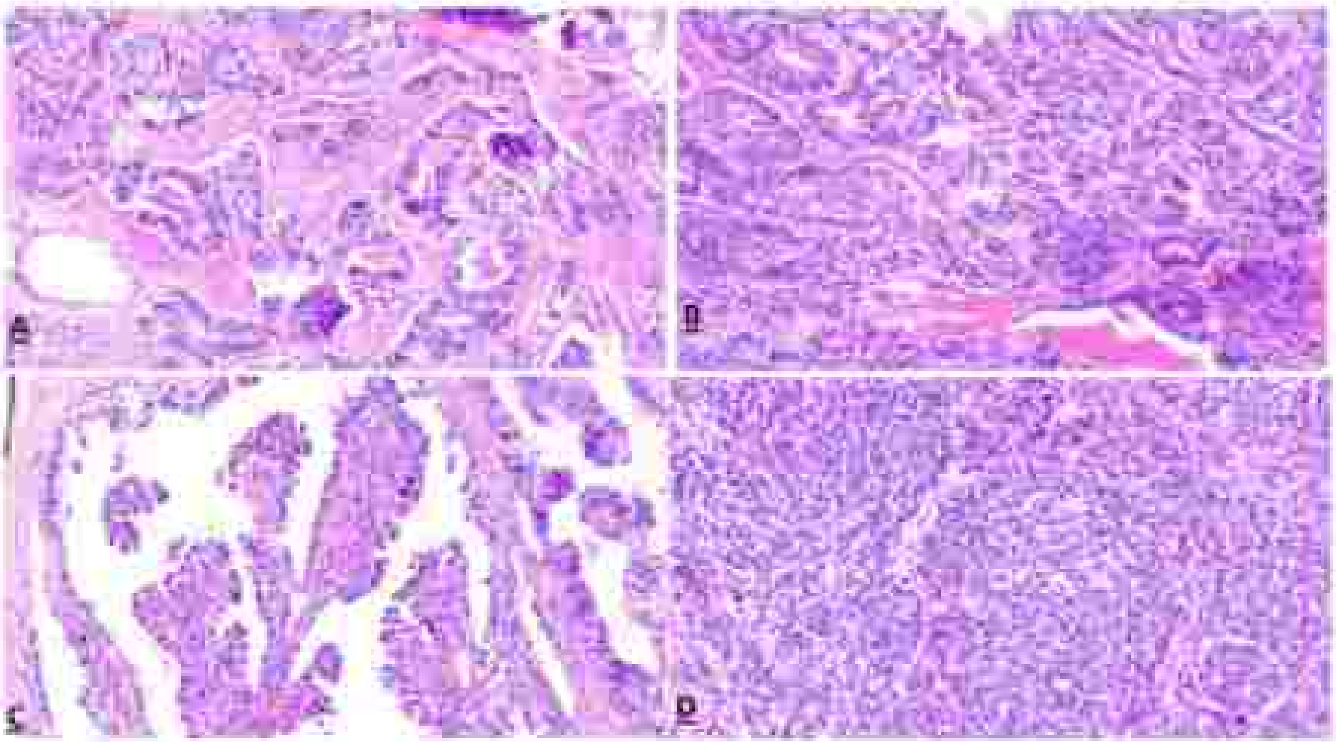

Fig. 2. Ovarian mesonephric-like adenocarcinoma. Tubular (A), glandular (B), papillary (C), solid (D) pattern.

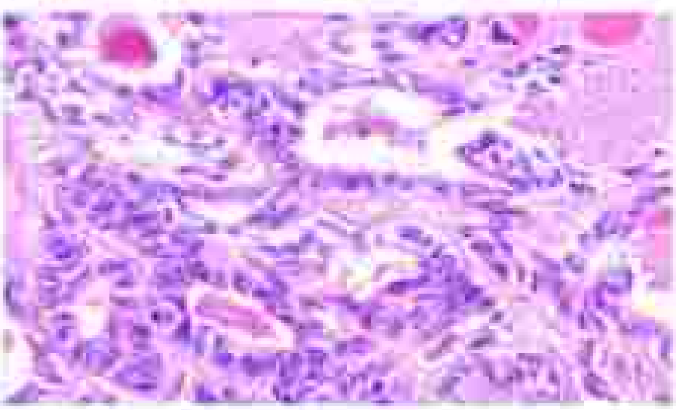

Fig. 3. Ovarian mesonephric-like adenocarcinoma (high power field), shows tubular pattern lined by cuboidal cells with nuclear groove and filled with eosinophilic colloid-like material.

account for approximately 1 % of endometrial carcinomas, with an average patient age of 55 years ([illegible] et al., 2022).

This tumor's clinical manifestations, such as abdominal or pelvic pain and distension, often manifest when the tumor attains substantial size or advances to higher stages ([illegible] et al., 2020). Detecting early-stage ovarian mesonephric-like adenocarcinoma remains challenging, akin to other ovarian malignancies. Therefore, vigilance towards suspected symptoms, coupled with precise physical examinations, is pivotal for raising suspicion of this condition. In-depth studies, encompassing imaging, assessment of pathological behavior, and immunohistochemical evaluations, are crucial steps for confirming or refuting the diagnosis ([illegible] et al., 2018). Consequently, monitoring serum tumor markers, utilizing imaging modalities like abdominal-pelvic ultrasonography, CT scans, and MRI, is imperative.

Distinct immunohistochemical markers specific to mesonephric-like adenocarcinoma—TTF1, GATA3, PAX8, and CD10—show diagnostic utility, as they exhibit positive expression, while ER and PR markers manifest negative expression, facilitating differentiation from other diagnoses ([illegible] et al., 2021). For instance, distinguishing this mass from suspected endometrioid adenocarcinoma or serous adenocarcinoma hinges on the over-expression of ER and PR and the absence of GATA-3 in the latter masses ([illegible] et al., 2020).

The pathogenesis of mesonephric-like adenocarcinoma remains enigmatic, prompting discussions among pathologists on whether these represent endometrioid adenocarcinomas closely imitating mesonephric adenocarcinoma or actual occurrences of mesonephric adenocarcinomas within the ovary/endometrium. Mesonephric-like carcinoma displays a range of histologic patterns, similar to endometrioid carcinoma, including a tubuloglandular pattern. These carcinomas are generally negative for hormone receptors, which helps distinguish them from low-grade endometrial endometrioid carcinoma. They express markers like GATA-3 and TTF1, which are typically absent in low-grade endometrial endometrioid carcinoma (Gynecologic Pathology book, 2020).

Ogawa's literature review revealed that all evaluated cases of ovarian MLA (33/33) were pMMR, contrasting with the 6–19 % dMMR rate observed in ovarian endometrioid carcinomas. This suggests that pMMR may serve as a distinguishing feature of MLA compared to endometrioid carcinoma. They also found that KRAS mutations were present in [illegible] % of the ovarian MLA cases (38 out of 42), suggesting that KRAS mutations could be a potential therapeutic target for recurrent or metastatic MLA ([illegible] et al., 2024).

Treatment guidelines for mesonephric-like adenocarcinoma are not definitive. Based on clinical experiences, a treatment protocol often includes hysterectomy, followed by bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, and omentectomy for most patients ([illegible] et al., 2022). The choice of treatment approach should consider patient age (reproductive period), tumor stage (FIGO staging), and patient satisfaction with the treatment protocol. Chemotherapy holds vital importance for tumor regression, akin to other ovarian malignancies. Recent reports suggest that a combination of surgery followed by chemotherapy, employing carboplatin plus

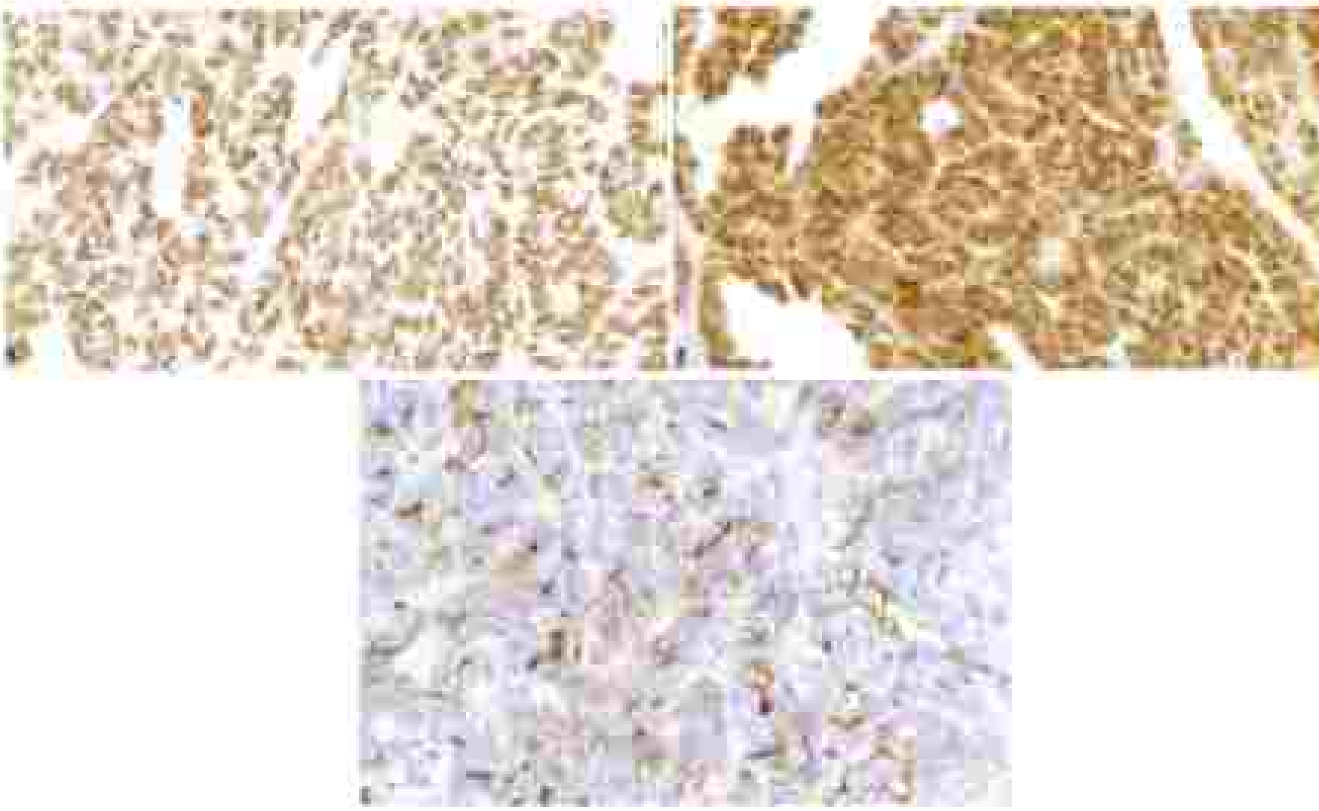

Fig. 4. ovarian mesonephric-like adenocarcinoma, TTF1 immunostaining is positive nuclear expression (A), PAX8 immunostaining is positive nuclear staining (B), CD10 immunostaining shows luminal expression in glands (C).

paclitaxel, could facilitate tumor regression (Mannipet et al., 2021). our case also underwent adjuvant chemotherapy with carboplatin, paclitaxel, and bevacizumab for one-year post-surgery. Follow-up CT shows no tumor involvement, and the patient is stable.

In our study, the case presented with entirely non-specific initial symptoms, such as anemia and dyspnea. Prolonged persistence of these symptoms led to sequential initial and imaging evaluations, ultimately culminating in specialized assessments involving histopathology and tumor marker tracking. This comprehensive approach led to a definitive diagnosis. Neglecting the initial manifestations or failing to suspect such a rare diagnosis can jeopardize patient outcomes. In managing such cases, it is imperative to heed even the subtlest non-specific symptoms, conduct diagnostic surgeries, employ highly accurate and sensitive imaging techniques, and initiate treatment approaches, including surgical interventions coupled with chemotherapy, at the earliest opportunity.

An exploration of existing literature reveals a limited number of similar cases, primarily within the last decade. Chen's case study from 2020 (Chen et al., 2020) details a 26-year-old female patient with a history of abdominal discomfort. Initial diagnosis using pelvic ultrasound identified a solid and cystic mass within the adnexal region, with the diagnosis confirmed through pathological and immunohistochemical examinations. The therapeutic plan involved total hysterectomy, left adnexectomy, pelvic and para-aortic lymphadenectomy, and omentectomy, succeeded by four cycles of combination chemotherapy with carboplatin and paclitaxel, resulting in complete tumor removal without recurrence during a 13-month follow-up.

Similarly, Koh's research in 2022[14] encompassed four patients with stage IC-II mesonephric-like adenocarcinoma. These patients underwent surgery and adjuvant chemotherapy, with three of them showing no recurrence within 12 months. Pors et al.'s 2021 study (Pors et al., 2021) reported that 39 % of mesonephric-like adenocarcinomas were found in the ovary, with a significant recurrence rate of 42 % in cases of untreated or delayed diagnosis. Their report indicated a 5-year disease-specific survival rate postoperatively at 71 %.

In conclusion, the available evidence underscores the importance of prompt evaluation of suspected cases of this tumor, focusing on histopathological findings and tracking immunohistochemical markers, while adopting a combined approach of surgery and chemotherapy to ensure the long-term survival of patients.

Ethical approval

Ethic clearance was not necessary in this study. No procedure was performed on the patient, therefore, no unnecessary costs or interventions was imposed on the patient. Also, the information about the patient remains confidential only with the researcher.

Consent

No procedure was performed on the patient and no images of the patient were included in this study. However, this study was conducted in an educational, therapeutic and research center and consent forms in Persian language are taken in the hospitalization records of all patients to carry out research projects. The image of the consent form is attached. Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. No patient's name, initial, or hospital numbers has been mentioned in this study.

Patient consent statement

The authors declare that they have obtained consent from the patient.

The authors declare that they have obtained consent from the patient's next of kin, as the patient is deceased.

The authors declare that they have obtained consent from the patient's legal guardians.

CRediT authorship contribution statement

Maryam Hosseinitad: Writing – original draft, Conceptualization, Resources, Visualization. **Elham Mirzaeian:** Conceptualization, Project administration, Resources, Supervision, Visualization. **Amirhossein Charejoo:** Writing – review & editing, Resources.

Declaration of competing interest

None.

Acknowledgements statement

– **Assistance with the study:** Assistance with the study: None.
– **Financial support and sponsorship:** Financial support and sponsorship: None.
– **Declarations of interest:** None.
– **Presentation (for original articles only):** None.

References

[illegible], 2021. Mesonephric-like adenocarcinoma of the ovary associated with low-grade serous carcinoma: a case report. Diagnostics (Basel) 11 [illegible]. https://doi.org/10.3390/diagnostics[illegible]. May 2.

[illegible], 2018. [illegible]. Int. J. Gynecol. Pathol. 37, [illegible].

Chen, [illegible], 2020. Mesonephric-like adenocarcinoma of the ovary: a case report and a review of the literature. Medicine 99 [illegible]. https://doi.org/10.1097/MD.[illegible]. Nov 25.

Choi, [illegible], 2023. [illegible]. Anticancer Res. [illegible].

[illegible] et al., 2023. A combined morphologic and molecular approach to [illegible] mesonephric-like adenocarcinoma of the endometrium. Am. J. Surg. Pathol. [illegible].

[illegible], 2020. Ovarian mesonephric-like adenocarcinoma arising in serous borderline tumor: a case report with complete morphological and molecular analysis. Diagn. Pathol. 15 [illegible]. https://doi.org/10.1186/s13000-020-[illegible]. Jul 22.

[illegible], 2021. Progress in the pathological arena of gynecological cancers. Int. J. Gynaecol. Obstet. 155 (Suppl. 1), [illegible]. https://doi.org/10.1002/ijgo.[illegible]. Oct, Suppl.

[illegible], 2020. [illegible].

[illegible], 2019. Cytologic features of upper gynecologic tract adenocarcinomas [illegible] mesonephric-like differentiation. Cancer Cytopathol. [illegible]. https://doi.org/10.1002/cncy.[illegible]. Aug; pub [illegible]. Jul [illegible].

Kim, [illegible], 2022. Mesonephric-like adenocarcinoma of the ovary: clinicopathological and molecular characteristics. Diagnostics 12 [illegible]. https://doi.org/10.3390/diagnostics[illegible]. Jan 27.

[illegible] et al., 2020. [illegible]. [illegible].

[illegible], 2024. Ovarian mesonephric-like adenocarcinoma: its prevalence in a Japanese high-volume cancer center and a literature review [illegible]. [illegible]. https://doi.org/10.3390/[illegible]. Aug 20.

[illegible], 2022. Clinicopathologic characteristics of mesonephric adenocarcinomas and mesonephric-like adenocarcinomas in the gynecologic tract: a multi-institutional study. Am. J. Surg. Pathol. [illegible]. https://doi.org/10.1097/PAS.[illegible]. Apr 1.

[illegible], 2022. Mesonephric-like adenocarcinoma: a rare tumor: the importance of diagnosis. [illegible]. https://doi.org/10.3390/[illegible]. Nov 4.

[illegible], 2020. Mesonephric-like adenocarcinoma of the ovary [illegible]: a case report and review of the literature. Gynecol. [illegible]. https://doi.org/10.1016/[illegible].

[illegible] Classification of Tumours, 5th Edition, Female Genital Tumours (2020).

[illegible], 2021. Mesonephric adenocarcinoma in female genital tract: a case series. Medicine 100 [illegible]. https://doi.org/10.1097/MD.[illegible]. Sep 3.