Clinicopathology and prognosis of mesonephric carcinomas

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Research Article

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Abstract

**Background:** Mesonephric adenocarcinoma (MNA) and Mesonephric-like adenocarcinoma (MLA) are rare malignant tumors of the female genital tract with extremely similar histopathological, immunohistochemical, and molecular characteristics. Differential diagnosis is therefore challenging, and experience in treatment and prognosis is lacking.

**Methods:** We collected clinicopathological features and immunohistochemical and follow-up information from 2 patients with mesonephric carcinomas (1 case of MNA and 1 case of MLA). A total of 139 cases of MNA and MLA were obtained from PubMed and CNKI through keyword searches. The clinicopathological features and prognostic information of 141 cases of mesonephric carcinomas were compared and analyzed. This detailed review of the literature provides a comprehensive overview of currently known mesonephric carcinomas.

**Results:** The median ages of MNA and MLA patients were 51 and 59 years, respectively. The most common clinical symptoms of both patients were irregular vaginal bleeding. Microscopically, these tumor cells are mostly arranged in mixed patterns, such as tubular, glandular and glomeruloid patterns. Tubular and glandular patterns are the most frequently described. MNA is characterized by mesonephric remnants adjacent to tumor tissue. Immunohistochemical staining is positive GATA3, PAX-8 and CD10 expression and negative ER, PR and P16 expression. TTF-1 expression is most common in MLA. The most common genetic change is KRAS gene mutation. The five-year survival rates of MNA and MLA are 73.5% and 68.5%, with recurrence rates of 33% and 58% and median times to recurrence of 20 and 12 months, respectively. Age affects the survival prognosis of MNA and MLA ($P=0.04$, $P<0.01$), and there is a significant difference in the DFS K-M survival curve between MNA and MLA ($P<0.01$).

**Conclusions:** The typical microscopic morphology and expression of immunomarkers support the diagnosis of MNA and MLA. Microscopically, mesonephric remnants adjacent to tumor tissue and immunohistochemical marker TTF-1 expression are key for the differential diagnosis of MNA and MLA. The recurrence and metastasis rates of MLA are much higher than those of MNA, and the prognosis is poor. Age is an important factor influencing the survival and prognosis of MNA and MLA. The most effective treatment for mesonephroid tumors remains to be further elucidated.

**Background**

Mesonephric carcinomas are rare diseases of the female genital tract. During embryonic development, females have two pairs of primitive genital ducts: Wolffian ducts (mesonephric ducts) and Müllerian ducts. The Müllerian duct becomes the female reproductive duct, and the mesonephric ducts eventually regress[1]. Mesonephric adenocarcinoma (MNA) is believed to derive from the remnants of the mesonephric ducts deep in the interstitial tissue of the cervix and vagina. Mesonephric-like adenocarcinoma (MLA) occurs in the uterus and ovary. Microscopically, MLA and MNA have very similar morphological characteristics, with the only difference being that benign mesonephric remnant tissue can
be found adjacent to the tumor of MNA. At present, no reports have described mesonephric remnants adjacent to MLA tumor tissue. The first case of MNA was reported by McGee in 1962[2], while the first reported case of MLA was by Yamamoto in 1995[3]. The WHO guidelines for cervical cancer (2020) have classified MNA as “adenocarcinoma HPV-independent mesonephric type”, while MLA occurring in uterine bodies is classified as “endometrioid carcinoma NOS, mesonephric-like adenocarcinoma”. To facilitate the earlier and better diagnosis and treatment of MNA and MLA, we describe a case of MNA and a case of MLA, summarize the clinicopathological and immunohistochemical characteristics and prognosis of these patients, and conduct a retrospective analysis of 141 cases of mesonephric carcinomas in the related literature.

Methods

Cases collected

By May 2021, 1 case of MNA and 1 case of MLA had been diagnosed in the First Affiliated Hospital of Bengbu Medical College. Information was collected, including patient age, tumor size, clinicopathological features, immunohistochemistry, and follow-up information. All medical and pathological records were reviewed by 3 experienced pathologists. Our patients agreed to undergo follow-up investigation, and both patients provided informed consent so that the details of their cases could be published. After a search of PubMed and CNKI, 68 cases of MNA and 71 cases of MLA were identified in the literature over the years. MNA refers to tumors that show typical morphological and immunohistochemical characteristics of mesonephric adenocarcinoma, primarily found in the cervix and mostly accompanied by remnants or hyperplasia of the mesonephric duct. MLA is a tumor that shows typical morphological and immunohistochemical characteristics of mesonephric carcinoma and is primarily found in the uterine body without mesonephric remnant or hyperplasia. This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Bengbu Medical College and was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

HE section preparation and immunohistochemical analysis

Tissue specimens were fixed with 10% neutral formalin, dehydrated, embedded in paraffin and stained with HE. Four-micron-thick sections were cut from representative formalin-fixed, paraffin-embedded tissue blocks. After dewaxing, sections were labeled with a set of antibodies against GATA3, PAX-8, CD10, TTF-1, Calretinin, P16, ER, PR, and Ki-67 (Table 1). IHC slides were interpreted by three experienced pathologists. All markers except Ki-67 were evaluated as positive or negative, and the Ki-67 index was analyzed as a cell nuclear marker in 1000 tumor cells in the region with the highest nuclear marker index and expressed in terms of the percentage of stained cells.
<table>
<thead>
<tr>
<th>Antibody</th>
<th>Source</th>
<th>Item Number</th>
<th>Clone</th>
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<td>GATA3</td>
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<td>L50-823</td>
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<td>MAB-0837</td>
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<td>MX002</td>
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<td>Maixin</td>
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<td>MX007</td>
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<td>Calretinin</td>
<td>Maixin</td>
<td>MAB-0716</td>
<td>MX027</td>
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<td>ER</td>
<td>Maixin</td>
<td>Kit-0012</td>
<td>SP1</td>
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<td>PR</td>
<td>Maixin</td>
<td>MAB-0675</td>
<td>MX009</td>
</tr>
<tr>
<td>TTF-1</td>
<td>Maixin</td>
<td>MAB-0677</td>
<td>MX011</td>
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<tr>
<td>Ki-67</td>
<td>Maixin</td>
<td>MAB-0672</td>
<td>MX006</td>
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</table>

**Molecular detection**

The KRAS gene of MNA cases was detected by fluorescence PCR, and the kit was purchased from Xiamen Eide Biological Company. The experimental steps were carried out in strict accordance with the kit instructions. The PCR instrument was a ThermoFisher ABI7500 system.

**Data analysis**

The clinicopathological features and prognostic information of 141 patients with mesonephric carcinoma (MNA69 cases, MLA72 cases) were compared and analyzed. OS (overall survival) was calculated for each patient from the date of diagnosis to the date of last known follow-up or death. DFS (disease-free survival) is from the date of diagnosis to the date of the first recurrence or, if there is no recurrence, to the date of the last known follow-up or death. The DFS-related Kaplan–Meier survival curves of patients with specific follow-up dates were analyzed using IBM SPSS Statistics 25 statistical software.

**Results**

**Clinical features**

Case 1: A 49-year-old female patient with MNA visited our hospital for treatment due to progressive dysmenorrhea for more than 4 years and frequent urination for more than 1 year. Physical examination revealed abdominal pain and an abdominal mass. Gynecological examination showed slight erosion of the cervix, slight hypertrophy, and irregular enlargement of the uterine body. Color ultrasound showed that the uterus was enlarged, and there were many low echoes in the muscularum area with a size of 4.4 cm×2.5 cm, with a regular shape and clear boundaries. There was a 1.9 cm×0.9 cm high echo area in the
endometrium area. Hysteroscopy showed uterine cavity enlargement, endometrial thickening, and local polypoid protrusion. The clinical diagnosis was uterine fibroids and endometrial polyps. Case 2: A 67-year-old MLA female patient visited our hospital complaining of irregular postmenopausal vaginal bleeding for more than 2 months. Physical examination showed no obvious abnormalities. Gynecological examination showed cervical atrophy and contact bleeding. Uterine atrophy was noted with no tenderness. MRI of the lower abdomen (plain scan + enhancement) revealed an abnormal intrauterine signal with mild enhancement (Figure 1). FIGO stage Ia endometrial cancer was considered.

**The gross and microscopic appearance of the tumor**

Case 1 showed mild erosion of the cervix with slight hypertrophy. For case 2, gross examination of the endometrial surface of the left uterine horn showed a polypoid protrusion, 3.0 cm×2.5 cm×0.8 cm in size, with a gray and red appearance in sections. Microscopically, the tumor tissue showed mixed growth of tubular and glandular tubular structures (Figure 2a). Glomeruloid structures were also seen in case 1 (Figure 2b), with atypia of tumor tissue and cells, lack of glycogen or mucus in cytoplasm, ground-glass appearance in some nuclei, and rare mitosis. The biggest difference between the two patients is the MNA patient had visible benign mesonephric remnants in the residual tumor tissues, mainly for the sample of the gland structure. The tumor was well-differentiated. The nonciliated epithelium cell monolayer cubic or columnar cells showed partial tufted or diffuse distribution in tubular structures (Figure 2c) lined with a single layer of flat or low cuboidal epithelium cells (Figure 2d), and the lumen had evenly distributed eosinophilic material. In case 2, no benign mesonephric remnants or hyperplasia tissue were found after resampling.

**Immunohistochemical marker results**

Immunohistochemical staining of the MNA patients showed that the tumor cells were positive for GATA3 (Figure 2e) and PAX-8 (Figure 2f), and the expression rate of Ki-67 was less than 5%. CD10, P16, TTF-1, ER (Figure 2g) and PR (Figure 2h) expression was negative. Immunohistochemical staining of MLA patients showed positivity for GATA3 (weakly positive), PAX8, and TTF-1 and negativity for calretinin, CD10, ER, PR, and P16. The Ki-67 expression rate was approximately 10%.

**Molecular detection results**

The KRAS gene of the MNA patient was analyzed by fluorescence PCR, and Pg12a mutation was found in exon 2 of the KRAS gene (Figure 2i). No relevant molecular tests were performed for the MLA patients.

**Treatment and follow-up**

MNA patients received postoperative radiotherapy in the pelvic lymph node drainage area 15 days after surgery, and cisplatin plus docetaxel synchronous chemotherapy was administered for 2 cycles, for which the patients returned to our hospital. After 15 months of follow-up, no recurrence has been observed. Follow-up remains ongoing. The MLA patients did not receive radiotherapy or chemotherapy after surgery. Three months after the operation, reexamination in the hospital showed normal findings. The
patients have been followed for 6 months, and no recurrence has been observed. Follow-up remains ongoing.

**Prognoses of the 141 MNA and MLA patients**

Combined with our two patients (MNA1 case, MLA1 case), a total of 141 patients (MNA69 cases, MLA72 cases) with mesonephric carcinoma were identified in the literature. The clinicopathological features, immunohistochemical markers and prognostic information of these patients were collected and analyzed (Tables 2 and 3).

Patients with MNA range in age from 1.5 to 78 years, with a median age of 51 years. The most common clinical symptom is irregular vaginal bleeding (92.3%, 36/39). Most tumor cells grow in a mixed form, with a tubular structure observed in 78% (22/28), glandular tubular structure observed in 39% (11/28), papillary structure observed in 53% (15/28), followed by a reticular structure, glomerular structure, sexual cord structure, etc.. The mixed growth of two or more structures is often noted. The tubular structure is lined with cubic or columnar cells, and eosinophilic secretions positive for PAS can be seen in the lumen. In this case, partially dilated tubular structures with monolayer ciliated cubic cells are also visible. Adjacent to the tumor, there were normal mesonephric remnants (n=33) and mesonephric duct hyperplasia (n=22). According to FIGO cervical cancer staging in 2018, 65.6% (n=63) of MNA were stage I, and all were stage IB. The 5-year survival rate of MNA was 73.5%, and 11 of 51 patients had recurrence, with a recurrence rate of 33%. The median time to recurrence is 20 months. Statistical analysis showed that age could affect the survival prognosis and recurrence of MNA ($P=0.024$, $P=0.04$).

The oldest and youngest MLA patients were 91 and 26 years old, respectively, with a median age of 59. The most common clinical symptom was irregular vaginal bleeding (96.4%, 27/28). Microscopically, MLA tumor cells are more pleomorphic and mitotic than MNA tumor cells. There is no residual middle renal duct tissue or middle renal duct hyperplasia found in MLA tumor tissue. According to the FIGO 2018 endometrial cancer staging, 47% (n=68) of these patients had stage II, III, or IV disease. The 5-year survival rate of MLA was 68.5%, the recurrence rate was 58%, and the median recurrence time was 12 months. Statistical analysis showed that age was an important factor influencing tumor recurrence ($P<0.01$).

The results of these studies revealed that MLA was more invasive and metastatic than MNA; the K-M survival curves of DFS of MLA and MNA are shown in Figure 3 ($P<0.01$).

**Table 2**

Result of clinicopathological and prognostic
### Table 3

Result of 141 cases immunohistochemical marks

<table>
<thead>
<tr>
<th>Clinicopathological and prognostic information</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MNA</td>
</tr>
<tr>
<td>Age(years)</td>
<td>max</td>
</tr>
<tr>
<td></td>
<td>min</td>
</tr>
<tr>
<td></td>
<td>mid</td>
</tr>
<tr>
<td>The most common clinical symptoms</td>
<td>92.5%</td>
</tr>
<tr>
<td>(irregular vaginal bleeding)</td>
<td></td>
</tr>
<tr>
<td>Tumor size cm</td>
<td>max</td>
</tr>
<tr>
<td></td>
<td>min</td>
</tr>
<tr>
<td></td>
<td>mid</td>
</tr>
<tr>
<td>Death rate</td>
<td>21.2%</td>
</tr>
<tr>
<td>OS 5years</td>
<td>73.5%</td>
</tr>
<tr>
<td>Recurrence rate</td>
<td>33%</td>
</tr>
<tr>
<td>Median time to recurrence month</td>
<td>20</td>
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### Antibody Expression

<table>
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<tr>
<th>Antibody</th>
<th>MNA</th>
<th>MLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>GATA3</td>
<td>Positive and diffuse positive</td>
<td>86.7% (n=15)</td>
</tr>
<tr>
<td>Pax-8</td>
<td>Positive and diffuse positive</td>
<td>100% (n=16)</td>
</tr>
<tr>
<td>CD10</td>
<td>Lumen stain</td>
<td>77.4% (n=31)</td>
</tr>
<tr>
<td>p16</td>
<td>Negative (patchy)</td>
<td>75% (n=12)</td>
</tr>
<tr>
<td>calretinin</td>
<td>positive</td>
<td>48% (n=25)</td>
</tr>
<tr>
<td>ER</td>
<td>negative</td>
<td>97.6% (n=42)</td>
</tr>
<tr>
<td>PR</td>
<td>negative</td>
<td>97.4% (n=39)</td>
</tr>
<tr>
<td>TTF-1</td>
<td>negative</td>
<td>100% (n=13)</td>
</tr>
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</table>

### Discussion

Mesonephric-associated adenocarcinoma is a rare disease of the female genital tract. In the embryonic development of the female reproductive system, the mesonephric tube degenerates completely after renal development, and incomplete degeneration forms mesonephric tube remnants distributed in the ovary, mesosalpinx, uterine ligament, uterine body, cervix, vagina and other parts [4]. Mesonephric remnants are most commonly found in the lateral wall of the cervix but can also be found in the lateral wall of the vagina or uterus, ovary hilum, and mesosalpinx. MNA most commonly occurs in the cervix, followed by the vagina. It is believed that MNA originates from mesonephric remnants and is often associated with mesonephric hyperplasia. Mesonephric carcinomas occurring outside the cervix are referred to as MLA. At present, the most widely accepted explanation for the origin of MNA and MLA is that MNA arises from the residual tissue of the mesonephric duct (Wolfe's duct), while MLA arises from the Müllerian duct and differentiates along the direction of the middle renal duct. Some scholars believe that KRAS gene mutation can not only cause the occurrence and development of MNA but also activate MLA. MLA also possesses genetic alterations that are frequently reported for Müllerian tumors, such as mutations in
PIK3CA, PTEN, and CTNNB1 genes. MLA and Müllerian duct lesions, such as endometrial carcinoma, serous borderline tumor, and low-grade serous ovarian cancer, share mutations in the KRAS gene and NRAS gene, reflecting the cloncity between MLA and Müllerian duct tumors. At present, most of the studies on MNA and MLA are case reports, and there is still a lack of studies focusing on the prognosis of MNA and MLA. To better diagnose and differentiate MNA and MLA, we collected a total of 141 cases of MNA and MLA since 1962 based on the relevant literature. Next, we discuss the clinicopathological features, immunohistochemical expression characteristics, prognosis and differential diagnosis of these two rare diseases.

MNA tends to occur in middle-aged and elderly women, with a median age of 51 years, and the common sites are the cervix, vagina and urethra. It has been reported that the onset age of MLA is older than that of MNA, with a median age of 59 years. The common onset sites are the endometrium and ovary, and the most common clinical symptoms of both are irregular vaginal bleeding. Unlike the common squamous cell carcinoma of the cervix, endophytic infiltrating MNA is rarely detected by ordinary cervical curettage and is usually found on conical or hysterectomy specimens. However, MLA generally presents as intrauterine exophytic masses, most of which are polypoid protrusions ranging from 1 to 14 cm in diameter accompanied by bleeding and necrosis. MLA is usually detected earlier than MNA by gynecological ultrasound, MRI and preoperative pathological biopsy. The structures of the MNA and MLA are both diverse and similar, including tubular, glandular, papillary, reticular, glomerular and sexual cord structures. The most common is a glandular tubular structure. The epithelial cells are nonciliated single cubic or low columnar, some nuclei show ground glass opacity, and hyaline eosinophilic secretion can be found in the glandular lumen. The cells are mostly mild to moderate atypia, and the nuclei can be vacuolar, nuclear overlap, nuclear grooves and other nuclear characteristics similar to papillary thyroid carcinoma. The number of mitotic figures vary somewhat, and MLA usually has more mitotic figures than MNA. The microscopic differentiation between MLA and MLA is mainly determined according to whether mesonephric remnants or hyperplasia can be found next to the tumor tissue. The presence of benign mesonephric remnants is helpful in diagnosis, but they are not always visible due to tumor overgrowth or because they are still too small to be detected microscopically. Therefore, we recommend that when suspected renal duct tumor tissue is found, all materials should be to the greatest extent possible.

MNA and MLA not only have similar microscopic structures but also express similar immunohistochemical markers. Both MNA and MLA tumors have positive GATA3 and PAX-8 expression, positive CD10 luminal expression, negative or focally positive p16 expression, and negative ER and PR expression. CD10 is considered to be a good marker of mesonephric remnant tissue and mesonephric adenocarcinoma. The expression of CD10 in mesonephric carcinomas is mainly located in lumencells. Ord et al. suggested that positive CD10 expression could be used as a marker of mesonephric remnants and mesonephric carcinomas in the female genital tract. Recently, Kenny et al., Tong et al. showed that PAX-8 is positively expressed in the male genital tract mesonephric epithelium and can be used as a reliable marker to distinguish mesonephric carcinoma. PAX-8 is strongly positive in benign mesonephric remnants, hyperplasia and malignant mesonephric tract lesions. Negative ER and PR immunomarker expression is an important clue for the diagnosis of mesonephric carcinomas and can
also help to differentiate between most female genital tract tumors, such as endometrioid adenocarcinoma. The expression of these immunomarkers is relatively stable in MNA and MLA tumors, and the expression of GATA3 and TTF-1 is worthy of further discussion. GATA3 is considered to be the best immunomarker for mesonephric carcinomas due to its high sensitivity and specificity[14]. According to our statistical analysis, the positive staining rate of GATA3 tumor cells in reported MNA cases is as high as 86.7%, and most of them show diffuse, strongly positive or positive expression. However, the GATA3 expression rate in MLA is only 71.7%, and diffuse, strongly positive expression is rare. TTF-1 was negative in all 13 MNA cases we collected, while the positive expression rate was as high as 78% in 41 MLA cases. Some studies[15, 16] have suggested that TTF-1 and GATA3 are inversely expressed in mesonephric carcinomas. Our data showed that the reverse expression rate of GATA3 and TTF-1 in MNA was 90.1% (10/11), with GATA3 expression being positive and TTF-1 expression being negative. The reverse expression rate of TTF-1 was 43.5% (17/39) in MLA, and TTF-1 was mostly positive. This finding indicates that GATA3 and TTF-1 expression levels are indeed different, which is worthy of further investigation by collecting more cases.

MNA and MLA are a group of diseases of the female genital system with a poor prognosis. MNA is mostly found in the early stage of the disease, while MLA is mostly found in the middle and late stages of the disease, with a worse prognosis than MNA. Porset et al.[15] conducted a comparative analysis of MNA cases with a group of HPV-associated cervical cancers and HPV-unrelated cervical cancers and found that MNA had poorer overall survival and tumor-free survival. Euscher et al.[17] conducted a retrospective analysis of MLA cases in the endometrium and showed that MLA is more aggressive and has a greater capacity for early recurrence and metastasis than low-grade endometrioid carcinoma. For the first time, we compared the prognosis of 141 patients with MNA and MLA. According to the 2018 FIGO cervical cancer staging system, 65.6% (n = 63) of MNA cases were stage I, and all were stage IB. The 5-year survival rate of MNA was 73.5%, the recurrence rate was 33%, and the median recurrence time was 20 months, with age being an important factor influencing survival and recurrence (P = 0.024, P = 0.04). According to the FIGO 2018 endometrial cancer staging, 47% (n = 68) of MLA patients have stage II, III, or IV disease. The 5-year survival rate of MLA is 68.5%, the recurrence rate is 58%, and the median recurrence time is 12 months. Age has also been found to affect tumor recurrence (P < 0.01). The final results showed that MLA was more invasive and metastatic than MNA and had the worst prognosis of all types of mesonephric carcinomas. Compared with previous reports, MNA most easily metastasizes to the lung[18]. In contrast, we believe that MNA is most likely to metastasize to the pelvis, while MLA is most likely to metastasize to the lungs. Perhaps due to the small number of cases, the distinction between the two has not been very clear. At present, there is no specific treatment for middle renal duct tumors, and most patients undergo extensive whole uterus plus bilateral adnexectomy. Through a literature review of 68 cases of MNA, we found that postoperative radiotherapy (P = 0.760) and postoperative chemotherapy (P = 0.965) did not show statistical significance in terms of treatment outcomes. MLA patients have been reported to be sensitive to platinum-based chemotherapy[18], while effective treatment for mesonephroid tumors requires further study.
Mesonephric carcinomas have been reported in the uterine body, cervix, broad ligament, bladder, urethra, and urethra diverticulum. Because the microscopic morphology of MNA and MLA is similar to that of clear cell carcinoma, serous carcinoma, malignant mixed Müllerian tumor, and endometrioid adenocarcinoma, the incidence of mesonephric carcinomas is most likely underestimated. We believe that it is necessary to differentiate MNA and MLA from the following tumors. 1. Benign mesonephric hyperplasia and MNA: Most carcinomas are diffuse mesonephric hyperplasia. The difference is that the nuclei of these carcinomas are malignant. The tubule pattern of MNA is similar to that of diffuse and vigorous mesonephric hyperplasia. MNA has an inconspicuous interstitial response and a pseudo infiltration pattern. The characteristics supporting the diagnosis of MNA include the presence of a mixture of other morphologies (solid, glandular, reticular, etc.), vascular or lymphatic infiltration, marked nuclear atypia, mitotic number > 1/HPF, and intracavitary necrotic debris. Mesonephric hyperplasia is almost incidental microscopically, while MNA mostly causes clinical symptoms and presents as a gross mass. 2. Cervical clear cell carcinoma and MNA: A small part of the clear cell carcinoma is confined to the myometrium, with various degrees of cystic papillary and solid structures. In the past it has been regarded as mesonephric carcinoma, but transparent nail cells cannot be seen in mesonephric carcinoma. Around the clear cells, there are no mesonephric remnants or hyperplasia, and immunohistochemistry shows CD10 negativity and ER and PR positivity. 3. Endometrioid carcinoma and MLA: It is necessary to distinguish endometrioid carcinoma with glandular hyperplasia from MLA. If there are no mesonephric remnants and a lack of scaling around the tumor and immunohistochemical ER and PR expression in MLA is negative, MLA tends to be the diagnosis. 4. Differentiation between MNA and MLA: MLA mainly occurs in the endometrium and ovary and lacks mesonephric remnants and hyperplasia near tumor tissue under a microscope. The occurrence of MLA seems unrelated. Negative expression of the immunohistochemical marker TTF1 tends to lead to a diagnosis of MNA, and positive expression tends to be diagnosed as MLA.

Conclusions

In summary, we reported 1 case of MNA and 1 case of MLA in detail and analyzed the clinicopathological characteristics, immunohistochemical characteristics and treatment prognosis of 141 cases of mesonephric carcinoma combined with relevant literature. The typical microscopic morphology of the tumor tissue exhibits atypical tubular, glandular, papillary, glomerular and other patterns; the typical immunophenotype is diffusely positive or positive GATA3 and PAX-8 expression, CD10 luminal staining, and negative ER and PR expression. These characteristics support the diagnosis of mesonephric carcinoma. Mesonephric remnants and immunohistochemical expression of TTF-1 can be used to differentiate MNA and MLA. The prognosis of MLA is poor, and the recurrence and metastasis rates of MLA are much higher than those of MNA. In addition, the prognosis is relatively worse as the age of patients increases. Effective treatments for both MLA and MNA remain to be further elucidated.

Abbreviations
Declarations

This study was approved by the Medical Ethics Committee of The First Affiliated Hospital of Bengbu Medical College and conducted following the ethical guidelines of the Declaration of Helsinki.

**Ethics approval and consent to participate**

Ethical approval for the study was obtained from the ethics committee of The First Affiliated Hospital of Bengbu Medical College (Bengbu, Anhui) and the exemption from informed consent was approved as well.

**Consent for publication**

Not applicable.

**Availability of data and materials**

The database generated and analyzed during this study is included in this article and its supplementary materials. Raw data are available upon reasonable request.

**Competing interests**

The authors have declared that no competing interests exist.

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**Authors’ contributions**

Rui Min was the main author on the paper, worked up the cases, and drafted the manuscript. Nan Li supervised the research and revised the manuscript. Shuai Sun, Fan Li, Qing Xia provided cytological smear and carried out immunohistochemistry study. Yan Su, Yuexin Han collected data. All authors have read and approved the final version of the manuscript.

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Figures
Figure 1

MRI images from our case 2. (a) T1W1 cross section abnormally low signal (b) T2W1 cross section abnormally high signal (c) T1W1 cross section heterogeneous enhancement (d) T2W1 sagittal plane abnormally high signal (e) T1W1 sagittal plane heterogeneous enhancement (f) DW1 cross section abnormally high signal
Figure 2

a. Tumor tissue is expressed as glandular tubular structure, high magnification, HE

b. Tumor tissue is expressed as glomerulus structure, medium magnification, HE

c. At high magnification, the wall of the glandular duct is a single cuboidal epithelium, and red eosinophilic tissue can be seen inside, high magnification, HE

d. Dilated tubular structures could be observed beside the tumor tissue, low magnification, HE

e. GATA3 positive tumor tissue, medium magnification, EnVision method

f. PAX-8 positive tumor tissue, EnVision method

g. ER negative tumor tissue, EnVision method
h. PR negative tumor tissue, EnVision method

i. Mutation of P. G12A in exon 2 of KRAS gene A: internal reference gene; B: P.g12a (exon2)

![Survival Proportions Graph](image)

**Figure 3**

DFS K-M survival analysis of 141 cases