Mesonephric Adenocarcinoma Arising From The Uterine Corpus：Case Reports and Literature Review

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Case report

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Abstract

Background Mesonephric adenocarcinoma (MNAC) is a rare carcinoma which arises from the mesonephric remnant of the gynecologic tract. It mainly occurs in the uterine cervix, barely locates in the uterine corpus, ovarian and vagina. To date, only a few cases of MNAC arising from of the uterine body (UB-MNAC) have been reported, and the clinicopathologic and molecular characteristics of UB-MNAC remain limited. A recent report suggested that series of UB-MNAC should be defined as Mesonephric-like adenocarcinoma carcinomas (MLAC), for they exhibited the classic morphologic features and immunophenotype of mesonephric carcinoma, but occurring outside of the cervix and without convincing mesonephric remnants. Thus, the histogenesis of UB-MNAC is not yet clear, they may originate in Müllerian tissue and exhibits the mesonephric differentiation phenotype, or arise from the mesonephric remnants in the uterine wall.

Case presentation To better understand the histogenesis of UB-MNAC, we presented three UB-MNAC cases from west china second university hospital, which exhibited typical morphologic, histologic as well as the immunohistochemical characteristics of MNAC. Notably, among the three cases, two cases arising from the myometrium layer of the uterine corpus found mesonephric remnants around the tumor. By reviewing the published UB-MNAC and UB-MLAC, we found that to our knowledge ,it is the first time finding mesonephric remnants around the MNAC cells in the reported literature, except one case that found mesonephric remnants in the cervix, and the tumors of the three cases were all arising from the myometrium layer, without endometrium involved. Then we compared the clinical characteristics of the UB-MNAC cases arising from the myometrium and endometrium, and the results showed that the two subgroups had most in common in the clinical characteristics except the myometrium subgroup had a higher elevated CA125 level, and this result was in consistent with the Kaplan-Meier survival analysis, which indicated that the myometrium subgroup had a poorer prognosis than the endometrium group. But this need more data and further study such as the molecular analysis.

Conclusion Though the pathogenesis of MLAC or MNAC of the uterine corpus is still under debate, according to our cases and the published literatures, We hypothesize two different pathways involved: the MNAC arising from the myometrium not affecting the endometrium may directly develop from the mesonephric remnant, the one occurred in the endometrium may not real mesonephric adenocarcinoma, but more likely arising from mesonephric transformation of Müllerian adenocarcinoma, and is better referred as MLAC. Besides, the two kinds of adenocarcinomas may have different clinical prognosis, while the MNAC arising from the myometrium may have a poorer prognosis than the MLAC originating from the endometrium, although they have identical morphologic and histologic characteristics.

Introduction

Mesonephric adenocarcinoma (MNAC) is a rare carcinoma that originates from mesonephric remnant of the female genital tract [1-3], and are predominantly located on the lateral walls of the cervix and vagina[4]. Of the cases reported to date, the vast majority of MNAC are from uterine cervix[1, 2, 4-19]., , comprising<1% of all carcinomas at this site[20], several cases of MNAC are from ovary [21-24], and rare cases are from vagina [4, 7, 25-29] and uterine corpus[4, 11, 21, 30-43]

MNAC is typically characterized by a combination of diverse growth patterns in histopathology, including tubulocystic, glandular, papillary, retiform, and glomeruloid architecture. Dense eosinophilic secretion is usually present in the tubulocystic components[6]. MNAC has a distinctive immunophenotype , it usually exhibits positive immunoreactivity for GATA binding protein 3 (GATA3), paired box 2 (PAX2), CD10, TTF1, and negative reactivity for estrogen receptor (ER), progesterone receptor (PR)[39, 44, 45].

Mesonephric-like carcinomas(MLAC) are a series of tumors that recently described by McFarland and colleagues. They reported a subset of 5 ovarian and 7 uterine corpus neoplasms which presented the typical histologic features of mesonephric carcinomas, but mesonephric remnants could not be found around it. Furthermore, some tumors were only confined to the endometrium layer without deep myometrim involved, where mesonephric remnants would exist theoretically. These tumors exhibited an immunophenotype same as mesonephric carcinomas, which were variably positive for CD10, calretinin, GATA3, and TTF1, but negative for ER and PR. Although the authors presume that these neoplasms might represent a new type of endometrioid adenocarcinomas, considering the immunohistochemical and histologic characteristics they found, they were in favor of that these tumors were “true” mesonephric neoplasms but admitted the uncertainty in their pathogenesis, so they termed them as “mesonephric-like” adenocarcinomas[21]. Molecular analyses suggest that MLACs are characterized by recurrent *KRAS*-mutations as well as unique immunohistochemical features and an aggressive clinical course[24, 44, 46].One research demonstrated that PIK3CA mutations, which have not previously been identified in cervical MNAC, were found in 3 of 7 (43%) MLAC in uterine corpus, and thus raised the question about possible Mullerian origin of the uterine corpus MLAC[46].

According to the published reports, the distant metastasis (5%)and recurrence rate(32%) of MNAC arising from the uterine cervix (UC-MNAC)is substantially higher than that of FIGO stage I cervical squamous cell carcinoma (11.0%) and usual-type endocervical adenocarcinoma (16.0%), suggesting that patients with UC-MNAC have a worse prognosis than those with more common types of cervical carcinoma[13]. But because of the limited number of cases reported, less is known regarding the clinical outcomes of UB-MNAC. Most publications on UB-MNAC are individual case reports or case series[4, 11, 21, 30-43]. A recent case series reported 11 cases of UB-MNAC , by investigating the clinicopathologic details, they concluded UB-MNAC displays an aggressive biological behavior, with a tendency to metastasize to the lungs[39]. But still, little is known about UB-MNAC, and it remains debated whether they represent mesonephric carcinomas arising in the uterus or Müllerian carcinomas that undergo mesonephric transformation. These findings led us to investigate UB-MNAC cases diagnosed in our institution and reviewed the published MNAC and MLAC arising from the uterine corpus, summarized and analyzed the characteristics of them. In this study, we presented three UB-MNAC cases diagnosed in our hospital, adding cases of UB-MNAC with morphologic and immunohistochemical analyses to the existing literature and to provide more data regarding clinical characteristics of UB-MNAC, hoping to help the clinician and pathologist have a better understanding of this rare carcinoma. And by presenting two special UB-MNAC cases, which mesonephric remnants were found around the corpus tumor for the first time, we add more evidence to better understand the pathogenesis of UB-MNAC.

Medical Record Review

Totally three patients of UB-MNAC were selected according to the diagnosis criteria, they were treated and monitored at the Gynecologic Department, West china children and women Hospital (Sichuan, China). We

thoroughly reviewed patients' medical records, pathology reports, and gross photographs. Clinical details, including age at initial diagnosis, presentation of symptoms and/or signs, serum cancer antigen-125(CA125) level, preoperative endometrial curettage diagnoses, surgical treatment, FIGO stage, postoperative treatment, development of metastasis, overall survival, and current status were examined (summarized in **supplementary Table1)**. The pathologic characteristics reviewed included tumor size, architectural pattern, and originate location; presence of sarcomatous component and so on.

Case Reports

Case1

A 67-year-old patient with past medical history of hypertension presented with postmenopausal vaginal bleeding and cough for one week. Transvaginal ultrasound and MRI examination revealed a hyperechoic endometrial mass in the cavity. Dilatation and curettage was performed and the mass was diagnosed as endometrial carcinoma with mixed clear cell and endometrioid components. PET-CT indicated metastatic lesion in the lung and the pubic bone. The patient then underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy, omentectomy, appendectomy, and pelvic and para-aortic lymphadenectomy. Grossly, a 9.0×6.0×3.5 cm solid mass was located in the fundus protruding into the uterine cavity **(Figure.1)**. Cervix and bilateral adnexa were unremarkable. Omentum and lymph nodes were grossly normal. Microscopically, the tumor exhibited a variety of growth patterns, including a characteristic tubular pattern with dense eosinophilic secretion, as well as a variety of morphologies, such as acinar, papillary, and ductal structures. The mass infiltrated into the outer half of myometrium, and was limited to the uterus with no serosal or cervical involvement, but lymphovascular space invasion was found. Immunohistochemical studies demonstrated that the tumor cells were immunoreactive for GATA3, CD10(luminal), TTF-1, PAX8, p16(patchy), and PTEN, and negative for ER, PR, AR, WT-1, P53, HNF1-β. The mismatch repair gene PMS2、MLH1、MSH2、MSH6 function retained well. All submitted lymph nodes were negative for carcinoma. The patient was diagnosed as stage IVB UB-MNAC, and she received postoperative systematic chemotherapy, and had no evidence of disease recurrence for 3 months after the surgery by now.

Case 2

A 55-year-old postmenopausal patient with unremarkable medical history complained of pink vaginal discharge, pollakiuria, and bilateral hip joint pain for several weeks. The ultrasound and CT scan revealed a 11*11*9cm heterogeneous hyperechoic mass in the posterior and fundal region of the uterus, with vague borderline. The CT scan also indicated metastatic lesion in the lung and right ischium. The para-aorta lymph node was enlarged. Laboratory workup showed a significantly increased CA125 level of 145.1 IU/ML. She received D&C and the pathologic result indicated poor to moderate differentiated adenocarcinoma. Then she was given three times neoadjuvant chemotherapy, and total laparotomy hysterectomy and bilateral salpingo-oophorectomy was performed later. Gross examination revealed a 11.0×7.0×7.0 cm ill-defined hemorrhagic mass lesion located in the myometrium of the posterior wall of the uterus **(Figure. 2)**. The mass grossly involved the serosa and the right sacrum ligament., the bilateral adnexa were totally normal. The endometrium and cervix were grossly normal too. Intraoperative frozen section was diagnosed as poorly differentiated cancer or carcinosarcoma, needing immunohistochemistry (IHC) to identify. Microscopically, the mass showed

a variety of growth patterns, including tubulocystic, papillary, solid, and retiform structures (**Figure. 2**). Densely eosinophilic secretions were focally present in the tubular and ductal structure of the tumor. The tumor cells penetrated beyond serosa and involved the right ovary as well as the lymphovascular system. Notably, normal **mesonephric remnant was found around the** adenocarcinoma cells. The entire endometrium was submitted for microscopic examination and showed focal pure hyperplasia and small focal complicated hyperplasia. Uterine cervix and the rest dissected part were negative for carcinoma. Immunohistochemical stains were performed, and indicate**d** that the adenocarcinoma component was positive for GATA3, CD10(luminal), TTF-1, PAX2, PAX8, p16(patchy), PTEN, CK-P, CK7,β-catenin and CyclinD, negative for ER, PR, Napsin-A, CD15, HNF1-β, Vimentin, caldesmon, Des, SMA, and WT-1, the Ki67% proliferation index was about 80%. The spindle cells component was negative for ER, PR,CK-P, CK7, EMA, CD10, CyclinD1, α-Inhibin, TTF-1, Des, caldesmon, GATA3, Pax-2, and positive for Vimentin, SMA, Pax-8(focal), and the Ki67 proliferation index was about 20%. A diagnosis of stage IVB UB-MNAC was made, including a small component of spindle cells, which partially showed leiomyosarcoma differentiation. At the most recent follow-up, the patient was scheduled chemotherapy, and showed no signs of recurrence for 4 months.

Case 3

The patient was 75 years old, and she received a laparoscopic salpingo-oophorectomy due to benign adnexal cyst several years before. The routine ultrasonography follow-up indicated a mass in the right wall of the uterus. The further CT scan showed a cystic-solid mass in the right adnexal region, which had no clear margin to the uterine wall. No other abnormality was found by the imaging test, and the CA125 level was also normal. A totally hysterectomy and abdominal multipoint biopsy was performed on her. The gross finding was a partial cystic partial solid mass measuring about 5cm in diameter in the right cornu of the uterus. The adenocarcinoma was arising from the myometrium layer of the right uterine cornu, invaded the serosal layer, and formed a mass in the right adnexal region. The endometrium was totally not affected. Noteworthy, mesonephric remnant was found around the adenocarcinoma cells. Metastatic lesion was found on the intestine surface. The adenocarcinoma was immunoreactive for GATA3, CD10(luminal), TTF-1, PAX2, PAX8, p16(patchy), CR(partial) and PTEN, and negative for ER, PR, WT-1, P53, AR, CK-20,CEA, CD56, Syn, CgA, α-Inhibin, Ki67 proliferation index was about 60%**(Figure. 3)**. The diagnosis for this patient was FIGO stage IVB UB-MNAC, and she received systematic chemotherapy after surgery. She was monitored in our hospital for 17 months by now, showing no signs of recurrence.

Discussion

MNAC is a typical rare malignancy which arises from the mesonephric remnant located in the female genital tract[1]. It was found mostly in the cervix [3] and rarely in the vagina [26] and uterine corpus[31]. These carcinomas have unique histologic and immunohistochemical characteristics. MNAC often presented varable histologic grown patterns from microscopic field to field within the same tumor, and as a result may be under-evaluated and misdiagnosed[4].The characteristic morphologic pattern include tubulocystic, retiform, papillary, ductal, sex cord, glomeruloid and solid components, the lumens contain dense periodic acid Schiff positive eosinophilic secretions[9, 11, 35]. Due to its rarity, these histologic patterns can easily be mistaken for a variety of other neoplasms to the unsuspecting pathologist. There may be a characteristic immunophenotype with consistent positive staining for GATA3 and PAX-8 as well as negativity staining for steroid hormone receptors,

both the ER and PR [39, 44, 47]. The staining for TTF1 is usually diffuse, and there is a luminal positivity for CD10 in the majority of cases.[48]

UB-MNAC is rare, and the diagnosis of UB-MNAC can be challenging, especially on biopsy materials and frozen sections. Morphologic differential diagnoses of UB-MNAC include cervical mesonephric adenocarcinoma with involvement of the uterine corpus and different morphological subtypes of endometrial adenocarcinomas. The distinction of a “true” cervical mesonephric adenocarcinoma depends on the tumor being located entirely or predominantly within the cervix or the uterine corpus. This can be determined by a detailed analysis of the hysterectomy specimen or preoperatively by a topographic evaluation of the imaging findings on CT and/or MRI[21]. To distinguish the UB-MNAC from other types of endometrial adenocarcinomas, such as clear cell carcinoma, endometrioid carcinoma, serous carcinoma, the characteristic grown pattern mentioned above and the classic immunohistochemical stains should be considered together. But by now, there are no antibodies that can distinguish UB-MNAC from Müllerian carcinomas.

The question about a real UB-MNAC has been raised by McFarland et al, who described a series of corpus mesonephric-like adenocarcinomas (MLAC) arising in the endometrium and infiltrating into the myometrium[21]. Given that these uterine cases appeared to arise from the endometrium rather than being located predominantly in the myometrium where the mesonephric remnant was supposed to be located in theory, these authors proposed that UB-MNAC do not actually arise from mesonephric remnants, but could arise from Mullerian structures and differentiate along a mesonephric pathway, and this tumor should be described as a ‘mesonephric-like” adenocarcinoma rather than MNAC.

To better understand this, we reviewed all the published cases of UB-MNAC or MLAC, and summarized them in **supplementary table1.** As shown in Table1, totally, 53 cases of UB-MNAC or MLAC, including the present three cases, have been reported by now, but only 46 patients had detailed clinical information. Generally, the patients with UB-MNAC or MLAC ranged in age from 31 to 91 years (mean, 59.8 years). The tumors measured 1.5 to 9.0 cm (mean, 5.3 cm) in size. Most of the patients complained of vaginal bleeding (27,58.4%).9 cases showed an elevated CA125 level, accounting for 19.6%, while the other 16 cases had a normal CA125 level. 23 cases (50%) were FIGO stage I, 5 cases (10.9%) were stage II,10 cases (21.7%) were stage III, and 7cases (15.2%) were stage IV. Only 7 cases were diagnosed as MNAC by D&C before operation, while 12 cases (26.1%) had be mistaken as EC. They all received operation therapy, but exact operation varied from TH + BSO to TH + BSO + PLND + PALND, depending on the stage and the patient general well beings. 20 cases, that was 43.4%, received postoperative therapy, either chemotherapy or radiotherapy or both. 15 cases (32.6%) showed metastasis, usually to lung(12cases,26.1%). Among them, 30 cases are arising from the endometrium, and /or infiltrating into the myometrium layer, accounting for 65.2%, while other 10 cases (21.7%) were completely confined in the myometrium layer, without endometrium involved. Respectively, evidence of mesonephric remnant was only found in 3(5.6%) cases, with two cases in our hospital found mesonephric remnant around the tumor, and the other one found mesonephric remnant in the cervix(summarized in **supplementary table1**).Notably, the tumors of the three cases were all arising from the myometrium, without endometrium involved. These three cases, especially the two cases in our hospital, which found mesonephric remnants around the tumor raised our interesting about whether these mesonephric or mesonephric-like adenocarcinomas arising from different parts of the uterine corpus have the same pathogenesis.

Table 1
Characteristics of patients with UB-MNAC or MLAC

Characteristics	n(%)
Total number	46
Mean age(range)	59.8(31 ~ 91)
Symptoms	
Vaginal bleeding	27(58.7)
Abdominal pain	2 (4.3)
Pollakiuria	1 (2.2)
None	2 (4.3)
NA	16(30.4)
CA125	
Elevated	9 (19.6)
Normal level	16(34.8)
NA	21(45.7)
Size(cm)	
Mean size(range)	5.3(1.5-9.0)
Stage	
I	23(50.0)
II	5 (10.9)
III	10(21.7)
IV	7 (15.2)
NA	1 (2.2)
D&C	
MNAC	7 (15.2)

EC	12(26.1)
AC	2 (4.3)
CS	2 (4.3)
None	2 (4.3)
NA	21(45.8)
Location	
Myometrium	10(21.7)
Endometrium, Myometrium Involved	30(65.2)
NA	6 (13.1)
Operation	
TH	1 (2.2)
TH + BSO	8 (17.4)
TH + BS0 + PLND	6 (13.0)
TH + BSO + OMT	1 (2.2)
TH + BS0 + PLND + PALND	12(26.1)
TH + BS0 + PLND + PALND + OMT	1 (2.2)
TH + BS0 + PLND + PALND + OMB	1 (2.2)
TH + BSO + PLND + PALND + OMT + APD	1 (2.2)
NA	15(32.6)
Post operation therapy	
None	9 (19.6)
CT	11(23.9)
RT	3 (6.5)
CT + RT	6 (13.0)

NA	17(37.0)
Metastasis	
None	15(32.6)
Lung	12(26.1)
Lymph node	3 (6.5)
NA	16(34.8)

Abbreviation: UB-MNAC: uterus body Mesonephric adenocarcinoma; MLAC: mesonephric-like adenocarcinoma; NA: not available; D&C: dilatation and curettage; EC: endometrioid carcinoma; AC: adenocarcinoma; CS: carcinosarcoma; TH :total hysterectomy; BSO: bilateral salpingo-oophorectomy; PLND: pelvic lymph node dissection; PALND: para-aorta lymph node dissection;OMT:omentectomy;OMB:omentalbiopsy;APD:appendectomy;CT:chemotherapy;RT:Radiotherapy;

To have a better understanding of this, we further analyzed the clinical characteristics and the survival rate of the two subgroup cases. Known that the MLAC arising from the endometrium had identical morphologic and immunohistochemical features with the UB-MNAC as the published literature indicated [21], our analyzed results showed the two subgroups most clinical characteristics were also identical (Table2), such as the age(60.6 ± 1.8 & 55.2 ± 4.3,P **= 0.19**),symptoms(most cases were presented with vaginal bleeding), stages(P **= 0.19**),and metastasis rate (P **> 0.99**)and metastasis site(a tendency to metastasize to the lung). Notably, 81.3% cases rising from the endometrium had normal CA125 level, while those originating from the myometrium had a higher elevated CA125 level (P **= 0.03**). This result was in consistent with the Kaplan-Meier survival analysis, which indicated that the cases from the myometrium layer had a poorer prognosis (Fig. 4, P **= 0.11**,). But this need more data, because the longest follow-up time was only 56 months as reported and the cases were limited so far.

Table 2
Correlation between different tumor location and various clinicopathological features of patients with UB-MNAC

Tumor Originate Location			
Endometrium	Myometrium	P value	
Number	30	10	
Age	60.6 ± 1.8,	55.2 ± 4.3	0.19
Stage			
I	18(60.0)	4(44.4)	0.61
II	3(10.0)	2(22.2)	
III	6(20.0)	1(11.1)	
IV	3(10.0)	2(22.2)	
CA125			
Normal	13(81.3)	3(33.3)	0.03*
Elevated	3(18.7)	6(66.7)	
Tumor size			
≤ 5	16(66.7)	4(40.0)	0.25
5	8(33.3)	6(60.0)	
Therapy			
Operation	8(42.1)	1(10.0	0.08
Operation + others	11(57.9)	9(90.0)	
Metastasis			
Yes	10(47.6)	4(44.4)	> 0.99
No	11(52.4)	5(55.6)	

By reviewing the literatures, we found that some theories do exist for the MLAC, one is the secondary trans-differentiation from Müllerian type carcinomas. The theory appears to be supported on a molecular basis. In the first sizeable series investigating the molecular alterations in MNAC, the authors showed that MLAC, similar to MNAC, are characterized by recurrent KRAS mutations, frequently PIK3CA mutations, and lack of PTEN mutations.PIK3CA mutations are mutations which have not been identified in MNAC previously [46] and PTEN and PIK3CA mutations are common in endometrial carcinomas, present in up to 95% of endometrial microsatellite instable and POLE mutated tumors[44]. These molecular features demonstrate biological overlap with carcinomas of both mesonephric and Mullerian (endometrioid) differentiation. Besides, one recent report presented a patient with coexisting endometrial MLAC and low-grade endometrioid carcinoma[40], which was treated using medroxyprogesterone acetate therapy, resulting in recurrence of MLAC alone. Another recently

published two papers presented two ovarian adenocarcinomas with combined low-grade serous and mesonephric morphologies, also suggest a Müllerian Origin for some Mesonephric Carcinomas.[22, 24]Given the previously documented association with endometriosis (ovarian neoplasms)[24] and the prominent endometrial involvement (uterine corpus neoplasms)[21], these tumors are best regarded as of Mullerian origin and representing adenocarcinomas which differentiate along mesonephric lines.

From the cases we presented in this study, we suggest that UB-MNAC arising from different part of the uterus have different pathogenesis, and may have different prognosis though they may have identical morphology and immunophenotype as well as other clinical characteristic. The tumor arise from the myometrium should be referred as “true” mesonephric carcinomas which is originated from the mesonephric remnant in the uterine wall, though in most cases, mesonephric remnants could not be found. That may be because of the overgrowth of the tumor. and those located in the endometrium layer are better to be diagnosed as “mesonephric-like” carcinomas, which may undergo mesonephric transformation of Müllerian adenocarcinoma. To date, only 53 cases of UB-MNAC or MLAC, including the present cases, have been reported. It might because many cases had been misdiagnosed as Müllerian adenocarcinoma. To better understand the pathogenesis and biological behavior, it is necessary to collect sufficient MNAC cases for clinicopathological and molecular study by keeping in mind the possible presence and classic histological features of MNAC or MLAC in the uterine corpus.

Conclusion

We described three cases of UB-MNAC in our hospital. Among them, two cases were completely confined within the corpus myometrium, without endometrium involved. And typically, mesonephric remnant was found around the tumor in the two cases. From our knowledge, it is the first time that find mesonephric remnants around the UB-MNAC cells, which has profound meaning for our understanding of the histogenesis of UB-MNAC. While the histogenesis of MNAC has not yet been confirmed in the uterine corpus, we propose two different pathways by which MNAC arises in the uterine corpus: 1) for those tumors arising from myometrium, it is directly developing from the mesonephric remnants and/or 2)for those originating from the endometrium, it is due to mesonephric transformation of Müllerian adenocarcinoma. Meanwhile, though limited information, by analyzing the two subgroups in the published literatures, we found that the two subgroups might have different clinical prognosis, which might further more support our hypothesis of the two different originations for the UB-MNAC and MLAC.

Abbreviations

UB-MNAC: uterus body Mesonephric adenocarcinoma; MLAC: mesonephric-like adenocarcinoma; IHC: immunohistochemistry; NA: not available; D&C: dilatation and curettage; EC: endometrioid carcinoma; AC: adenocarcinoma; CS: carcinosarcoma; TH :total hysterectomy; BSO: bilateral salpingo-oophorectomy; PLND: pelvic lymph node dissection; PALND: para-aorta lymph node dissection;OMT:omentectomy;OMB:omentalbiopsy;APD:appendectomy;CT:chemotherapy;RT:Radiotherapy;

Declarations

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Availability of data and materials

There are no additional supporting data available.

Authors' contributions

Hu Qian and Guo Tao designed the study, carried out histopathological evaluation and drafted the manuscript. Wu Xiu Li assisted with the pathological analysis. Xu Qin collected the clinical and surgical data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of West China Second University Hospital.

Consent for publication

Written informed consent for publication of clinical details and clinical images was obtained from the patient.

Competing interests

The authors declare that they have no competing interests

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Figures

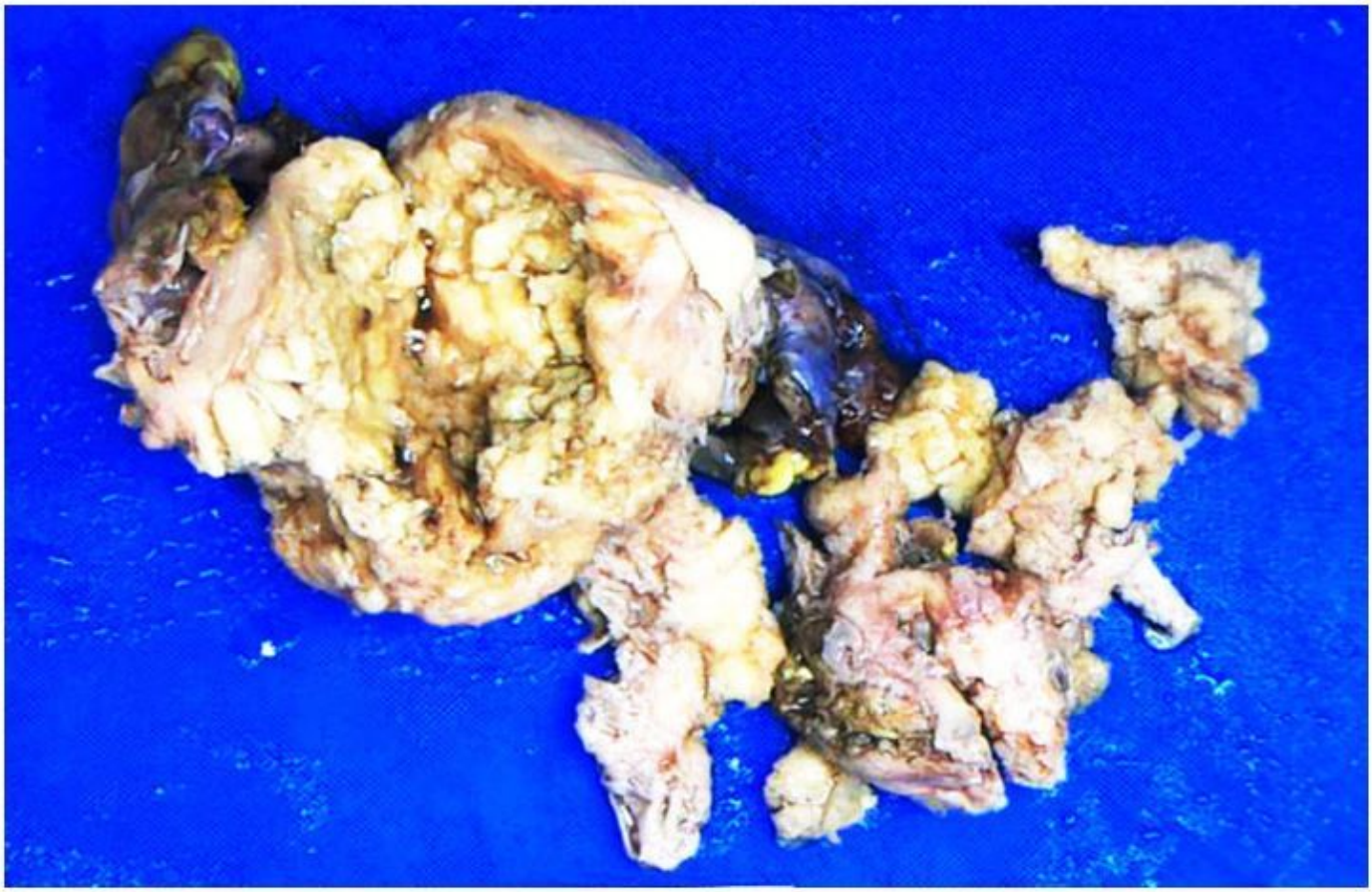

Figure 1

Gross findings of UB-MNAC: the 9.0×6.0×3.5 cm solid mass was located in the fundus protruding into the uterine cavity and into the outer half of myometrium, the cut surface was gray and yellow; Cervix and bilateral adnexa were unremarkable. Greater Omentum and lymph nodes were grossly normal;

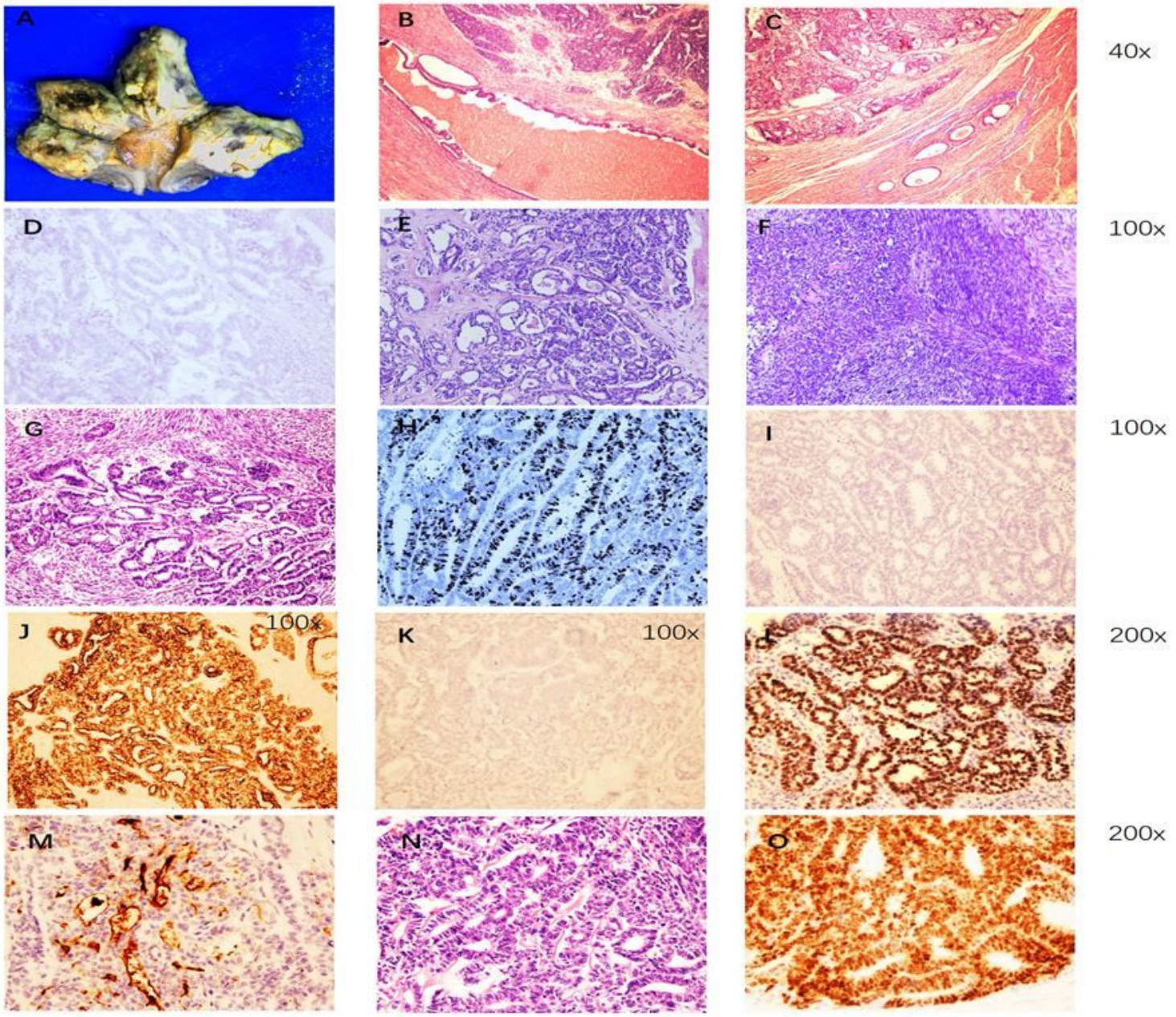

Figure 2

A:Gross findings of UB-MNAC: the tumor located in the myometrium layer, the tumor was solid, presented as multinodular shape, the cut surface was gray and yellow, and cystic cavity can be found focally; B:Dilated glands, focally showed atypical hyperplasia；C:The left upper glands were arranged crowded as clusters；the normal mesonephric remnants were seen in the right lower region.；D:Lack of ER expression；E: Densely eosinophilic secretions were focally present in the tubular and ductal structure of the tumor；F:Spindle cells component；G:Small and round gland lumen in different size, partially shaped in retiform structure；H:The Ki-67 proliferation index was almost 80%；I:Lack of P16 expression；J:Strong immunoreactivity of PCK；K:Lack of PR expression；L:Strong immunoreactivity of TTF；M:Uniform CD10 immunoreactivity along the luminal surface； N:The tumor cells were arranged in disorder, with marked cellular atypia and enlarged hyperchromatic nuclei, without cilia. No glycogen was seen in the cytoplasm; O: Strong immunoreactivity of PAX-8;

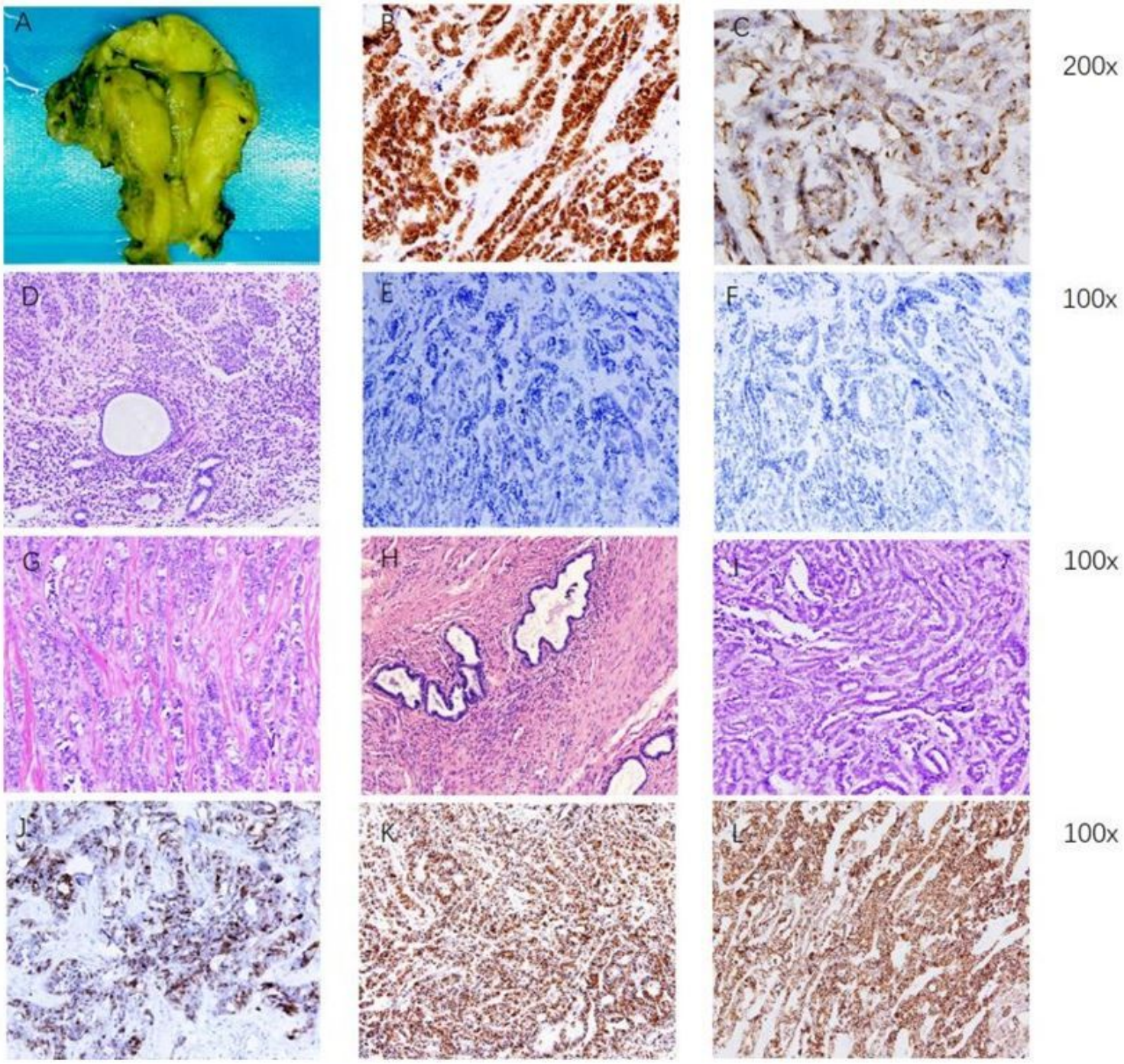

Figure 3

A:Gross finding: the tumor located in the posterior wall of the uterus, presented as nodular and solid, protruding into the surface of the serosal layer; B:Positive staining of PAX-8;C:Luminal staining of CD10;D:HE staining of normal endometrium; E: Negative staining of PR; F: Negative staining of ER; G:Tubular structure; H:Normal mesonephric remnant in the myometrium; I:Glandular structure, glands are arranged crowded; J:Patchy positive staining of P16;K:Positive staining of Vimentin; L:Positive staining of CK-P;

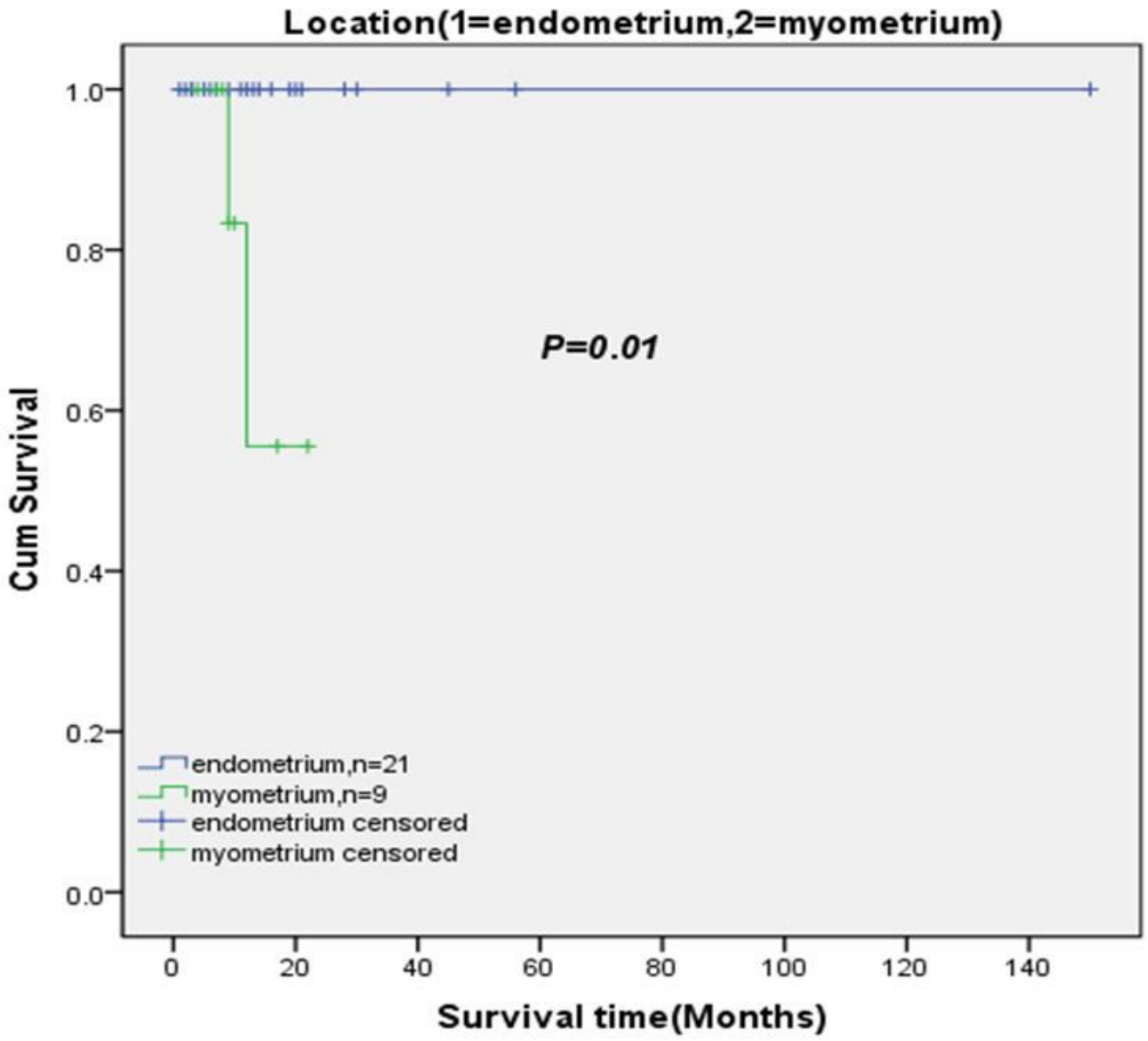

Figure 4

Kaplan-Meier survival analysis of survival of cancer patients according to different tumor location. Totally,30 patients had exactly follow-up time, among them, 21 cases tumor were arising from the endometrium, with or without myometrium involved; other 9 cases tumor were arising from the myometrium, without endometrium involved, and the result showed that the myometrium subgroup had poorer prognosis (P =0.01).

Supplementary Files

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