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Clinicopathological analysis of ovarian mucinous tumor

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Abstract: *the clinical and pathological data of 45 patients with ovarian mucinous tumors were analyzed retrospectively, and their clinicopathological features were summarized in order to analyze the clinicopathological features of ovarian mucinous tumors. There were 30 cases of benign ovarian mucinous tumors (66.67%), 4 cases of borderline tumors (8.89%), 11 cases of malignant tumors (24.44%), 9 cases of primary malignant tumors (20%) and 2 cases of secondary malignant tumors (4.44%). The morphological spectrum of ovarian mucinous tumors is widely expressed, and the close combination of pathological examination and clinical examination is of great significance for diagnosis and treatment.*

Keywords: *ovarian mucinous tumor, Borderline ovarian mucinous tumor, ovarian mucinous adenocarcinoma*

1. Introduction

From June 2019 to June 2023, 45 cases of ovarian mucinous tumors were treated in our hospital, aged from 13 to 85 years old.All of them had complete clinical and follow-up data, and were confirmed by surgical pathological examination. Serum CA125 level and CA199 level were detected before surgery.

All patients received surgical treatment, including conservative surgery and extensive surgery.The surgically resected specimens were fixed with 10% formaldehyde solution, and the diagnosis was made by routine HE staining and light microscopy. Pathological diagnosis was made according to WHO diagnostic criteria for ovarian mucinous tumors, and was diagnosed and reviewed by two experienced pathologists. Forty-five cases of ovarian paraffin specimens were stained by HE and SP immunohistochemical methods. The specific operation steps are carried out according to the kit instructions, DAB staining, hematoxylin restaining. The antigen was repaired by citrate heating. Immunohistochemical sP kit and ready-to-use murine anti-human monoclonal antibodies CK7, CK20, CDX-2, villin, etc. were purchased from Fuzhou Maixin Company.

All patients were followed up for 1 to 12 months to understand the changes of clinical symptoms and signs, improve pelvic examination, ultrasound and tumor markers, and calculate the age, sex, changes of serum markers, surgical procedures and pathological features of the two groups.

2. Data and Methods

Clinical features Forty-five patients with ovarian mucinous tumors ranged in age from 13 to 85 years old, with a median age of 60 years old. Thirty patients with benign tumors ranged in age from 13 to 85 years, four with borderline tumors ranged in age from 28 to 60 years, and 11 with malignant tumors ranged in age from 15 to 65 years. The average preoperative serum CA125 of 45 patients was (22.02±1.34) kU/L, of which 6 patients were elevated (> 35kU/L). The mean CA199 before operation was (21.34±2.05) kU/L, of which 10 cases were elevated (> 37kU/L). Of the 45 cases, 41 showed abdominal distension and pelvic mass, 3 showed hematochezia, diarrhea and other intestinal cancer symptoms, and 1 showed vaginal bleeding, 12 were bilateral, 33 were unilateral, and 23 were right. Of the 45 patients, 2 had metastases outside the ovary (Table 1).

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Table 1 Clinicopathological features of ovarian mucinous tumors (n=45)

Group	ovarian primary	ovarian metastasis
Median age (years)	60	64
Mean maximum tumor diameter (cm)	12.2	13.4
Site of disease		
Right side	23/45	1/45
Left side	20/45	1/45
Bilatera	0/45	0/45
With external ovarian metastases	/	2/45

The tumor is cystic or solid in the eye, and the inside is a viscous jelly-like substance or a yellowish viscous liquid. In benign patients, the inner surface of the lesion is smooth and the wall is thin, while in borderline tumors, the inner surface is basically smooth and doped with more clusters of papillary hyperplasia. The internal surface of patients with malignant lesions is multilocular cystic lesions, and solid areas are more common than borderline lesions, often accompanied by bleeding and necrotic lesions, and only a few tumors are mainly solid and doped with mucoid substances.

Microscopic examination of 30 cases (66.67%) of benign ovarian mucinous tumors showed that the epithelium was arranged in a single layer, mainly composed of columnar epithelial cells, the cell boundaries were clear, and obvious mucus could be observed in the cytoplasm, and the nuclei were distributed in the base area, small and deeply stained, and there was no mitotic phase (Figureure 1 A). In 4 cases (8.89%), the epithelial layers of borderline tumors were significantly increased, and there were bud or clumpy changes, atypical cells, irregular nuclei and deep staining, and reduced mucous in the cytoplasm. Compared with benign tumors, there were more mitotic phases (Figure 1 B). The epithelium of 11 patients (24.44%) with malignant tumors showed atypia (Figure 1 C), and there were obvious interstitial infiltration, which could be divided into expansive infiltration and destructive infiltration. 2.4 Immunohistochemical markers CK7, CK20(Figure 1 F), MUC-1, MUC-2, villin positive staining indicates brown-yellow particles in cytoplasm, and CDX-2 positive staining indicates brown-yellow particles in nucleus (Table 1, Figure 1 E. F).

3. Results

Clinical Features Of 45 patients with ovarian mucinous tumors, 30 with benign tumors ranged in age from 13 to 85 years, 4 with borderline tumors ranged in age from 28 to 60 years, and 11 with malignant tumors ranged in age from 15 to 65 years. The average preoperative serum CA125 of 45 patients was (22.02±1.34) kU/L, of which 6 patients were elevated (> 35kU/L). The mean CA199 before operation was (21.34±2.05) kU/L, of which 10 cases were elevated (> 37kU/L).

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In 30 cases (66.67%) of benign ovarian mucinous tumors, the epithelium showed a single layer arrangement, mainly composed of columnar epitheliumThe cell was composed, the cell boundary was clear, and obvious mucus could be observed in the cytoplasm. The nucleus was distributed in the base area, with small volume and deep staining, and no fission phase (Figureure 1 A). In 4 cases (8.89%), the epithelial layers of borderline tumors were significantly increased, and there were bud or clumpy changes, atypical cells, irregular nuclei and deep staining, and reduced mucous in the cytoplasm. Compared with benign tumors, there were more mitotic phases (Figureure 1 B). The epithelium of 11 patients (24.44%) with malignant tumors showed atypia (Figureure 1 C), and there were obvious interstitial infiltration, which could be divided into expansive infiltration and destructive infiltration.

Immunohistochemical markers CK7, CK20(Figureure 1 E.F), villin positive staining indicates brown-yellow particles in cytoplasm, and CDX-2 positive staining indicates brown-yellow particles in nucleus (Table 2).

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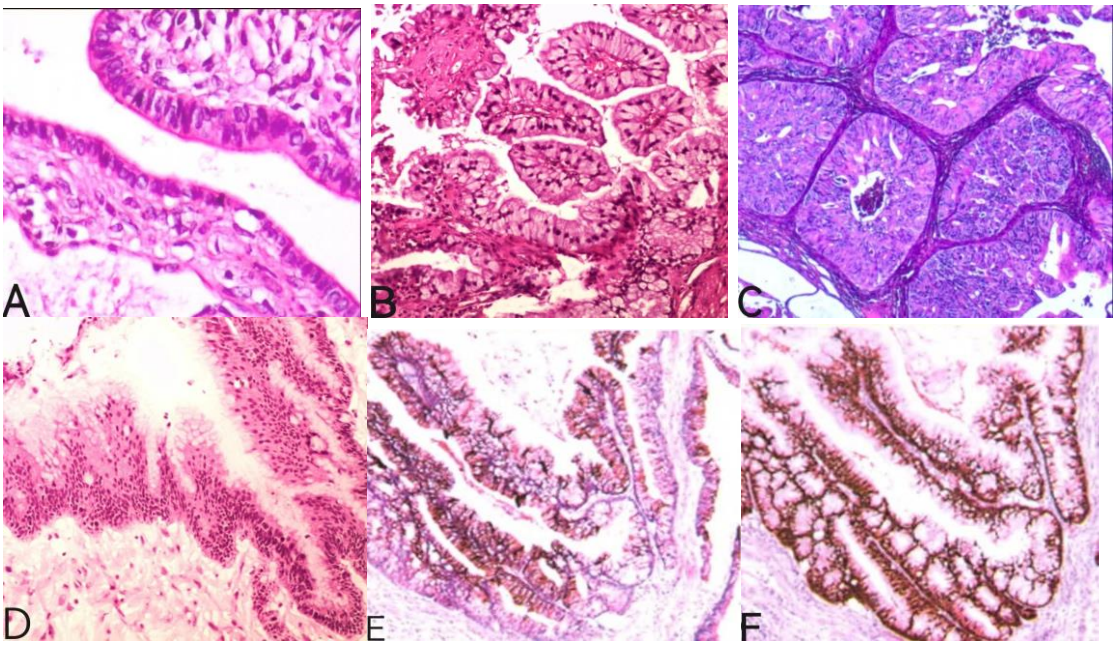

(A: Mucinous cystadenoma of the ovary. B: borderline mucinous cystadenoma of the ovary. C: Mucinous adenocarcinoma of the ovary. D: Metastatic mucinous adenocarcinoma of the ovary. E: CK20 diffuse cytoplasm strongly positive,SP method. F: CDX-2 diffuse cytoplasm strongly positive, SP method)

Figure 1 Mucinous tumor of ovary.

4. Discuss

Mucinous tumors account for about 15% of all ovarian tumors, mostly benign tumors, accounting for about 85% of ovarian mucinous tumors. Borderline and malignant tumors are relatively rare [1-2]. Of the 45 cases of ovarian mucinous tumors, 66.67% were benign, 8.89% borderline, 24.44% malignant, 9 primary malignant tumors (20%), 2 secondary malignant tumors (4.44%). That's pretty much what we've been reporting. - Yeah. Ovarian mucinous tumors are more common in young and middle-aged women aged 20-50 years, while borderline and malignant tumors are more common in women aged 30-80 years. Due to the mixed characteristics of benign, borderline and malignant tumors in ovarian mucinous tumors, ovarian diagnosis is difficult, especially borderline tumors are difficult in clinical diagnosis. Under normal circumstances, the nature of tumors can be directly observed by the naked eye as cystic or solid, the nature of intracapsular fluid, the state of tumor surface and whether there is papillary mass in the inner wall of the capsule, etc., which are of great significance for the diagnosis of benign and malignant tumors [3]. Microscopic observation shows that benign tumors are mostly cystic, can be unilocular or multilocular, and the cyst wall is relatively smooth inside and outside, lined with a single columnar epithelium without papillary growth. It is worth noting that in multilocular cases, it often shows the dense distribution of tiny ovary, and can also show realistic viscous fluid on fresh specimens, and the specimen texture is relatively delicate. It is often misdiagnosed as malignant tumor, so it should be carefully observed and identified during pathological examination [4]. The tissue sections of typical malignant tumors are often cystic-solid, and the distribution of the inner chamber in the cystic area is more dense, while the solid area can appear gray-white area, and the texture is brittle, and there are usually solid areas and small cystic cavities at the same time, and some patients can be complicated with hemorrhage and necrosis. The inner wall of cysts may be accompanied by papillary hyperplasia , which is relatively fragile and easy to fall off [2-3].Borderline tumors are difficult to diagnose because of the common characteristics of benign and malignant tumors. Microscopically, epithelial hyperplasia is seen without significant stromal infiltration and with any two of the following: villous adenoid hyperplasia, presence of mitotic signs or atypical cells, and cell organization within 4 layers. For patients with suspected borderline tumors, adequate sampling should be ensured to detect small infiltrating lesions, avoid misdiagnosis and missed diagnosis, and improve diagnostic accuracy [5-6].

The morphological profile of metastatic mucinous tumors of the ovary is widely expressed, and may have obvious mucinous adenocarcinoma or borderline mucinous tumor morphology, or even

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benign cystadenoma morphology, showing the so-called maturation phenomenon [7]. Sometimes microscopic images show the presence of follicle-like lacunae in the ovarian stroma, which can appear in a variety of metastatic mucous tumors of the ovary at different primary sites, so it is easy to misdiagnose. In this group, 1 of the 2 metastatic myxoid tumors had cells that were gently arranged into a single layer, and local epithelial hyperplasia presented multiple layers, which was easily misdiagnosed as primary myxoid cystadenoma of the ovary or borderline myxoid cystadenoma of the ovary (Figure 1D), which brought great difficulties for differential diagnosis. Therefore, when intraoperative freezing encountered benign ovarian myxoid tumors, Clinicians should be reminded to explore the digestive tract and other prone areas. Due to the overlap in HE morphology between primary and metastatic mucinous tumors of the ovary, this group expected to explore the differences between the two through immunohistochemical markers, so that suspected cases of unexplored patients could be detected by immunohistochemical screening in postoperative pathological diagnosis, providing clues for clinical investigation of primary lesions. As can be seen in Table 2, CK7- / CK20+ and CDX-2+ / villin+ are the expression characteristics of metastatic mucinous tumors of the ovary from the colon and stomach, which are similar to the phenotypes of metastatic mucinous tumors from the digestive tract reported in most literatures [8-10]. The phenotypes of ovarian metastatic mucinous tumors of cervical origin reported in the literature were CK7+ / Cl(20-, MUC.1 - / MUC-2+ and CDX-2- / villin-, which were not significantly different from those of primary mucinous tumors of ovary [11-15]. To sum up, the clinicopathological features of metastatic mucinous tumors of the ovary can be summarized as follows: (1) bilateral lesions, or unilateral lesions <13cm in diameter, and the right side is more common; (2) The surface of the ovary is incomplete with mucus or nodular growth in the superficial layer of the cortex; (3) With PMP or abdominal pelvic implant metastasis; (4) destructive interstitial infiltration; (5) Immunophenotypes: CK7- / CK20+, MUC-1- / MUC-2+, CDX-2+ / villin+; (6) Preoperative surgical history or intraoperative extra-ovarian lesions [16]. Some studies have found that most metastatic mucous tumors of the ovary can be screened during intraoperative freezing with an accuracy of nearly 90% according to the above article only. However, even if all the above conditions are met, there is still at least 5% misdiagnosis rate and the probability of diagnostic uncertainty [17].

Table 2 Immunophenotype of metastatic mucinous adenocarcinoma of the ovary

Immune marker	Primary colon	Primary stomach
CK7	+	+
CK20	+	+
CK20	+	-
Villin	+	+
CEA	+	+
Inhibin	-	-

In 2020, WHO diagnosed those with the maximum diameter of stromal infiltration lesion under the microscope exceeding 5mm as invasive myxocarcinoma, and those lacking the above criteria were classified as "microinfiltration" of borderline myxoid tumors [18]. According to the growth and invasion patterns of tumors, ovarian mucinous carcinoma can be divided into two types: expansive and invasive . The dilatation microscope shows a dense distribution of fused or complex malignant glands (back-to-back phenomenon) with little interstitial separation between the glands. The infiltrating type destroys and invades the interstitium in the form of glands, cell clusters or single cells, and is more aggressive than the dilatant type [19-22]. 80% of ovarian mucinous carcinomas are metastatic mucinous carcinomas of the ovary, 45% of which are derived from primary tumors of the gastrointestinal tract, 20% from the pancreas, 18% from the cervix and/or endometrium, and 8% from breast cancer [23]. The histological features of ovarian mucinous carcinoma are very similar to those of ovarian metastatic mucinous carcinoma, especially those of colorectal carcinoma. Ovarian mucinous carcinoma often co-exists with a variety of components and growth patterns, such as benign and borderline components, expansive and invasive, or other pathological types. Metastatic mucinous carcinoma of the ovary has an obvious fibroproliferative reaction, showing nodular or invasive growth, and clusters of tumor cells can be seen in the corpus luteum or the white body of the ovary [24]. More than 90% of ovarian mucinous carcinoma tumor cells contain a large amount of mucin, while metastatic ovarian mucinous carcinoma is rich in extracellular mucus, accounting for more than 50% of the tumor volume. Mucinous carcinoma of the ovary is mostly unilateral and larger than metastatic mucinous carcinoma of the ovary (16 ~ 20cmvs.11 ~ 12cm). However, size alone is not enough to diagnose primary or metastatic tumors, and 32%-48% of metastatic mucinous carcinoma of the ovary have tumor diameter > 10cm [24]. Seidman et al. established a model for differentiating ovarian

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mucinous carcinoma from metastatic mucinous carcinoma based on tumor size and lateral classification: more than 90% of bilateral tumors were metastatic regardless of their diameter. The tumors were more than 10cm in diameter on one side, and 82% were primary. Unilateral tumors <10cm in diameter, 87% were metastatic. This suggests that the possibility of metastatic mucinous carcinoma of the ovary cannot be ruled out even if it is unilateral mucinous carcinoma. Other valuable features in the diagnosis of metastatic mucinous carcinoma of the ovary include bilateral ovarian involvement, ovarian surface involvement, mucin presence outside the cell, destructive interstitial infiltration, nodular growth, hilar involvement of the ovary, vascular invasion, sig-ring cells, and extensive necrosis [25]. Expert consensus: ovarian mucinous carcinoma is mostly unilateral ovarian mass, which is cysticThe pathology is divided into two types: dilatation type and infiltration type. The Seidman model can be used to differentiate ovarian mucinous carcinoma from metastatic mucinous carcinoma based on tumor size and side to some extent, but it still needs to be combined with other pathological features.

5. Conclusions

In conclusion, the morphological spectrum of ovarian mucinous tumors is widely expressed, and the close integration of pathological examination with clinical practice is of great significance for diagnosis and treatment.

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