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Seromucinous ovarian tumor A comparison with the rest of ovarian epithelial tumors☆

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ABSTRACT

Background: Seromucinous ovarian tumors are rare and not adequately described in the literature and this is especially true for seromucinous carcinomas.
Aim of the study: To describe histological and clinical features of these tumors in comparison with the rest of ovarian epithelial tumors.
Materials and methods: Two hundred and forty one (241) ovarian tumors, borderline ($n = 92$) or malignant ($n = 149$), treated surgically without neoadjuvant chemotherapy, were examined.
Results: Seromucinous borderline (SMBT) and malignant tumors (SMC) comprised 7.8% ($n = 7$) and 4% ($n = 6$) of all borderline tumors and carcinomas, respectively, studied. Mean age of diagnosis was 63.2 and 68.3 years and mean size was 6.4 cm and 12 cm for SMBT and SMC, respectively. Seromucinous tumors were associated with endometriosis in 23.1% of the cases and they were bilateral in 30.8%. Microscopically, variety in cellular composition, papillary architecture and development into thick walled, occasionally muscular, cysts were the main findings. Medullary/paraovarian/tubal or deeply cortical localization was also characteristic. Stage predicted overall and progression-free survival ($p < 0.0001$ and $p = 0.03$, respectively). Five-year survival was 62% for patients with high grade serous carcinoma, 55% for seromucinous carcinoma, 100% for endometrioid carcinoma, 75% for clear cell carcinoma, and 80% for patients with mucinous carcinoma. Differences were not however statistically significant.
Conclusion: Seromucinous tumors have unique features that support their classification as a different entity. Their localization and their often thick fibrous or/and muscular wall provides further evidence for an histogenesis from the secondary Müllerian system or vestigial structures.

1. Introduction

Seromucinous ovarian tumors, benign, borderline or carcinomas, are rare neoplasms formerly classified with mucinous tumors, as the Müllerian or endocervical subtype, but now comprise a new category of ovarian epithelial tumors in the 2014 World Health Organization (WHO) classification [1]. Due to their rarity and their variety in morphology, they are occasionally difficult to diagnose and this is especially true for carcinomas, for which there are very few cases series in the literature.

Borderline seromucinous tumors are characterized by complex papillae with a fibro-oedematous stroma rich in neutrophils; the papillae are lined by various cell types- mucinous, serous, clear cells, squamous cells or often eosinophilic indifferent cells [2]. Carcinomas have a similar morphology as borderline tumors, but they are diagnosed in the basis of their architectural complexity (expansile type of invasion) or their destructive stromal invasion [3].

In about one third of seromucinous tumors, endometriosis is also found; this, the immunophenotypic similarity (CK7+, ER+, PR+, WT1-), the occasional morphological similarity and the inactivation of the tumor-suppressor gene *ARID1A* in a proportion - 8 out of 24 cases immunohistochemically studied [4] - of these tumors, as seen in endometrioid tumors too, have led to the hypothesis that seromucinous tumors are also associated to endometriosis [5].

In this study, we evaluated a series of seromucinous borderline and malignant tumors to better describe their characteristics, clinical and pathological, comparing them with the rest of ovarian epithelial tumors.

☆ Conflict of interest: The authors have no conflict to disclose.

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2. Materials and methods

2.1. Study population

Specimens from 241 patients diagnosed with an ovarian borderline or malignant tumor, treated surgically without neoadjuvant chemotherapy, were included in the study. Clinical information was collected through the electronic medical records. Local ethics committee of the University Hospital of St-Etienne approved the study.

2.2. Histopathological evaluation and immunohistochemical analysis

All available slides from the formalin fixed paraffin embedded tissues were histopathologically re-evaluated [6]. Complementary immunohistochemical staining was performed in selected cases in order to establish the correct diagnosis. Tumor classification was done in accordance with the 2014 WHO Classification [1] and staging was performed according to the TNM and FIGO classification [7,8].

2.3. Statistical analysis

Data were analyzed using the StatView software (Abacus Concepts, Berckley Ca, USA). Relationship between two groups was investigated using chi-square test for categorical data. Analysis of variance (Anova) was used for age and tumor size. Survival probability was estimated by Kaplan–Meier analysis with log-rank product limit estimation. For all analyses, statistical significance was indicated at a p value of <0.05.

3. Results

3.1. Patients' and tumors' characteristics

Patients' and tumors' characteristics are presented in Tables 1-3. The age at diagnosis in the whole sample ranged from 15 to 90 years, with a median age of 62 years. The mean age at diagnosis was higher for all carcinomas than for borderline serous or mucinous tumors (Fig. 1). Seromucinous borderline and malignant tumors were diagnosed later

Table 1
Features of the current seromucinous tumors.

	Age	Type	pT	Grade	Cell types	Mitoses/10HPF	Architecture	Localization	Wall	Follow up
1	78	Border	T1a	NA	1. Mucinous 2. Eosinophilic	NA	Papillary	Cortex	Thin	ANED at 3 months
2	58	Border	T1a	NA	1. Eosinophilic 2. Mucinous 3. Serous	NA	Papillary	Meso-ovarium	Thick muscular	ANED at 5 months
3	85	Border	T3b	NA	1. Serous 2. Clear 3. Mucinous	NA	Papillary. Small cysts around. Exophytic component	Mostly cortex	Not defined	ANED at 110 months
4	25	Border	T1c	NA	1. Serous 2. Mucinous 3. Eosinophilic	NA	Papillary	Mostly cortex	Thick fibrous	ANED at 12 months
5	84	Border	T1a	NA	1. Serous 2. Mucinous 3. Clear	NA	Papillary	Mostly cortex	Thick fibrous	ANED at 78 months
6	57	Border	T1a	NA	1. Serous 2. Mucinous	NA	Papillary. Small cysts around	Mostly cortex	Thin	ANED at 171 months
7	56	Border	T1a	NA	1. Eosinophilic 2. Serous 3. Mucinous	NA	Papillary	Medulla	Thick fibrous	Lost at follow up
8	49	Ca	T1a	2	1. Mucinous 2. Serous 3. Eosinophilic	2	Papillary and glandular. Expansile	Medulla/cortex	Thick	ANED at 22 months
9	73	Ca	T2a	1	1. Serous 2. Mucinous 3. Clear 4. Eosinophilic	1	Papillary. Expansile	DTD	Thick fibrous	ANED at 28 months
10	76	Ca	T3b	3	1. Eosinophilic 2. Serous	4	Solid, papillary and glandular. Destructive	DTD	Thick fibrous	Died at 44 months
11	88	Ca	T1c	2	1. Clear 2. Eosinophilic 3. Mucinous 4. Squamoid	5	Papillary and glandular. Destructive	DTD	Thick muscular	Died at 10 months
12	74	Ca	T1a	2	1. Serous 2. Mucinous	1	Papillary and glandular. Expansile	DTD	Thick fibrous	ANED at 110 months
13	54	Ca	T2a	3	1. Clear 2. Serous 3. Eosinophilic	5	Papillary and solid. Expansile and destructive	DTD	Thick fibro-muscular	Recurrence (lymph nodes) at 24 months

NA: Not applicable. HPF: high power field. Grading was performed as previously suggested similar to endometrioid carcinomas [3]. Border: borderline, Ca: carcinoma. Cell types are presented in descending frequency. DTD: difficult to determine. ANED: alive with no evidence of disease.