International Journal of Clinical and Diagnostic Pathology

ISSN (P): 2617-7226
ISSN (E): 2617-7234
www.patholjournal.com
2023; 6(4): 01-04
Received: 02-07-2023
Accepted: 06-08-2023

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Immunohistochemical expression of vimentin monoclonal antibody in ovarian surface epithelial tumors in correlation with clinicopathological parameters

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DOI: https://doi.org/10.33545/pathol.2023.v6.i4a.542

Abstract
Background: Ovarian epithelial tumors, comprising 90% of Western ovarian cancers, have subtypes like serous, endometrioid, clear cell, mucinous, seromucinous, and Brenner. Risk factors include genetics, reproductive history, and lifestyle factors. Prognosis depends on stage, residual disease, and grade, with over 90% 5-year survival in stage 1 and 30% in stage 3; vimentin plays a key role in maintaining cell shape and cytoskeletal stability. The research examines vimentin monoclonal antibody immunohistochemistry in ovarian surface epithelial tumours and its connection with clinicopathological characteristics.
Method: A retrospective cross-sectional study at Babylon Training Center for Pathology examined 55 ovarian epithelial tumor cases, using formalin-fixed paraffin-embedded tissue blocks primarily obtained through excisional biopsy at Al-Hilla Teaching Hospital. Immunohistochemical staining with vimentin antibody (Clone: BSB-v9) was employed, with parallel positive and negative controls, including leiomyoma for positive control. Vimentin scoring relied on color intensity in over 50% of the cell population.
Results: Among 55 ovarian surface epithelial tumors, 65.4% were benign, with serous cystadenoma being the most common. Malignant cases constituted 20%, primarily serous cystadenocarcinoma. Borderline tumors accounted for 14.5%, with mucinous and serous subtypes being the most prevalent at 50% and 37.5%, respectively.
Conclusion: Vimentin expression varies between benign, borderline, and malignant ovarian surface epithelial neoplasms, epithelial-mesenchymal transition processes may be implicated in the pathogenesis of serous ovarian tumours, and all serous borderline tumours and carcinomas express vimentin.

Keywords: Ovarian surface epithelial tumor, vimentin monoclonal antibody

Introduction
Ovarian epithelial tumors are a significant portion of ovarian neoplasms, comprising approximately two-thirds of all cases, and about 90% of ovarian cancers in Western countries [1]. These tumors are further classified based on their cell type, which includes serous, endometrioid, clear cell, mucinous, seromucinous, and Brenner tumors. Additionally, within each histotype, tumors are categorized as benign, borderline, or malignant based on their cellular characteristics [2]. Benign tumors are characterized by non-cancerous nuclear features and differentiated cytoplasm [3], while borderline tumors display cytologic atypia without evidence of invasion [4]. Several risk factors contribute to the development of ovarian epithelial tumors, including genetic factors, reproductive history, alcohol consumption, smoking, and the use of oral contraceptive pills, among others [5]. The prognosis of these tumors depends on factors such as the stage at the time of diagnosis, the presence of residual disease after treatment, and the tumor grade. For instance, the 5-year survival rate for stage 1 disease exceeds 90%, while it drops to 30% for stage 3 disease [6]. Vimentin, a protein present in its monomeric form, consists of a central α-helical domain flanked by non-helical amino (Head) and carboxyl (Tail) domains. Vimentin plays a crucial role in maintaining cell shape, cytoplasmic integrity, and stabilizing cytoskeletal interactions [7].

The objective of this study is to assess the immunohistochemical expression of vimentin monoclonal antibody in ovarian surface epithelial tumors and investigate its correlation with clinicopathological parameters.

Methodology

This retrospective cross-sectional study was conducted at the Babylon Training Center for Pathology. The study group consisted of formalin-fixed paraffin-embedded tissue blocks obtained from 55 cases of ovarian epithelial tumors. These tissue samples were collected from excisional biopsies performed on patients, and they were sourced from the histopathology laboratory at Al-Hilla Teaching Hospital. The immunohistochemical staining method employed in this study involved the use of a primary antibody (vimentin). Specifically, a Mouse monoclonal antibody with cytoplasmic expression, 3 ml in volume, Ready-To-Use, was utilized. This antibody was sourced from Bio SB, with the Clone designation: BSB-v9. In each round of immunostaining, parallel positive and negative control sections were processed. For the positive controls, leiomyoma of the uterus was used, as this tissue type is known to express vimentin. These positive controls were included in every run of the experiment to ensure the reliability of the staining process. Conversely, sections that were not treated with the primary antibody (vimentin) served as negative controls in each set of slides. The scoring of vimentin expression was based on the intensity of the color produced by staining in more than 50% of the cell population. The scoring system used was as follows:

- 1+ indicated weak staining
- 2+ indicated moderate staining
- 3+ indicated strong staining

This methodology was employed to assess the immunohistochemical expression of vimentin in the ovarian epithelial tumors under investigation in this study.

Statistical analysis was performed by using SPSS version software 24. *P* values less than 0.05 were considered as statistically significant.

Results

Fifty-five cases of surface epithelial tumors of the ovary were studies. In this study of the 55 ovarian tumors, 36 (65.4%) cases were benign, 8 (14.5%) cases were borderline and 11 (20%) cases were malignant. Serous cystadenoma (21, 85.3%) was the most common benign lesion-followed by mucinous cystadenoma (12, 33.3%) and followed by Brenner tumor 3 cases (8.3%) (Categorized as others in table 1). Of the total malignant cases (11, 20%), serous cystadenocarcinoma was most common, followed by 4 cases of mucinous cystadenocarcinoma and 1 clear cell carcinoma and 2 endometrioid carcinoma (categorized as others in table (1). Out of the 8 cases of borderline lesions 4 (50%) were mucinous followed by 3 (37.5%) of the serous type.

Table 1: Histopathological Classification and distribution of surface epithelial tumors

Types	Benign	Borderline	Malignant	Total
Serous	21 (58.3%)	3 (37.5%)	5 (45.45%)	29
Mucinous	12 (33.3%)	4 (50%)	4 (36.36%)	20
Others	3 (8.3%)	1 (12.5%)	2 (18.18%)	6
Total	36 (65.45%)	8 (14.5%)	11 (20%)	55

Out of 55 cases of surface ovarian epithelial tumors were studies, age range from (14-76) years, the most common age of the patients affected by SOET at age between 40-49 (19, 34.5%) followed by the age 30 – 39 (10, 18.1%), while the SOET at age below 20 years were 2 cases (3.6%) and above 70 years 4 cases (7.2%) as show in table 2

Table 2: Distribution of surface epithelial ovarian tumors in different age groups

Age	Number of tumors
<20	2 (3.6%)
20-29	8 (14.5)
30-39	10 (18.1%)
40-49	19 (34.5%)
50-59	8 (14.5%)
60-69	4 (7.2%)
>70	4 (7.2%)
Total	55

In study of 49 cases of serous and mucinous surface ovarian epithelial tumors the gross histopathological finding, were found that 30 out of 49 cases have smooth external surface, 19 (63.33%) serous tumors and 11(36.66%) were mucinous, and 19 cases appear to have nodular external surface, 10 (52.63) serous and 9 (47.36%) mucinous. According to locularity 23 cases out of 49 were unilocular, 20 (86.95%) serous and 3 (13%) mucinous. 26 cases out of 49 show multilocularity with 17 (65.38%) mucinous and 9 (34.61%) serous tumors, the relation between locularity and types of ovarian tumor were statistically significant as show in table (3)

Table 3: Correlation between serous and mucinous ovarian epithelial tumors and gross features

Types	External surface				Locularity			
	Smooth	Nodular	Total	p-value	Unilocular	Multilocular	Total	p-value
Serous tumors	19 (63.33%)	10 (52.63%)	29	0.4 > 0.05 Not significant	20 (86.95%)	9 (34.61%)	29	0.0001 < 0.05 significant
Mucinous tumors	11 (36.66%)	9 (47.36%)	20		3 (13%)	17 (65.38%)	20	
Total	30	19	49		23	26	49	

In correlation between histopathological subtypes of SOET and the location of the ovarian tumors the result were in 29cases of serous tumors 16 (72.7%) at the right side and 13 (52%) at the left and no any case of serous tumor presented bilaterally, while of the 20 cases mucinous tumors were 3 (13.6%) at right side and 11 (44%) at left, 6 (75%) bilateral, of 3 cases of Brenner tumors 1(4.5%) right side, 1 (4%) left side and 1 (12.5%) bilateral, clear cell borderline tumor 1 case at right side, and of endometeroid carcinoma 1 case (4.5%) at right and 1 (12.5%) bilateral, the correlation between histopathological subtypes of ovarian epithelial tumors and location whether left or right sides or bilateral were statistically significant as shown in table (4)

Table 4: Correlation between histopathological subtypes of surface ovarian epithelial tumors and side

Types of tumor	Side		Bilateral	p-value
	Right	Left		
Serous	16 (72.7%)	13 (52%)	0 (0%)	0.02 < 0.05 significant
Mucinous	3 (13.6%)	11 (44%)	6 (75%)	
Brenner	1 (4.5%)	1 (4%)	1 (12.5%)	
Clear cell	1 (4.5%)	0 (0%)	0 (0%)	
Endometroid	1 (4.5%)	0 (0%)	1 (12.5%)	
Total	22 (40%)	25 (45.45%)	8 (14.54%)	

Discussion

In the present study, vimentin expression was observed in 36.36% (20/55) of cases involving surface epithelial ovarian tumors, with a noted association between the type of tumor and its degree of differentiation. Particularly in serous ovarian tumors, there was an inverse relationship between vimentin expression and the degree of differentiation. Vimentin was weakly positive in benign serous tumors, with 85.7% (18/21) of cases showing negative expression and 14.2% (3/21) exhibiting 1+ positivity. This contrasted with borderline and malignant tumors, suggesting that the absence of vimentin is a strong indicator of benign differentiation in serous ovarian tumors [8]. No borderline serous ovarian tumors showed 3+ positivity for vimentin, but 66.66% (2/3) exhibited 2+ positivity and 33.3% (1/3) displayed 1+ positivity. In malignant serous tumors, 60% (3/5) demonstrated a 3+ staining pattern. This indicates that higher vimentin staining intensity is associated with malignant differentiation of serous ovarian tumors (8). This observation aligns with recent studies that have associated vimentin overexpression with inhibited differentiation [9]. A study conducted by Viale *et al.* supported this view, showing a relationship between vimentin expression and the degree of differentiation in serous ovarian tumors [10]. However, there was a difference noted; while Viale *et al.* reported consistent vimentin expression in better-differentiated tumors, our study found its expression in both borderline and malignant serous ovarian tumors. Studies by Matsuzaki *et al.* and Dr. Ankita Goel *et al.* displayed similarities with our findings, showing vimentin expression in 21.73% (5/23) and 14.2% (3/21) of benign ovarian serous cystadenoma cases, respectively [11, 12]. In our study, all borderline and malignant serous tumors were vimentin positive, with varying degrees of positivity. Specifically, 62.5% (5/8) showed 3+ grade, and 28.57% (2/8) exhibited 2+ grade in cases with serous adenocarcinoma [12]. These findings correlate with our current observations. Regarding ovarian mucinous tumors, vimentin expression was related to the tumor type but not to the degree of differentiation. Consistent with the findings of Viale *et al.* and Dr. Ankita Goel *et al.* [10, 12], no cases of 3+ vimentin expression were observed in benign, borderline, or malignant mucinous tumors. Kir G *et al.* reported vimentin expression in 18% of mucinous ovarian carcinomas [13]. In our study, 75% (3/4) of malignant mucinous tumors were vimentin negative, and 25% (1/4) showed weak 1+ positivity. Matsuzaki *et al.* did not observe any vimentin expression in 20 benign mucinous tumors studied [11], whereas our study and that of Dr. Ankita Goel *et al.* [12] reported weak 1+ vimentin positivity in 16.6% (2/12) of benign mucinous tumors. The current study did not analyze vimentin expression in endometrioid, clear cell, and Brenner ovarian tumors due to the limited number of these cases available. In terms of bilaterality of serous and mucinous ovarian epithelial tumors (SOET), our study revealed 14.54% (8/55) were bilateral, aligning with the 11.29% reported by Vaidya *et al.* [14]. This incidence was lower in studies by Tejeswini *et al.* [15] and Pradhan SB *et al.* [16], reporting bilaterality in 5.40% and 7.69% of cases, respectively. Our study also confirmed the distribution of left-sided tumors at 45.45% compared to right-sided tumors at 40%, consistent with findings by Madan *et al.* [17] and Pradhan SB *et al.* [16]. In the gross histopathological examination, 63.33% (19/30) of serous tumors exhibited a smooth external surface, with the majority being unilocular (86.95%, 20/23), while mucinous tumors showed 47.36% (9/19) nodularity and 65.38% (17/26) multilocularity, attributed to their inherent multilocularity [18]. Age is recognized as an independent prognostic factor in ovarian tumors [19], with cancer rates rising exponentially with age [20]. In this study, the mean age of diagnosis was 42.4 years, ranging from 14-76 years. This age distribution mirrored the findings of studies conducted by Pilli *et al.*, Zaman *et al.*, and Jha *et al.* [21].

Conclusion

The expression patterns of vimentin distinctly vary across benign, borderline, and malignant surface epithelial ovarian tumors. This differential expression suggests the potential role of the epithelial-mesenchymal transition in the pathogenesis of serous ovarian tumors. Given that all ovarian serous borderline tumors and serous carcinomas exhibited vimentin expression, it is evident that these tumors should be included among the epithelial neoplasms known to express vimentin. This discovery could have implications for diagnostic and therapeutic strategies in ovarian neoplasms.

Conflict of Interest
Not available

Financial Support
Not available

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How to Cite This Article
Shaker OA, AL-Mosawi HM, Al-Hilly NM. Immunohistochemical expression of vimentin monoclonal antibody in ovarian surface epithelial tumors in correlation with clinicopathological parameters. International Journal of Clinical and Diagnostic Pathology. 2023;6(4):01-04.