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EpCAM Expression in Epithelial Ovarian Cancer: Immunohistochemical and Histopathological Study

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Abstract

Background: Ovarian epithelial cancer is a dreadful gynecologic malignancy, with a usual late diagnosis and humble therapy response. EpCAM over-expression in epithelial ovarian cancer could be considered as a hopeful cancer target therapy.

Aim of Study: Detection of EpCAM over-expression in ovarian cancer and correlate it with the clinic-pathological tumor features.

Material and Methods: 42 paraffin blocks of ovarian cancer were immunostained with EpCAM antibody.

Results: EpCAM showed high expression in 54.7% of the studied cases, and it was significantly correlated with the patients' age, tumor size, tumor grade, the presence of lymphovascular emboli, extension to the serosal surface, and FIGO stage.

Conclusion: EpCAM is overexpressed in epithelial ovarian cancer, which could be a future target therapy.

Key Words: *EpCAM – Ovarian cancer – Prognosis.*

Introduction

OVARIAN cancer (OC) is the third most common female genital tract cancer, following cervical and uterine cancers **[1]**. Epithelial ovarian cancer (EOC) represents 85%-90% of OC and it remains a major cause of death from female genital tract cancers **[2]**. On the basis of the GLOBOCAN appraisal **[3]**, about 313,959 new cases and 207,252 deaths from ovarian cancer were evaluated in 2020. In Egypt, 2787 new cases and 1839 deaths from ovarian cancer were estimated in 2020 based on GLOBOCAN appraisal **[4]**.

OC in the early stages is usually asymptomatic **[5]**, whereas 85% of OC patients are diagnosed at advanced stages, when the tumor has reached the abdomen (stage III) or beyond the abdomen and to the liver (stage IV) **[6]**. The principal treatment of OC is cytoreductive surgery in addition to platinum-paclitaxel combination chemotherapy, with nearly 25% of patients being unresponsive to chemotherapy, and many of them having a recurrence. Therefore, OC has a high death rate, associated with a five-year survival rate of around 45% **[5]**.

OC has complicated biological behavior; therefore, the identification of new molecular therapeutic agents is increasingly needed at present for the management of OC **[7]**. Among them is the epithelial cell adhesion molecule (EpCAM) or (CD326). It is a 3942kDa calcium-independent transmembrane glycoprotein that was initially discovered as an antigen in human colonic carcinoma and acts as an epithelial-specific intercellular homophilic adhesive molecule **[8]**.

EpCAM is involved in cell adhesion, signal transduction, and gene regulation processes **[9]**. The expression of EpCAM leads to increased cell proliferation and metabolism via upregulation of the proto-oncogene c-myc **[10]**, and it also helps in cell and tissue differentiation through interactions with E-cadherin **[11]**. Overexpression of EpCAM is detected in various human carcinomas **[12]**, including breast **[13]**, pancreatic **[14]**, and liver cancers **[15]**. Such over-expression makes EpCAM a novel molecular target for oncologic therapy **[16]**.

Aim of the work:

This study was designed to elucidate the immunohistochemical expression of EpCAM in epithelial ovarian cancer and correlating EpCAM expression with other clinic-pathological parameters to detect its utility as a molecular therapeutic agent in the treatment of EOC.

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Material and Methods

The study group: A retrospective study included 42 cases of epithelial ovarian cancer obtained through the collection of archived paraffin blocks from the Department of Pathology, Faculty of Medicine, Cairo University, Egypt, during the period from January 2018 to March 2021. Cases with deficient clinical data or poorly fixed specimens were excluded from the study. The medical records, including the clinical and histopathological data, were revised. The study attained approval from the Local Ethics Committee of the Faculty of Medicine, Cairo University.

Histopathological evaluation:

Each paraffin block was re-cut at 5 thicknesses with a rotator microtome and mounted on glass slides to be stained with Haematoxylin and Eosin (H&E) for histopathological re-evaluation by two pathologists. Histological classification and grading of EOC into low and high grades were done according to WHO classification 2014 **[17]**.

The histopathological types of the tumors were as follows; 24 cases (57.2%) were serous, 8 cases (19%) were mucinous, 6 cases (14.3%) were endometrioid, and 4 cases (9.5%) were clear cell carcinoma.

The immunohistochemical procedure of EpCAM:

The archived 42 paraffin-embedded blocks of EOC cases were sectioned on adhesive-charged microscopic slides; sections of 5µm were obtained. According to the Dako standard protocol, heat-mediated antigen retrieval was performed with citrate buffer pH 6 in an automated water bath (Dako PT link, PT101). The primary antibody was a mouse monoclonal antibody diluted at (1:100) against EpCAM. Catalogue No.: abx019080 (0. 1ml) against the cell membrane region. It was manufactured by Abbexa Ltd, Cambridge, UK. Phone: +44 1223 755950. Fax: +44 1223 755951. Abbexa LLC, Houston, TX, USA. Phone: +1 832 327 7413. www.abbexa.com Email: info@abbexa.com. Immunohistochemical staining was performed in an autostainer (Dako autostainer link 48) using a polymer-based detection system (DakoEnVisionTM FLEX, K8000) (Dako, Colorado, USA) Dako Colorado, Inc. 4850 Innovation Drive Ft. Collins, CO 80525 USA970-226-2200.

Diaminobenzidine was used as chromogen and Mayer's hematoxylin was used as a counterstain, after that coverslips and the DPX mounting medium were used for mounting and preserving sections. All sections were examined using an Olympus BX51 light microscope with x40 objective eyepieces (Olympus, Tokyo, Japan). The positive control used for EpCAM was normal ovarian serosal tissue.

Evaluation of the expression of EpCAM:

EpCAM positive staining was detected in the cell membrane of the epithelial ovarian cancer cells. In each section, the ovarian serosal surface acted as a positive internal control. The immunostaining of EpCAM was performed by applying the scoring system used by Tayama et al. (2017), who combined the proportion score and the intensity score. The proportion score was performed semi-quantitatively to estimate the percentage of positively stained tumor cells. The intensity score evaluates the intensity of staining. The EpCAM expression immunoreactive score (IRS) was determined by the multiplication of both scores as illustrated in (Table 1) **[16]**.

Immunoreactive score (IRS):

Table (1): The immunoreactive score (IRS).

A- The Proportion score (percentage of positive cells)	B- The Intensity score (intensity of staining)	IRS score (multiplication of A and B)
0 = 0% of cells are positive	0 = No staining	0-2 = Negative
1 = 1-25% of cells are positive	1 = Weak staining	3-4 = Weak positive
2 = 26-50% of cells are positive	2 = Moderate staining	6-8 = Moderate positive
3 = 51-75% of cells are positive	3 = Strong staining	9-12 = Strong positive
4 = >75% positive cells	Final IRS score (A x B): 0-12	

The categorization of EpCAM expression into low-EpCAM expression, which was defined as a total IRS score of (0-4) and high EpCAM expression, which was defined as a total IRS score 6 E was done **[16]**. The results of EpCAM immunostaining were correlated with the clinic-pathological variables.

Statistical methods:

Data management and analysis were performed using the Statistical Package for Social Sciences (SPSS) vs. 24. Comparisons between two groups with respect to normally distributed numeric variables were made using the *t*-test. Non-normally distributed numeric variables were compared by the Mann-Whitney test. For categorical variables, differences were analyzed with 2 (Chi-square) tests and Fisher's exact test when appropriate. All *p*-values are two-sided. *p*-values <0.05 were considered significant.

Results

This retrospective study was conducted on forty-two cases diagnosed as epithelial ovarian cancer. As regards the histological subtypes of the enrolled cases, 24 cases (57.2%) were serous, 8 cases (19%) were mucinous, 6 cases (14.3%) were endometrioid, and 4 cases (9.5%) were clear cell carcinoma.

Patients' ages ranged from 35 to 72 years, with a mean of 50.4 (8.1 years) and a median of 45 years. Statistical analysis showed that (25 cases; 59.6%) <50 years and (17 cases; 40.4%) 50 years. The size of the lesion ranged from 5cm to 25cm in maximal diameter; (22 cases, 52.3%) measured 10cm and (20 cases; 47.7%) were <10cm. As regards the laterality of the lesion, 25 cases (57.5%) were unilateral, while 17 cases (42.5%) were bilateral.

In the present study, the tabulated analysis of the tumor histopathological features revealed the following: The tumor grade was high in 31 cases (73.7%), and low in 11 cases (26.2%). Tumor necrosis was detected in 32 cases (76.1%). Lymphovascular emboli were evident in H &E sections in 27 cases (64.3%). In 18 cases (42.8%), the ovarian serosal surface was seeded by malignant tumor deposits. In 15 cases (35.7%), associated omental metastatic tumor deposits were found, and malignant cells were found within the ascetic fluid in 11 cases (26.2%).The FIGO staging system classified the tumor into 24 cases (57.1%) as stage 1, 3 cases as stage II (7.2%) and 15 cases (33.9%) as stage 3.

EpCAM immunostaining expression was detected within the cell membrane in 35 cases (83.3%) of EOC. According to IRS score, 23 cases (54.7%) showed high expression (IRS 6) and 1919 cases (45.3%) showed low expression (IRS 4) (Table 2).

Age constituted a statistically significant factor in EpCAM expression. High EpCAM expression was detected in (5 cases; 11.9%) 50 years and (18 cases; 42.9%) <50 years, while low EpCAM expression was detected in (12 cases; 28.6%) 50 years and (7 cases; 16.7%) 50 years (p-value= 0.006).

Greater tumor size was more associated with high EpCAM expression. High EpCAM expression was detected in (17 cases; 40.4%) with tumor sizes 10cm and in 6 cases (14.3%) <10. The correlation was statistically significant (p-value=0.002).

Correlating EpCAM expression with the tumor laterality revealed a statistically insignificant correlation. High EpCAM expression was found nearly in equal percentages in unilateral and bilateral tumor masses; (11 cases; 26.2%), and (12 cases; 28.6%) respectively, while low expression was predominating in unilateral cases (14 cases; 33.3%) (p-value=0.8) (Table 2).

The correlation of EpCAM with the tumor histological subtype revealed an insignificant correlation. High expression was detected in 13 serous cases (31%), 6 mucinous cases (14.3%), 3 clear cases (7.14%) and 1 endometrioid case (2.4%) (p-value=0.1) (Table 2).

Table (2): Relationship between EpCAM and other clinicopathological variables.

Factors	High expression No=23 %=54.7%	Low expression No=19 %=45.2%	p-value
Age:			
50 ysy:	5 (11.9%)	12 (28.6%)	0.006
<50 ys	18 (42.9%)	7 (16.7%)	
Size:			
10cm	17 (40.4%)	5 (11.9%)	0.002
<10cm	6 (14.3%)	14 (33.3%)	
Laterality:			
Unilateral	11 (26.2%)	14 (33.3%)	0.08
Bilateral	12 (28.6%)	5 (11.9%)	
Histological variant:			
Serous	13(31%)	11 (26.2%)	0.1
Mucinous	6 (14.3%)	2 (4.8%)	
Clear	3 (7.14%)	1 (2.4%)	
Endometrioid	1 (2.4%)	5 (11.9%)	
Necrosis:			
Negative	6 (14.3%)	4 (9.5%)	0.7
Positive	17 (40.4%)	15 (35.7%)	
Grading:			
Low	3 (7.14%)	8 (19 %)	0.03
High	20 (47.6%)	11 (26.2%)	
LVI:			
Negative	5 (11.9%)	10 (23.8%)	0.03
Positive	18 (42.9%)	9 (21.4%)	
Serosal involvement:			
Negative	10(23.8%)	14 (33.3%)	0.04
Positive	13(31%)	5 (11.9%)	
Omental deposits:			
Negative	12 (28.6%)	15 (35.7%)	0.07
Positive	11 (26.2%)	4 (9.5%)	
Ascetic fluid:			
Negative	14 (33.3%)	7 (16.7%)	0.3
Positive	9 (21.4%)	2 (4.8%)	
FIGO:			
I	9 (21.4%)	15 (35.7%)	0.03
II	2 (4.8%)	1 (2.4%)	
III	12 (26.8%)	3 (7.14%)	

The presence of tumor necrosis was directly proportionate to EpCAM expression as it was detected in 17 cases (40.4%) displaying high expression and 15 cases (35.7%) displaying low expression. The relationship was statistically insignificant (p-value=0.7) (Table 2).

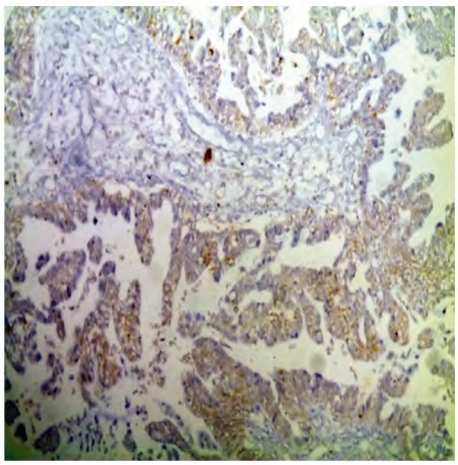
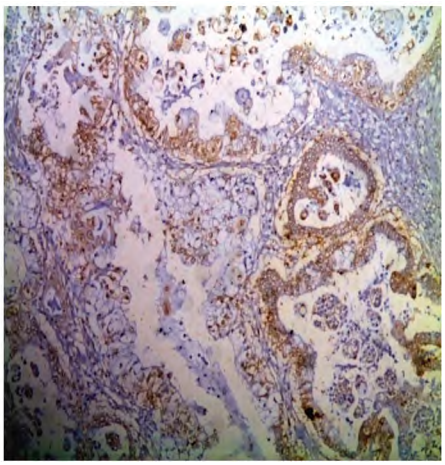
The grade of EOC was significantly associated with EpCAM expression. High grade EOC showed high EpCAM expression in 20 cases (47.6%) and low expression in 3 cases (7.14%) (p-value=0.03) (Table 2).

The greater the lymphovascular invasion, the greater the expression of EpCAM. EOC associated with lymphovascular emboli showed high EpCAM expression in 18 cases (42.9%), and low expression in 9 cases (21.4%). The correlation was statistically significant (p-value=0.03) (Table 2).

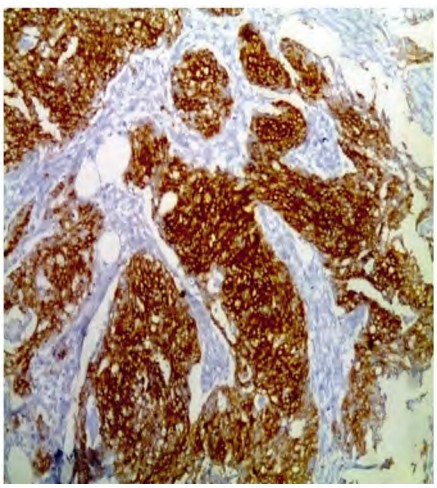
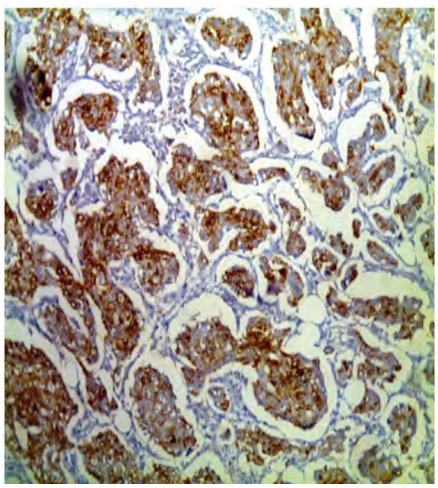
The extension of the tumor to the ovarian serosal surface was associated with high EpCAM expression in 13 cases (31%), and low expression in 5 cases (11.9%). The correlation was statistically significant (p-value=0.04) (Table 2).

Both malignant metastatic omental deposits and malignant cells in ascetic fluid were directly proportionate to the degree of EpCAM expression, but with a statistically insignificant correlation. Omental deposits were detected in 11 cases (26.2%) displaying high and in 4 cases (9.5%) displaying low expression (p-value=0.07). Malignant ascetic fluid was detected in 9 cases (21.4%) displaying high and in 2 cases (4.8%) displaying low EpCAM expression (p-value=0.3) (Table 2).

Correlating EpCAM expression with FIGO staging revealed that high grade expression was statistically significantly associated with advanced tumor stage. It was detected in 9 cases (21.4%) of stage I, 2 cases (4.8%) of stage II, and 12 cases (26.8%) of stage III (p-value=0.03) (Table 2).

(A)  (B) 

(A,B): Ovarian serous carcinoma showing low EpCAM expression (x400 original magnification).

(C)  (D) 

(C,D): Ovarian serous carcinoma showing high EpCAM expression (x200 original magnification).

Discussion

EpCAM acts as a mitogenic signal transducer through induction of cell proliferation by direct control of the cell cycle, upregulation of the cell cycle regulating genes cyclin A and E and the proto-oncogene c-myc, and increasing signal transduction into the nucleus via the Wnt-signaling pathway, EpCAM acts as a mitogenic signal transducer through induction of cell proliferation by direct control of the cell cycle **[18]**. Many studies have proved that EpCAM enhances invasion and metastasis of tumor cells, and that EpCAM positive cells have a stronger affinity for cell proliferation compared with EpCAM negative cells **[19]**. EpCAM intensity of expression is associated with tumor differentiation, disease stage, and metastasis **[20-22]**.

Many studies have found that ovarian cancer cells overexpress EpCAM when compared to normal ovarian cells **[23-27]**, and EpCAM overexpression is significantly associated with a lower survival rate in patients at stage III or IV of the disease **[28-30]**.

In our study; EpCAM expression was diffusely detected within the cell membrane of 23 cases (54.7%), which was in keeping with the results obtained by Tayama et al., **[16]**, who showed high EpCAM expression was detected in 97 cases (57.7%), and low EpCAM-expression in 71 (42.3%) of their studied cases. More than half of the cases (n=23; 54.7%) showed high (IRS score 6) and fewer cases (n=19; 45.2%) showed low expression (IRS score 4) These results come in accordance with Spizzo et al., **[31]** who detected that ovarian cancer are high EpCAM expressers (TIS >4) in 73% (n=236) and weak EpCAM expressors (TIS 1-4) in 19% (n=63). And similar to, but lower than, the results reported by Zheng et al., **[7]**, who detected it in 80% of the cases studied. The lower percentage of the highly expressed cases could be attributed to the smaller comparable sample size.

The age range in the current study was 35 to 72 years, with a mean age of 50.4 (8.1 years) and a median of 48 years. The correlation between the age incidence and EpCAM expression was statistically significant (p-value=0.006), which was slightly different from the study performed by Tayama et al., **[16]**, in which the age range in the EpCAM-high group was between 27 and 87 years with a median of 55.0 years, while in the EpCAM-low group was between 22 to 79 years with a median of 51 years (p-value=0.331), and was in disagreement with the study that was performed by Zheng et al., **[7]**, who detected an insignificant correlation between EpCAM expression and age (p-value >0.05).

The size: The current study showed a significant correlation (p-value=0.002) between the tumor size and the grade of EpCAM expression, which showed approval with that obtained by Tayama et al., **[16]**, as in their study both high and low groups of EpCAM expression attained more or less similar incidences in tumor sizes of 1 0cm and 10cm but with a statistically insignificant correlation (p-value=0.6).

The current study showed that EpCAM high-expression was independent of the histological tumor types. The highest EpCAM over-expression was detected in serous carcinoma (n=13; 31%), and the least for endometrioid (n=1 case; 2.4%). The relationship was statistically insignificant (p-value=0.1). These results showed concordance with Woopen et al., **[32]** who detected an insignificant correlation between EpCAM over-expression and the histological subtypes, but with a different order of frequency as they showed EpCAM over-expression in the endometrioid (n=18, 94.7%), the serous (n=36, 87.8%), and the mucinous tumours (n=11, 78.6%). Also, the results showed approval with Zheng et al., **[7]** who also reported a statistically insignificant correlation (p-value >0.05). Furthermore, the findings were consistent with Spizzo et al., **[23]**, who reported that EpCAM over-expression in OEC differs according to histological subtype, with mucinous having the lowest rate (TIS >4; 55%, n=32) compared to serous, endometrioid, or other histologies (TIS >4, 76%, n=204). This discrepancy in histological predominance may be attributed to the difference in the tumor grade and stage.

The current study revealed that the grade of EOC was statistically significantly related to EpCAM expression. (p-value=0.03), which agreed with Zheng et al., **[7]**, who discovered a statistically significant association between EpCAM expression and tumor grade (p-value 0.05), but disagreed with Woopen et al., **[32]**, who stated that EpCAM did not correlate with tumor grade.

Correlating EpCAM expression with FIGO staging revealed a significantly significant correlation (p-value=0.03). This showed concordance with Zheng et al., **[7]**, who found a statistically significant association between EpCAM expression and FIGO stage. (p-value 0.05), but disagreed with Woopen et al., **[32]** and Tayama et al., **[16]**, who all stated that EpCAM expression and FIGO stage

were not significantly correlated (*p*-value=0.4) for Tayama et al., **[16]**.

Conclusion:

EpCAM is over-expressed in EOC and this over-expression is correlated with the increased malignant potential of the tumor. These results further indicate that the expression of EpCAM may act as a potential biomarker for the assessment of the progression of epithelial ovarian cancer and may provide a molecular therapeutic target for advanced-stage epithelial ovarian cancer. However, larger group investigations at a wider scale and different histological types and stages are needed.

Conflict of Interest: The authors declare no conflict of interest.

References

1- BRAY F., FERLAY J., SOERJOMATARAM I., SIEGEL R.L., TORRE L.A. and JEMAL A.: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin., 68 (6): 394-424, 2018.

2- TORRE L.A., BRAY F., SIEGEL R.L., FERLAY J., LORTET-TIEULENT J. and JEMAL A.: Global cancer statistics, 2012. CA Cancer J. Clin., 65: 87-108, 2015.

3- The Global Cancer Observatory - March 2021. https://gco . iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf

4- The Global Cancer Observatory - March 2021. https://gco . iarc.fr/today/data/factsheets/populations/818-egypt-fact-sheets.pdf

5- SIEGEL R.L., MILLER K.D. and JEMAL A.: Cancer statistics, 2015. CA Cancer J. Clin., 65: 5-29, 2015.

6- NAROD S.: Can advanced-stage ovarian cancer be cured? Nat. Rev. Clin. Oncol., 13: 255-261, 2016.

7- ZHENG J., ZHAO L., WANG Y., ZHAO S. and CUI M.: Clinicopathology of EpCAM and EGFR in human epithelial ovarian carcinoma. Open Med., 12: 39-44, 2017.

8- VAN DER GUN B.T., MELCHERS L.J., RUITERS M.H., DE LEIJ L.F., MCLAUGHLIN P.M. and ROTS M.G.: EpCAM in carcinogenesis: The good, the bad or the ugly. Carcinogenesis, 31: 1913-1921, 2010.

9- DOROTHEA MAETZEL 1, SABINE DENZEL, BRIGITTE MACK, MARTIN CANIS, PHILIP WENT, MICHAEL BENK, CUONGKIEU, PEER PAPIOR, PATRICK A. BAEUERLE, MARKUS MUNZ and OLIVIER GIRES: Nuclear signalling by tumour-associated antigen. EpCAM. Nat. Cell Biol., 11 (2): 162-71, 2009.

10- MUNZ M., KIEU C., MACK B., SCHMITT B., ZEIDLER R. and GIRES O.: The carcinoma-associated antigen EpCAM upregulates c-myc and induces cell proliferation. Oncogen, 23 (34): 5748-58, 2004.

11- WINTER M.J., NAGTEGAAL I.D., VAN KRIEKEN J.H. and LITVINOV S.V.: The epithelial cell adhesion molecule (Ep-CAM) as a morphoregulatory molecule is a tool in surgical pathology. Am. J. Pathol., 163 (6): 2139-48, 2003.

12- SPIZZO G., FONG D., WURM M., ENSINGER C., OBRIST P., HOFER C., MAZZOLENI G., GASTL G. and WENT P.: EpCAM expression in primary tumour tissues and metastases: An immunohistochemical analysis. J. Clin. Pathol., 64: 415-420, 2011.

13- AL-HAJJ M., WICHA M.S., BENITO-HERNANDEZ A., MORRISON S.J. and CLARKE M.F.: Prospective identification of tumorigenic breast cancer cells. Proc. Natl. Acad. Sci. USA, 100: 3983-3988, 2003.

14- LI C., HEIDT D.G., DALERBA P., BURANT C.F., ZHANG L., ADSAY V., WICHA M., CLARKE M.F. and SIMEONE D.M.: Identification of pancreatic cancer stem cells. Cancer Res., 67: 1030-1037, 2007.

15- YAMASHITA T., JI J., BUDHU A., FORGUES M., YANG W., WANG H.Y., JIA H., YE Q., QIN L.X., WAUTHIER E., REID L.M., MINATO H., HONDA M., et al.: EpCAM-positive hepatocellular carcinoma cells are tumor-initiating cells with stem/progenitor cell features. Gastroenterology, 136: 1012-1024, 209.

16- TAYAMA S., MOTOHARAT., NARANTUY D., LI C., FUJIMOTO K., SAKAGUCHI I., TASHIRO H., SAYA H., NAGANO O. and KATABUCHI H.:The impact of EpCAM expression on response to chemotherapy and clinical outcomes in patients with epithelial ovarian cancer. Oncotarget, 8 (27): 44312-44325, 2017.

17- WHO Classification of Tumours Editorial Board. Female Genital Tumours: WHO Classification of Tumours, 5 th ed.; IARC: Lyon, France, Volume 4, 2020.

18- IMRICH S., HACHMEISTER M. and GIRES O.: EpCAM and its potential role in tumor-initiating cells, Cell Adh-Migr, 6: 30-38, 2012.

19- MITRA M., KANDALAM M., HARILAL A., VERMA R.S., KRISHNAN U.M., SWAMINATHAN S., et al.: EpCAM is a putative stem marker in retinoblastoma and an effective target for T-cell-mediated immunotherapy, Mol. Vis, 18: 290-308, 2012.

20- BAE J.S., NOH S.J., JANG K.Y., PARK H.S., CHUNG M.J., PARK C.K., et al.: Expression and role of epithelial cell adhesion molecule in dysplastic nodule and hepatocellular carcinoma, Int. J. Oncol., 41: 2150-2158, 2012.

21- CHAN A.W., TONG J.H., CHAN S.L., LAI P.B. and TO K.F.: Expression of stemness markers (CD133 and EpCAM) in prognostication of hepatocellular carcinoma, Histopathology, 64: 935-950, 2014.

22- NI J., COZZI P.J., DUAN W., SHIGDAR S., GRAHAM P.H., JOHN K.H., et al.: Role of the EpCAM (CD326) in prostate cancer metastasis and progression, Cancer Metastasis Rev., 31: 779-791, 2012.

23- VAN DER GUN B.T., MELCHERS L.J., RUITERS M.H., DE LEIJ L.F., MCLAUGHLIN P.M., et al.: EpCAM in carcinogenesis: The good, the bad or the ugly. Carcinogenesis, 31: 1913-1921, 2010.

24- VAN DER GUN B.T., DE GROOTE M.L., KAZEMIER H.G., ARENDZEN A.J., TERPSTRA P., et al.: Transcription factors and molecular epigenetic marks underlying EpCAM overexpression in ovarian cancer. Br. J. Cancer, 105: 312-319, 2011.

25- HEINZELMANN-SCHWARZ V.A., GARDINER-GARDEN M., HENSHALL S.M., SCURRY J., SCOLYER R.A., et al.: Overexpression of the cell adhesion molecules DDR1, Claudin 3, and Ep-CAM in metaplastic ovarian epithelium and ovarian cancer. Clin. Cancer Res., 10: 4427-4436, 2004.

26- SPIZZO G., GASTL G., OBRIST P., FONG D., HAUN M., et al.: Methylation status of the Ep-CAM promoter region in human breast cancer cell lines and breast cancer tissue. Cancer Lett, 246: 253-261, 2007.

27- KOBEL M., KALLOGER S.E., BOYD N., MCKINNEY S., MEHL E., et al.: Ovarian carcinoma subtypes are different diseases: Implications for biomarker studies. PLoS Med., 5: e232, 2008.

28- SPIZZO G., WENT P., DIRNHOFER S., OBRIST P., MOCH H., et al.: Overexpression of epithelial cell adhesion molecule (Ep-CAM) is an independent prognostic marker for reduced survival of patients with epithelial ovarian cancer. Gynecol. Oncol., 103: 483-488, 2006.

29- OSTA W.A., CHEN Y., MIKHITARIAN K., MITAS M., SALEM M., et al.: EpCAM is overexpressed in breast cancer and is a potential target for breast cancer gene therapy. Cancer Res., 64: 5818-5824, 2004.

30- VARGA M., OBRIST P., SCHNEEBERGER S., MUHLMANN G., FELGEL-FARNHOLZ C., et al.: Overexpression of epithelial cell adhesion molecule antigen in gallbladder carcinoma is an independent marker for poor survival. Clin. Cancer Res., 10: 3131-3136, 2004.

31- SPIZZO G., FONG D., WURM M., ENSINGER C., OBRIST P., HOFER C., MAZZOLENI G., GAST G. and WENT P.: EpCAM expression in primary tumour tissues and metastases: An immunohistochemical analysis, J. Clin. Pathol., 64: 415e420. doi:10.1136/jcp.2011.090274, 2011.

32- WOOPEN H., PIETZNER K., RICHTER R., FOTOPOULOU C.H., JOENS T., BRAICU E.I., MELLSTEDT H., MAHNER S., LINDHOFER H., DARB-ESFAHANI S., DENKERT C. and SEHOULI J.: Overexpression of the epithelial cell adhesion molecule is associated with a more favorable prognosis and response to platinum-based chemotherapy in ovarian cancer, J. Gynecol. Oncol., Vol. 25, No. 3: 221-228, 2014.

التعبير عن EPCAM فى سرطان المبيض الظاهرى
(دراسة هستوباثولوجية ومناعية نسيجية كيميائية)

المقدمة: يعتبر سرطان المبيض الظاهرى من أكثر الأورام المميتة التى تصيب الجهاز التناسلى للمرأة، مع تشخيصه المتأخر كالمعتاد واستجابته المتواضعة للعلاج. فيمكننا الاعتبار أن التعبير الزائد لـ EpCAM فى سرطان المبيض الظهارى كعلاج مستهدف للسرطان.

الهدف: الكشف عن التعبير الزائد لـ EpCAM فى سرطان المبيض وربط تعبيره مع مختلف السمات الإكلينيكية.

المواد والطرق: تم إجراء صبغ كيميائى منا عى لـ EpCAM على بلوكات البارفين لـ ٤٢ حالة من سرطان المبيض الظاهرى.

النتائج: أظهر EpCAM تعبيراً زائداً فى ٥٤.٧٪ من الحالات المدروسة، وكانت هناك علاقة ذات دلالة إحصائية مع سن المرضى، حجم الورم، درجة الورم، الغزو اللمفاوى للأوعية الدموية، التمدد إلى السطح المصلى، ومرحلة FIGO.

استنتاج: أوضح البحث أن EpCAM يظهر بشكل زائد فى سرطان المبيض الظهارى، والذى يمكن أن يكون علاجاً مستهدفاً فى المستقبل.