# VALUE OF E-CADHERIN AND DESMIN IMMUNOCYTOCHEMISTRY IN DISTINGUISHING METASTATIC ADENOCARCINOMA FROM REACTIVE MESOTHELIAL CELLS IN SEROUS EFFUSIONS

**Thesis**

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# بسم الله الرحمن الرحيم

"يُؤْتِي الْحِكْمَةَ مَنْ يَشَاءُ وَمَنْ يُؤْتَ
الْحِكْمَةَ فَقَدْ أُوتِيَ خَيْراً كَثِيراً وَمَا يَذَّكَّرُ
إِلاَّ أُولُو الْأَلْبَابِ"

صدق الله العظيم
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# *Abstract*

One of the problems in studying serous effusion cytological samples is differentiation of reactive mesothelial cells from metastatic adenocarcinoma cells. In this study, the immunohistochemical diagnostic value of E-cadherin and desmin markers in differentiation of these 2 groups of cells was studied.

**Material and methods**: Fifty cases of serous effusions were examined on Papanicolaou-stained and Diff quick-stained smears as well as Paraffin-embedded cell blocks. 30 cases were diagnosed as metastatic adenocarcinoma and 20 cases were diagnosed as reactive mesothelial hyperplasia with typical cytomorphologic features. All the cases were studied for E-cadherin and desmin immunoreactivity.

**Results:** The all cases of metastatic adenocarcinoma reacted to E-cadherin and only 3 cases reacted to desmin, whereas among the 20 cases of reactive mesothelial cell hyperplasia, 18 cases stained with desmin and only one case was stained with E-cadherin. Considering the staining of the E-cadherin and desmin under conditions that the cells were stained with E-cadherin but not with desmin, sensitivity=90%, specificity=100%, positive predictive value (PPV)=100%, negative predictive value (NPV)=87% and accuracy=94% to identify metastatic adenocarcinoma. While under conditions that the cells were stained with desmin but not with E-cadherin, sensitivity=85%, specificity=100%, positive predictive value (PPV)=100%, negative predictive value (NPV)=90% and accuracy= 94% to identify reactive mesothelial cell hyperplasia.

**Conclusion:** Employing this short panel can be helpful for better differentiation of adenocarcinoma and reactive mesothelial cells in serous effusions.

**Key words:**

**Adenocarcinoma, reactive mesothelial cell, E-cadherin, desmin, immunohistochemistry, serous effusion**

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# *List Of Abbreviation*

| | |
|---|---|
| **AIDS** | **Acquired immunodeficiency syndrome** |
| **ALCL** | **Anaplastic large cell lymphoma** |
| **B72-3** | **Cell membrane associated antigen** |
| **BER-EP4** | **Anti-human epithelial antigen** |
| **BG-8** | **Blood group-8** |
| **CB** | **Cell Block** |
| **CD** | **Cluster of differentiation** |
| **CDH1** | **Cadherin 1, type 1, E-cadherin (epithelial)** |
| **DLBL** | **Diffuse large B-cell lymphoma** |
| **EBER** | **EBV-encoded RNA** |
| **EBV** | **Epstein-Barr virus** |
| **ECAD** | **E-cadherin (Epithelial cadherin)** |
| **EPS** | **Epithelioid sarcomas** |
| **GFAP** | **Glial fibrillary acidic protein** |
| **HBME1** | **Anti- human mesothelial cell (Hector Battifora Mesothelial -1)** |
| **H & E** | **Hematoxylin and eosin** |
| **HHV-8** | **Human herpes virus 8** |
| **HIV** | **Human immunodeficiency virus** |
| **ICC** | **Immunocytochmistry** |
| **IFPs** | **Intermediate filament proteins** |
| **LE** | **Lupus erythematosus** |
| **ME1** | **Malic enzyme 1** |

| | |
|---|---|
| **MOC-31** | **Epithelial surface antigen** |
| **MPNSTs** | **Malignant peripheral nerve sheath tumors** |
| **N/C** | **Nuclear /cytoplasmic** |
| **N-cadherin** | **Neuronal cadherin** |
| **NFPs** | **Neurofilament proteins** |
| **OB-cadherin** | **Osteoblastic cadherin** |
| **OV-CAR3** | **Human ovarian cell line** |
| **P-cadherin** | **placental cadherin** |
| **PAL** | **Pyothorax associated lymphoma** |
| **Pap** | **Papanicolaou** |
| **PEL** | **Primary effusion lymphoma** |
| **PENs** | **Pancreatic endocrine neoplasms** |
| **PTLD** | **Post-transplant lymphoproliferative disorder** |
| **SLE** | **Systemic lupus erythematosus** |
| **R-cadherin** | **Retinal cadherin** |

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# INTRODUCTION

The major purpose of cytological examination of serous effusion is to determine whether malignant cells are present or not. This is an extremely important task since in most cases the presence of malignant cells in effusion indicates an advanced or terminal stage of malignancy and usually associated with poor survival **(Naylor et al., 2008).** Adenocarcinomas are by far the commonest type of neoplastic cells to be found in serous effusion. Some tumors have a greater tendency than others to spread to the pleura, pericardium or peritoneum. The most common metastatic adenocarcinomas in pleura are lung cancer in men and breast cancer in women while those in peritoneum are gastrointestinal tract cancers in men and ovarian cancer in women **(Cibas, 2014).**

Whenever the serous membranes are irritated in a process of inflammation or longstanding effusion, mesothelial cells proliferate, shed in the fluid and show morphological changes in cytoplasm and nucleus including enlargement of the nucleus, binucleation, multinucleation or mitotic figures. In some cases, morphological differentiations of reactive mesothelial cells from adenocarcinoma in serous effusions are extremely difficult **(Lisa et al., 2003).**

Adoption of complementary methods will increase diagnostic accuracy in distinguishing between reactive mesothelial and adenocarcinoma cells. Nowadays, immunocytochemistry (ICC) is one of the most suggested methods **(Rahmani et al., 2011).** Employing the immunocytochemical methods, the markers have been used separately or in multiple panels, to help differentiation of the reactive mesothelial cells and metastatic adenocarcinoma has been investigated in many studies, in

some of which the markers have been found to be helpful **(Metzgeroth et al., 2007) & (Murugan et al., 2009).**

E-Cadherin and desmin may be used for discriminating between reactive mesothelial cells and adenocarcinoma cells obtained from serosal cavity fluids. E-cadherin is a member of family called intracellular calcium-dependent adhesion molecules: a transmembrane protein-expressed in epithelial cells. Its extracellular terminal amino acid binds to the same structure of neighboring homotypic cells where calcium ion exists, mediating the epithelial cell-cell adhesion **(Malle et al., 2005).**

Many studies have shown alterations in E-cadherin expression in many types of cancer specifically "lobular carcinoma of the breast and poorly differentiated gastric carcinomas". Theoretically, only the exfoliated cells originating from epithelial tissues can express E-cadherin, therefore, detection of E-cadherin expression is helpful for determining cells from epithelia. Because under normal conditions, epithelial cells are rarely present in benign effusions, the appearance of epithelial cells in effusions means a metastasis of carcinoma developed from epithelia **(He et al., 2004).**

The intermediate filament protein desmin is a known marker for smooth and skeletal muscle differentiation **(Dabbs, 2006).** Several studies have reported positive staining of benign mesothelial cells in serous fluid and tissue sections for desmin **(King et al., 2006).** The exact etiology for expression of desmin in mesothelial cells is not known; however, the multipotential role of mesothelial cells with possible muscle differentiation and coexpression of desmin have been proposed by some studies **(Bolen et al., 1986).**