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THE ROLE OF VIMENTIN IN DIFFERENTIATING ENDOMETRIAL ADENOCARCINOMA AND CERVICAL ADENOCARCINOMA

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Abstract : The histopathological features of endometrial adenocarcinoma sometimes overlap with those of endocervical adenocarcinoma, making it difficult to distinguish between the two. Patterns of immunohistochemistry allow for a more accurate identification of the tissue origin, one of which is vimentin. The aim of this study is to determine the role of vimentin in differentiating the primary tumor location in patients with cervical adenocarcinoma and endometrial adenocarcinoma. This is an analytical observational study with a cross-sectional design conducted at Adam Malik General Hospital from November 2022. The study involved two groups consisting of cervical adenocarcinoma and endometrial adenocarcinoma in paraffin blocks. Immunohistochemical examination of vimentin was performed on each group. Our results showed a significant difference in the expression of vimentin between the group with endometrial adenocarcinoma and cervical adenocarcinoma ($p < 0.001$). The vimentin test has a sensitivity of 100%, specificity of 91%, positive predictive value of 92%, and negative predictive value of 100%. These findings indicate that vimentin can differentiate the tumor location in endometrial adenocarcinoma, but not in cervical adenocarcinoma.

Keywords **- Cervical adenocarcinoma, endometrial adenocarcinoma, vimentin**

I. INTRODUCTION

Endocervical adenocarcinoma accounts for 10-20% of all cervical cancers worldwide and approximately 20-25% in developing countries, while endometrial adenocarcinoma constitutes about 80-90% of endometrial cancers.[1,2] The histopathological features of endometrial adenocarcinoma sometimes overlap with those of endocervical adenocarcinoma, making it challenging to differentiate between endometrial cancer and endocervical cancer, especially in limited specimens such as biopsies and endocervical and endometrial curettage stained with hematoxylin-eosin. The results obtained from these procedures have some limitations, including the contamination of endometrial cells with endocervical cells. Due to the mixture of endocervical and endometrial specimens in these preparations, histopathological examination with hematoxylin-eosin staining alone is sometimes unable to differentiate the origin of the tumor, whether the cancer cells originate from the endometrium and spread to the endocervix or vice versa.[2,3]

Immunohistochemical patterns allow for more accurate identification of tissue origin compared to hematoxylin-eosin examination alone. There are several immunohistochemical tests available to differentiate between endometrial adenocarcinoma and endocervical adenocarcinoma, such as vimentin. Immunohistochemical examination of vimentin, which is believed to recognize endometrial cancer tissue while differentiating it from endocervical cancer tissue, can be used as an initial diagnostic procedure and simplify diagnostic curettage procedures.[4,5,6]

Previous research has reported that immunohistochemical panel examination as a complement to conventional histopathological examination, including ER, Vimentin, mCEA, and p16, can distinguish between histopathological types of cervical adenocarcinoma and endometrial adenocarcinoma. Tumors originating from the endometrium have the characteristic of Vimentin (+), while tumors originating from the cervix have the characteristic of Vimentin (-).[7,8,9]

It is important to differentiate the origin of the tumor cells. This distinction plays a significant role in determining clinical decisions, including treatment selection. In this study, we will explore the role of vimentin as a valuable biomarker in differentiating between endometrial adenocarcinoma and cervical adenocarcinoma.

II. METHODS

2.1Population and Sample

The target population consists of paraffin blocks of adenocarcinoma types from patients diagnosed with cervical adenocarcinoma and endometrial adenocarcinoma. The accessible population includes paraffin blocks from patients diagnosed

with cervical adenocarcinoma and endometrial adenocarcinoma at Adam Malik General Hospital. The research sample comprises paraffin blocks of adenocarcinoma types from patients diagnosed with cervical cancer and endometrial cancer at Adam Malik General Hospital in Medan, who received therapy at the same hospital and have complete clinical data. The samples should also meet the inclusion and exclusion criteria for vimentin immunohistochemistry staining.

2.2 Data and Sources of Data

The data collected consist of primary data (vimentin staining) and secondary data from patients' medical records. The research data were obtained from the Obstetrics and Gynecology Department of Adam Malik General Hospital in Medan, and the vimentin immunohistochemistry staining was conducted at the Pathology Anatomy Laboratory of Adam Malik General Hospital starting from November 2022.

2.3 Procedure

The sample collection included paraffin blocks of cervical adenocarcinoma and endometrial adenocarcinoma types, confirmed through histopathology, and with complete medical data. Failed immunohistochemistry staining were excluded from this study. There are two groups: a group of paraffin blocks with histopathological diagnosis of cervical adenocarcinoma and a group of paraffin blocks with histopathological diagnosis of endometrial adenocarcinoma. Each group underwent immunohistochemistry staining for vimentin.

2.4 Statistical tools

This study is an analytical observational research with a cross-sectional design. Prior to data analysis, the accuracy and completeness of the subject's data were verified. The data were then coded, tabulated, and included in the data analysis, which involved descriptive analysis and hypothesis testing. In descriptive analysis, nominal scale data were presented as frequency distributions and percentages. The relationship between variables was assessed using the chi-square test. If the conditions for the chi-square test were not met, the Fisher exact test or other appropriate alternatives would be used. The data analysis was performed using statistical software.

III. RESULTS AND DISCUSSION

3.1 Expression of Vimentin in Endometrial Adenocarcinoma and Cervical Adenocarcinoma

In this study, there were 2 observers with kappa test analysis yielding an agreement of 91%. The study included 12 samples of endometrial adenocarcinoma and 12 samples of cervical adenocarcinoma. Based on the results of immunohistochemical examination (Table 3.1), 13 samples showed positive Vimentin expression, while 11 samples showed negative Vimentin expression.

Table 3.1: Expression of Vimentin in immunohistochemical examination

Histopathology	**Immunochemistry result**						**p value***
	Positive		Negative		Total		
	n	%	n	%	n	%	
Endometrial	12	100.0%	0	0.0%	12	100.0%	<0.001
Cervical	1	1.0%	11	99.0%	12	100.0%	

The Fisher's exact test results showed a significant difference in Vimentin expression between the endometrial adenocarcinoma group and the cervical adenocarcinoma group ($p < 0.001$). From this, it can be concluded that Vimentin can differentiate tumor location in endometrial adenocarcinoma but not in cervical adenocarcinoma.

Table 3.2: Vimentin Test against histopathological results

		Histopathology		
		Endometrial Adenocarcinoma	Cervical Adenocarcinoma	Total
Vimentin	Positive	12	1	13
	Negative	0	11	11
Total		12	12	24

Vimentin was found to have a sensitivity of 100%, while the specificity was 91% (table 3.2). Based on the sensitivity results obtained in this study, the vimentin test has a 100% ability to determine positive results and a specificity of 91%, meaning that the vimentin test has a 91% ability to determine negative results. The positive predictive value obtained from this study was 92%, and the negative predictive value was 100%. The results of this study indicate that the Vimentin test has a 100% ability to determine the histopathological results of endometrial adenocarcinoma and provides a 91% negative result for histopathological results that are not adenocarcinoma.

3.2 Discussion

Endometrial adenocarcinoma (EMA) and cervical adenocarcinoma (ECA) often present with similar clinical features. In routine histopathological examination with stains like hematoxylin-eosin, the characteristics of both types frequently overlap, making it difficult for clinicians to distinguish between the two conditions. Therefore, a marker is needed to differentiate between EMA and ECA. Vimentin expression has been reported to be frequently used to distinguish between these two types of tumors.[10,11]

In this study, histopathological examination was conducted on samples from patients with EMA and ECA, followed by vimentin staining on all samples, and data analysis was performed. The results showed that vimentin was positive in 13 samples,

while 11 samples were negative for vimentin. The statistical analysis also showed a significant difference ($p < 0.001$). Similar results were reported in a study conducted by Hernandez-Caballero et al. In that study, immunohistochemical examination was performed on 9 samples of cervical adenocarcinoma and 81 samples of endometrial adenocarcinoma. The immunohistochemical examination results showed that only 1 out of 9 samples were confirmed with cervical adenocarcinoma and tested positive for vimentin. Among the endometrial adenocarcinoma samples, 62 out of a total of 81 samples were found to be positive for vimentin. The statistical analysis in that study showed a significant difference ($p = 0.002$).[12,13,14]

These findings are consistent with a previous study by Amru Sofian et al. in 2006, which examined the role of vimentin immunohistochemistry as a marker for the origin of endometrial cancer tissue. The results of the study showed that vimentin immunohistochemistry could differentiate the tissue origin of endometrial cancer. This method had a sensitivity of 93.7% and a specificity of 94.4% in recognizing endometrial tissue.[15]

These results are also in line with a study conducted by Esheba, where positive vimentin expression was found in 16 out of 20 samples of EMA (80%), while in ECA, vimentin expression was only found in 1 out of a total of 10 samples (10%). The statistical analysis also showed a significant difference in vimentin expression between EMA and ECA samples ($p = 0.004$).[14]

A study by Yanaranop et al. also reported similar results to this research. In that study, immunohistochemical examination was performed on 44 samples of ECA and 66 samples of EMA. The study found that all ECA samples had negative vimentin expression, while all EMA samples were positive for vimentin. The statistical analysis also showed a significant difference between ECA and EMA samples ($p < 0.001$). The reported sensitivity and specificity of vimentin in differentiating EMA from ECA were 84.5% and 97.4%, respectively. The positive predictive value (PPV) and negative predictive value (NPV) for diagnosing EMA were 98% and 80.9%, respectively. Overall, the accuracy of vimentin expression reached 89.7%.[15]

Vimentin is a type III intermediate filament protein widely expressed in mesenchymal tissue. Vimentin expression in immunohistochemical examination can be used as a strong marker for diagnosing endometrial adenocarcinoma. Based on a study by Desouki et al., the sensitivity, specificity, PPV, and NPV of vimentin expression in diagnosing EMA were 82%, 97%, 99%, and 59%, respectively.[17,18]

Overall, it has been found that vimentin expression is almost always present in cases of EMA. Based on the findings of this research and previous studies, it can be concluded that vimentin can be a very good marker for distinguishing between EMA and ECA. In cases where vimentin expression is found positive in both specimens, the diagnosis of EMA can be aided by clinical examination or HPV testing. In clinical examination, patients with endometrial adenocarcinoma will have an enlarged uterus, whereas patients with cervical adenocarcinoma may have a mass on the cervix. In cases where there is suspicion of an endocervical adenocarcinoma, HPV testing may be considered, as approximately 70% of HPV DNA has been reported to be found in cases of endocervical adenocarcinoma.[18]

III. CONCLUSION

Distinguishing between EMA and ECA based on routine histopathological examination can be challenging due to overlapping characteristics. However, vimentin expression has shown promise as a reliable marker for differentiation. Multiple studies have reported significant differences in vimentin expression between EMA and ECA, with high sensitivity and specificity. Vimentin can serve as a valuable tool in diagnosing EMA, complemented by clinical examination or HPV testing in ambiguous cases of positive vimentin expression in both specimens.

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