

Matrix Metalloproteinases 9 Expression of Thyroid Follicular Neoplasm FNAB and Its Relationship with Thyroid Malignancy Histopathology

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ABSTRACT

Background

Fine-Needle Aspiration Biopsy (FNAB) thyroid nodules is not easy to distinguish between follicular malignancy and follicular benign lesion. Malignancy diagnosis can only be made from histopathology examination by examining tumor invasion to capsule and vaskular. Matrix Metalloproteinase 9 (MMP-9) examination can be added to help making initial diagnosis. MMP-9 is a proteolytic enzyme that plays important role in cancer progressivity, especially in thyroid. High MMP-9 expression will lead to earlier degradation of thyroid and its will make the cell metastasist easier. This study is to examine MMP-9 expression of thyroid follicular neoplasm related tomalignancy through histopathology examination and the diagnostic test of FNAB MMP-9 expression and histopathologic examination.

Methods

We used 42 sample FNAB follicular thyroid in Anatomic Pathology laboratories RSUP M Djamil Padang and histopathologic examination was performed. Immunohistochemical was staining with primary antibody MMP-9 then its expression were assessed in stroma and cytoplasmic cell tumour.

Results

MMP-9 expression was found positive in malignancy histopathologic (80.9%). Expression of MMP-9 at FNAB folikullar neoplasm thyroid is significant in malignant histopathologic thyroid ($p=0.017$). MMP-9 Sensitivity in thyroid follicular nodule FNAB is quite good (88.575) and its specificity is 51.14%.

Conclusion

Increased MMP-9 expression of FNAB follicular thyroid neoplasm is associated with histopathologic malignancy.

Key words: Fine-Needle Aspiration Biopsy (FNAB), follicular neoplasm thyroid, MMP-9

INTRODUCTION

Fine-Needle Aspiration Biopsy (FNAB) thyroid nodules are difficult to distinguish between follicular malignancy and follicular benign lesions.¹ The diagnosis of malignancy can only be made from histopathology examination by examining tumor invasion to the capsule and vascular.^{2,3} Matrix Metalloproteinase 9 (MMP-9) examination can be added to help to make an initial diagnose. MMP-9 is a proteolytic enzyme that plays important role in cancer progressivity, especially in the thyroid. High expression of MMP-9 will lead to earlier degradation of the thyroid and it will make the cell metastasis easier.⁴ This study aims to examine the MMP-9 expression of thyroid follicular neoplasm FNAB and its association with malignancy on pathological examination.

We used 42 samples of follicular thyroid neoplasm FNAB obtained from the Pathology Anatomic laboratories in M Djamil Hospital Padang, West Sumatera. The immunocytochemical was staining with primary antibody MMP-9 then its expression was assessed in the stroma and cytoplasmic tumor.

METHODS

This study was an observational study using a cross-sectional study method consist of 42 FNAB samples that were diagnosed with follicular neoplasms at M. Djamil Hospital Padang, West Sumatera. The preparations are reviewed and representative preparations will be stained with MMP-9 antibodies.

Immunocytochemical staining has been carried out in the Anatomy Pathology laboratories of RSUPN Dr. Cipto Mangunkusumo, Jakarta. We used primary antibody MMP-9 rabbit monoclonal (*Dual Endogenous Enzyme Block, Labelled Polymer-HRP, DAB + Substar buffer dan DAB + Chromogen, PB*) then its expression is assessed in the stroma and cytoplasmic tumor. And preparations have been analyzed at the Baiturrahmah Faculty of Medicine. MMP-9 expression of thyroid follicular neoplasm was associated with malignancy by histopathology examination.

RESULTS

Based on Bethesda, 42 cases were diagnosed and used as research samples, consisting of 5 men (11.9 %) and 37 women (88.1%). This study showed that the mean age of patients was 41 years old, with the minimum age was 17 years old, and the maximum age was 63 years old. The proportion of patients based on age, divided into 4 age groups, including <20 years old, 21-45 years old, 46-70 years old, and >70 years old. The results of this study showed that there were 2 (4.8%) patients of <20 years old, 24 (57.1%) patients of 21-45 years old, 16 (38.1%) patients of 46-70 years old, and 0 patients of >70 years old.

In this study, 34 cases (80.9%) of the thyroid follicular neoplasm stained with MMP-9 were obtained. The FNAB and immunocytology stain of thyroid follicular neoplasm FNAB can be seen in Figures 1 and 2. We found that the malignant histopathological types was more common and dominated by papillary types (73,8%) (Table 1). Expression of MMP-9 at FNAB folikular neoplasm thyroid is significant in malignant histopathologic thyroid ($p=0.017$). (Table 2) MMP-9 Sensitivity in thyroid follicular nodule FNAB is quite good (88,575) and its specificity is 51.14%.

Table 1. Characteristic based on age, gender, MMP-9 expression and histopathological of FNAB thyroid neoplasm follicular nodule.

Characteristics	n	%
Age		
<20 years old	2	4.8
21-45 years old	24	57.1
46-70 years old	16	38.1
≥70 years old	-	-
Gender		
Men	5	11.9
Women	37	88.1
Ekspresi MMP-9		
Negative	8	19.1
Positive	34	80.9
Type of histopstologic		
Benign	7	16.7
Inflamation	1	2.4
Folicullar adenoma	4	9.5
Adenomatous gaoiter	2	4.8
Maligna	35	83.3
Folikular carcinoma	4	9.5
Papillary carcinoma	31	73.8

Tabel 2. Expression of MMP-9 in thyroid follicular nodules examined with FNAB and presented with histopatological type.

Histopatological type	MMP-9		Total	p
	Negative f (%)	Positive f (%)		
Benign	4 (9.5)	3 (7.1)	7 (16.7)	0.017*
Malignant	4 (9.5)	31 (73.8)	35 (83.3)	
Total	8 (19)	34 (80.9)	42 (100)	

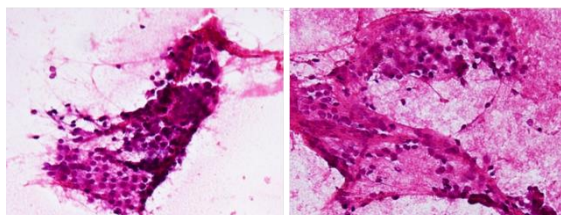


Figure 1. Microscopic of thyroid follicular neoplasm FNAB with H&E stain (100 times and 200 times).

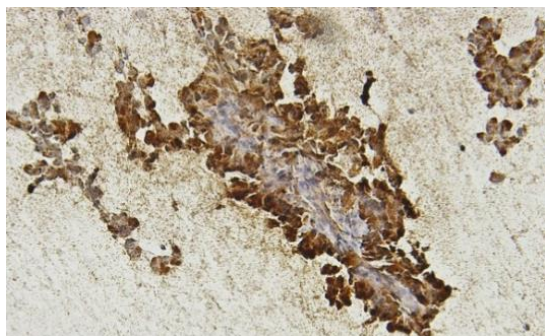


Figure 2. Microscopic of thyroid follicular neoplasm FNAB were positive with MMP-9 stain.

DISCUSSION

The study consisted of 42 cases diagnosed based on FNAB of thyroid follicular neoplasm including 88.1% women and 11.9% men. The same as a study Lim Hyeyeun et al in the United States (1974-2013) there were 97% (77.276) cases of thyroid cancer diagnosed in women.⁵

The higher thyroid nodule found in women than men is often associated with the role of female sex hormone factors, although until now through epidemiological studies this has not been proven. The role of female sex hormones that has been widely studied is the role of estrogen in the well-differentiated carcinogenesis of thyroid carcinoma. Estrogen has a proliferative effect on papillary thyroid carcinoma *in vitro*, but where there is cell proliferation that is mediated by the α (ER α) estrogen receptor, there will be an inhibitory effect by the β estrogen receptor (ER β). These findings also prove that estrogen is involved in the differentiation process of thyroid carcinoma.⁶ The role of hormonal factors in

thyroid carcinogenesis became clearer after it was discovered that pregnancy increases the risk of thyroid carcinoma due to increased thyroid hormones and serum estrogen levels.⁷

This study showed that the mean age of patients was 41 years old, with the minimum age was 17 years, and the maximum age was 63 years. The results of this study showed that there were 2 (4,8%) patients of <20 years old, 24 (57,1%) patients of 21-45 years old, 16 (38,1%) patients of 46-70 years old, and no patients of >70 years old. Savafi Ali, 2017 in Iran found that the highest rate of prevalence in thyroid cancer was observed at the age of 45 years at the time of diagnosis.⁸ Along with the aging process, cells will undergo DNA mutations including mitochondrial DNA which can increase the production of free radicals (ROS). The oxidative damage cycle that instructs ROS will play a direct role in the initiation of carcinogenesis and increase the potential for metastatic tumors.⁹

Fine needle aspiration biopsy (FNAB) is important in evaluating thyroid nodule patients, reducing unnecessary surgery in patients with benign nodules, proper interpretation, and therapy for patients with malignant nodules. Agcaoglu *et al* reported that the factors that can determine the success of thyroid FNAB and reduce false-negative scores are the expertise of cytopathologists.¹⁰ Metalloproteinase matrix is also used as a marker of the progression of malignancy. MMP can play an important role in the process of carcinogenesis, invasive cell tumors penetrate the basement membrane to the stroma and metastases.^{4,11} In this study, 34 cases (80.9%) of the thyroid follicular neoplasm stained with MMP-9 were obtained. The expression of MMP-9 stains positively on the cytoplasm and cell membrane with varying intensities.

Expression of MMP-9 at FNAB folikullar neoplasm thyroid is significant in malignant histopathologic thyroid (p=0,017). In this study, proves that deeper invasion and metastasis will attract more MMP-9 activity and significantly related to the aggressiveness of tumor cell, the presence of lymph nodes and distant metastasis and the degree of tumor.

CONCLUSION

In this study, increased MMP-9 expression of FNAB follicular thyroid neoplasm is associated with histopathologic malignancy.

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