Association of Alpha Methylacyl CoA racemase Expressed withThyroid Tumors

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Abstract

Thyroid cancer is a cancer originating from follicular or parafollicular thyroid cells. Alpha-methyl acyl-CoA racemase in humans is encoded by the AMACR gene. This study was aimed to detect the expression of AMACR in thyroid tumor using immunohistochemistry.Fifty sampleswere collected from blocks of patients previously diagnosed as thyroid tumors, 25 samples were benign andthe remaining 25 samples were malignant.There ages were ranged between 14 to 66 years with mean age 40 years. Out of them 16 were male (32%) and 34 were female (68%). Five micron was taken on positively coated slide for immunohistochemicalto detect the expression of AMACR. SPSS version 11.5 computer programs were used to analyze the data, frequencies, and means, the P. value was calculated by Chi square test.

AMACR expression inmalignant was positive in 8 (16%) and negative in 17 (34%)case, while the expression was negative in all benign cases. with a significant association betweenAMACR expressions and type of thyroidtumor($P<0.05$).the results of AMACR expressionin different types of thyroid cancer, were revealed the following: in papillary carcinoma 4(16%) were positive and 11(44%) were negative,while in follicular carcinoma 4(16%) were positive and 6(24%) were negative,with insignificant relation betweenAMACR expression and type of thyroid cancer ($P>0.05$).

The study concludes there is a significant association between AMACR expressions and thyroid tumors, but no significant relation between AMACR expression and type of thyroid cancer.

Key words: AMACR, thyroid tumors, Immunohistochemistry

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Introduction

Thyroid cancer is more common in people who have a history of exposure to high doses of radiation, family history of thyroid cancer, and are older than 40 years of age. [1]

According to the National Cancer Institute, there are about 56,000 new cases of thyroid cancer in the US each year, and the majority of those diagnoses are papillary thyroid cancer. Females are more likely to have thyroid cancer at a ratio of 3:1. Thyroid cancer can occur in any age group, although it is most common after age 30, and its aggressiveness increases significantly in older patients. [2]Thyroid cancer exhibits low biological aggressiveness in patients younger than 45 years. [3]

Papillary thyroid cancer or papillary thyroid carcinoma is the most common type of thyroid cancer,[4] representing 75 percent to 85 percent of all thyroid cancer cases.[5] [6]

Follicular thyroid cancer, which makes up about 10% to 15% of all thyroid cancers in the United States, tends to occur in somewhat older patients than does papillary cancer. [1]

Medullary thyroid cancer (MTC) is a form of thyroid carcinoma which originates from the parafollicular cells (C cells), which produce the hormone calcitonin.[4] Medullary thyroid carcinomais the third most common of all thyroid cancers. They make up about 3% of all thyroid cancer cases.Approximately 25% of medullary thyroid cancer is genetic in nature, caused by a mutation in the RET proto-oncogene. [7]Anaplastic thyroid cancer (ATC) is a form of thyroid cancer which has a very poor prognosis due to its aggressive behavior and resistance to cancer treatments. [8] [4]

Most first symptom of thyroid cancer is a nodule in thyroid region of neck in addition to an enlarged lymph node. Later symptoms that can be present are pain in neck and changes in voice.[4]

Thyroid pathological problems diagnosed by various methods such as measurement of thyroid stimulating hormone and anti-thyroid antibody, [9] measurement of calcitonin to exclude presence of medullary thyroid cancer. Finally fine needle aspirating cytology test

is usually performed and reported.[10]Radioactive Iodine-131 is used in patients with papillary or follicular thyroid cancer for ablation of residual thyroid tissue after surgery and for the treatment of thyroid cancer. [11]

Most thyroid cancers are very curable. In younger patients, both papillary and follicular cancers have a more than 97% cure rate if treated appropriately. Both papillary and follicular thyroid cancers are typically treated with complete removal of the lobe of the thyroid that harbors the cancer, in addition to the removal of most or all of the other side. [2]

AMACR is located in mitochondria and peroxisomes. Within peroxisomes, it plays a role in the oxidation of branched-chain fatty acids. It is also responsible for the racemization of an intermediate in the synthesis of bile acids. AMACR deficiency in humans has been linked to adult-onset sensory motor neuropathy and to infantile-onset liver dysfunction. Intriguingly, in neoplasia AMACR is most often expressed in tumors associated with a high fat diet, such as colonic and prostatic carcinoma.[12] Alpha-methyl acyl-CoA racemase in humans is encoded by the AMACR gene. [13]

AMACR expression inprostate,liver, salivary gland, thyroid and renal tubular epitheliumis occasional and at a lower level than in malignant glands.In the thyroid, AMACR expression was found in 42% of the follicular carcinomas but in only 16% of follicular adenomas. However, a more detailed analysis on a thyroid tissue microarray did not confirm a significant difference of AMACR expression in follicular adenoma and carcinomas.[14]The aim of this study was to detect the expression of AMACR in thyroid tumor using immunohistochemistry.

Materials and Methods

This is a descriptive retrospective case control study was conducted in Khartoum hospital -Sudan. The study was conducted during the period between Januarys to May 2016. Fifty formalin fixed paraffin embedded blocks were collected from laboratory archive previously diagnosed as thyroid tumors, 25 samples were benign andthe remaining 25 samples were malignant. From each block only one section with 3µm in diameter was cut and attached to salinized slides (Thermo manufacture), to detect AMACR using modified indirect immunohistochemical method. Following deparaffinization in xylene, slides

were rehydrated through a graded series of alcohol and placed in running water. Samples steamed for antigen retrieval using PT, slides were placed in sodium citrate buffer (pH 9.0), then were boiled at 97oC for 10 minutes, then sections were cooled at RT. Endogenous peroxidase activity was blocked with 3% hydrogen peroxidase and methanol for 10 min,then sections were incubated with 100µl of primary antibodies for 20 min at room temperature in a moisture chamber, and then rinsed in phosphate buffer saline. Then the linker was added for 10 minutes and washed in three changes of PBS, followed by addition of 3, 3 diaminobenzidine tetra hydrochloride (DAB) chromogen for 5 minutes. Sections were counterstained with haematoxylin. Concerning positive result, more than 5 cells per field showed brown cytoplasmic stain considered as positive result and less than 5 cells per field considered as negative result, all quality control measurements were obtained during staining procedure.The patient data were collected from patient file`s. Data was analyzed using SPSS computer program, frequencies, mean, chi square test were calculated.Ethical clearance obtained from Alneelain university ethical committee.

Results

Table 1 Shows sex distribution among study population this study found that 11 (68%) of patient were female and (32%) were male. The results of histopathological diagnosis showed benign in (50%) and malignant in (50%) ,the result of age group found less than or equal 40 years was 27(54%) and above 40 years 23(46%), the distribution of patients according to the region found as follow north Sudan (46%), east Sudan (12%) and center of Sudan (42%), AMACR immune expression was positive in (32%) and negative in (68%).

Table 2 Shows the results AMACR expression which were positive in (16%) and negative in (34%) of malignant. While it was negative in all case of benign, with no significant association between AMACR expression and histopathological diagnosis ($P<0.05$).

Table 3 Shows the results of AMACR expression which was positive in (16%) and negative in (44%) of papillary carcinoma. While it was positive in (16%) and negative in (24%) of follicular carcinoma, with insignificant association between AMACR expression and types of thyroid cancer (P>0.05).

Table1: Frequency of histopathological diagnosis, AMACR results, age group, sex and regions among study population

Results		frequency	Percent
Histopathological diagnosis	Benign	25	50%
	malignant	25	50%
AMACR immune expression	Positive	8	32%
	Negative	17	68%
Age group	Less than or equal 40	27	54%
	Above 40	23	46%
Sex group	Male	16	32%
	Female	34	68%
Region	North	23	46%
	East	6	12%
	Center	21	42%
Total		50	100%

Table2: Relation between AMACR expression and histopathological diagnosis

Histopathological diagnosis	AMACR results		Total	P.value
	Positive	Negative		
Benign	0	25	25	0.002
Malignant	8	17	25	
Total	8	42	50	

Table3: Relation between AMACR expression with types of thyroid cancer

Types of thyroid cancer	AMACR results		Total	P.value
	Positive	Negative		
Follicular	4	6	10	0.484
Papillary	4	11	15	
Total	8	17	25	

Discussion

This study aimed to evaluate express of AMACR in thyroid nodule and thyroid cancer usingimmunohistochemistry. In the present studyAMACR expression gave positive result in 8/50 of thyroid malignanttissues,in contrast, no expression of AMACR in benign thyroid tissues, with significant association between AMACR expression and thyroid tumor (p. value 0.002).This result similar to study of Went, who reported that AMACR was expressed in 42% of the follicular carcinomas but in only 16% of follicular adenomas. However, a more detailed analysis on a thyroid tissue microarray did not confirm a significant difference of AMACR expression in follicular adenoma and carcinomas [15].

This study found the expression of AMACR in different types of thyroid cancer were positive in 4/25 of papillary carcinoma , 4/25 of follicular carcinoma samples was identified, with no association between AMACR expression and types of thyroid carcinomas. This result agreed with abundant expression of AMACR in many distinct tumor typesPhilip T. Wenta*, Guido Sauterb, M. Oberholzera & Lukas Bubendorfa And disagreed with Expression of alpha-methylacyl-CoA racemase in papillary renal cell carcinoma.Tretiakova MS1, Sahoo S, Takahashi M, Turkyilmaz M, Vogelzang NJ, Lin F, Krausz T, Teh BT, Yang XJ The present study found 54% of patients were less than 40 years, this result agreed with Predictors of thyroid tumor aggressiveness.

Conclusion

The study concludes there is a significant association between AMACR expressions and thyroid tumors, but no significant relation between AMACR expression and type of thyroid cancer.

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