Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 1431-1437 | ISSN:2251-6727

Immunohistochemical Expression of Prostate-Specific Membrane Antigen in Malignant Thyroid Lesions

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(Received: 04 February 2024 Revised: 11 March 2024 Accepted: 08 April 2024)

KEYWORDS

Immunohistochemical expression, prostate-specific membrane antigen, thyroid lesions

ABSTRACT:

Introduction:

Prostate-specific membrane antigen (PSMA) is a zinc-dependent peptidase overexpressed in prostate cancers, making them amenable to imaging and targeted radionuclide therapy. However, its expression is not only restricted to prostate cancer but has also been demonstrated in tumor neovasculature (vascular endothelium), gliomas, and lung cancers.

Objectives:

1. To study the immunohistochemical expression of PSMA in malignant thyroid lesions.
2. Correlation of expression of PSMA among different grades of malignant thyroid tumor.

Methodology:

The present Hospital-based cross-sectional study was carried out in the histopathology section, pathology department of the tertiary center. Vijayapura during the period from 1st September 2022 – 31st December 2023 involved 30 cases who underwent excision of the thyroid gland.

Results

The most common malignant thyroid lesion is papillary carcinoma followed by follicular, medullary, and anaplastic carcinoma. According to gender-wise distribution, most of the malignant thyroid lesions are more common in females when compared to males. The expression of PSMA is seen in the lining endothelial cells of the blood vessels within the tumor. The expression is considered positive when the endothelial cell shows brown discoloration, the expression is considered negative when the endothelial cell shows no staining. PSMA is seen in 100% of cases of papillary carcinoma, 75% of follicular carcinoma, 50% of cases of medullary carcinoma, and negative expression in anaplastic carcinoma.

Conclusion:

These results help to explore novel biomarkers such as PSMA in thyroid cancer diagnosis and management.

Journal of Chemical Health Risks

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JCHR (2024) 14(3), 1431-1437 | ISSN:2251-6727

Introduction

Prostate-specific membrane antigen (PSMA) is a type II transmembrane glycoprotein highly restricted to the prostate epithelium.[1,2] It is also known as FOLH1 (folate hydrolase-1) or glutamate carboxypeptidase II. Immunohistochemical studies reported that PSMA is strongly expressed by normal and neoplastic prostatic epithelium, along with the epithelium of other genitourinary organs (bladder, kidney, fallopian tubes) and intestine.[3-5] Several recent studies found that PSMA is expressed not only by epithelial cells, but also by vascular endothelium of various malignancies including oral cavity, gastric and colorectal, lung, breast, endometrium, ovary, kidney, urothelial, and glial tumors.[6]

Prostate-specific membrane antigen (PSMA) is a zinc-dependent peptidase overexpressed in prostate cancers, making them amenable to imaging and targeted radionuclide therapy. However, its expression is not only restricted to prostate cancer but has also been demonstrated in tumor neovasculature (vascular endothelium) of gliomas, and lung cancers. Abundant PSMA expression in the tumor vasculature with relative sparing of normal tissue makes it a potential agent for targeted imaging and radionuclide therapy for solid tumors. [7]

PSMA expression in thyroid tumors is less studied. Overall survival rates for patients with differentiated thyroid cancer (DTC) are good. However, the prognosis of patients with loss of differentiation and metastatic disease is poor. Limited treatment options are available for patients with iodine-refractory thyroid cancer, for example, chemotherapy and tyrosine kinase inhibitors. [7]

Hence the present study was planned to study the immunohistochemical expression of PSMA in the thyroid lesions.

Objectives:

3. To study the immunohistochemical expression of PSMA in malignant thyroid lesions.
4. Correlation of expression of PSMA among different grades of malignant thyroid tumor.

Materials and methods: The present Hospital-based cross-sectional study was carried out in the histopathology section, pathology department, during the period from 1st September 2022 to 31st December 2023 involving 30 cases who underwent excision of the thyroid gland.d.

The specimen will be preserved in 10% formalin and processed routinely. 4-5 micron thick sections will be prepared from the most suitable tissue block. Stained slides are studied for morphological diagnosis, histopathological type (according to WHO classification), and staging of thyroid carcinoma (pTNM stage).

One more section of the slide will be mounted on a poly L lysine-coated slide from paraffin-embedded tissue blocks, subjected to PSMA immunohistochemical staining. Immunohistochemical expression of prostate-specific membrane antigen in the neovasculature of thyroid tumors will be correlated with prognostic factors such as tumor size, histological grade, and lymph node status.

Inclusion criteria: All excised malignant thyroid gland specimens received in the histopathology section of the Department of Pathology

Exclusion criteria: Improperly preserved/autolyzed thyroid tissues.

Statistical analysis: Data was collected by using a structured proforma. Data was entered in an MS Excel sheet and analyzed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of proportions.

Results

In our study, out of 30 cases, 03 cases are Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), 13 cases are papillary carcinoma, 05 cases are follicular carcinoma, 05 cases are medullary carcinoma and 04 cases are anaplastic carcinoma**. (Table 1)**

The mean age of the cases was 41.7±11.3 years. The age-wise distribution shows that papillary, follicular, and medullary carcinomas are seen in the 2nd to 6th decade, whereas Anaplastic carcinoma is more commonly seen after the 6th decade. **(Table 2)**

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According to gender-wise distribution, most of the malignant thyroid lesions are common in females when compared to males. In cases of papillary carcinoma, women predominate over men. On the other hand, follicular, medullary, and anaplastic carcinomas have equal distribution. **(Table 3)**

Interpretation of PSMA : The expression of PSMA is seen in the lining endothelial cells of the blood vessels within the tumor. The expression is considered positive when the endothelial cells show brown discoloration, the expression is considered negative when the endothelial cells show no staining. **(Table 5)**

The expression is classified into two types:

Focal expression: only a few blood vessels show positivity.

Diffuse expression: > 95% of blood vessels show positivity.

In NIFTP lesions, PSMA expressions are seen as focal, diffuse, as well as negative expressions. In papillary carcinoma, all the lesions show PSMA expression and are of diffuse type. Hence, it plays a very good diagnostic tool in cases of the dilemma in the diagnosis.

In follicular carcinoma, all the lesions show PSMA expression but focally. Hence, when papillary and follicular carcinomas are in differential diagnosis, PSMA helps in confirming the diagnosis as no Immunohistochemical marker is currently available for confirmation of histological subtype of malignant thyroid lesions.

In medullary carcinoma, out of 5 cases, 4 shows positive expression and one shows negative expression. Out of 4 positive cases, 2 cases show diffuse expression whereas 2 cases show focal expression. In anaplastic carcinoma, all the 4 cases are negative for PSMA expression. The control tissue showed positive expression. Hence, in poorly differentiated and high-grade tumours like anaplastic carcinoma, the expression is negative. It will be helpful in a proper diagnosis of the lesion. We found a correlation between the PSMA expression and the staging of various malignant tumours. We found that a greater number of pT 2 malignant tumours have positive PSMA expression. **(Table 5).**

Discussion

The malignancies of the thyroid gland are more common in hilly regions and in few ethnical people. Early diagnosis of these malignancy has a very good prognosis. Extensive research is going on for the immunohistochemical markers for thyroid malignancies. However, no single marker is available for diagnosis as well as for prognosis. Prostate specific membrane antigen (PSMA) is widely used for all the malignancies. It will stain the lining endothelial cells of tumor vasculature. Currently, in our pilot project study, we have used PSMA for thyroid malignancies to study its expression.

In our study, the most common malignant thyroid lesion is papillary carcinoma followed by follicular, medullary, and anaplastic carcinoma. Out of 30 cases, 03 cases are NIFTP, 13 cases are papillary carcinoma, 05 cases are follicular carcinoma, 05 cases are medullary carcinoma and 04 cases are anaplastic carcinoma. **(Table 1)**

The mean age of the cases was 41.7±11.3 years. The age-wise distribution shows that papillary, follicular, and medullary carcinomas are seen in the 2nd to 6th decade, whereas Anaplastic carcinoma is more commonly seen after the 6th decade. (Table 2). Ryu YJ et al[8] reported a similar mean age of the study population as 43.7±12.4 years.

Klein Nulent TJW et al[9] reported that four men and five women had an average age at diagnosis of 51 ± 15 years (range 31–76 years).

In our study, according to gender-wise distribution, most of the malignant thyroid lesions are more common in females when compared to males. (Table 3) . Ryu YJ et al[8] reported that 66.7% were females and 33.3% were males.

Sollini M. et al[10] reported that PSMA immunostaining in 77% of papillary carcinoma showed positive staining whereas 23% showed negative staining. The expression of PSMA is highest in papillary followed by Follicular carcinoma, medullary and anaplastic carcinoma. Our study also showed similar results with the highest staining in papillary followed by other malignancies.

Saffar H. et al[11] in their study reported that 63 cases of thyroid follicular neoplasms were evaluated including 48

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JCHR (2024) 14(3), 1431-1437 | ISSN:2251-6727

cases of follicular thyroid adenoma and 15 cases of follicular thyroid carcinomas (FTC). Among FTCs, 11 cases revealed both capsular and vascular invasion. In one case only capsular and in two cases only vascular invasions were observed. One case also revealed suspicious vascular invasion with further bone metastasis. The average age of the patients in the adenoma and carcinoma groups was 35.8± 10.1 and 43.8 ± 13.4 years, respectively. PSMA expression in follicular carcinoma is focal in the positive cases, same as seen in our study. A few cases also showed negative staining.

The expression is classified into two types: Focal expression: only a few blood vessels show positivity. Diffuse expression: > 95% of blood vessels show positivity. In NIFTP lesions, focal, diffuse, and negative expressions of PSMA are seen. Similar results have been shown by Segal K et al [12.]

Medullary carcinomas are among the rare tumors of the thyroid. In the study conducted by Bychkov et al [13,] the expression of PSMA is observed in 40% of cases, whereas in the present study, 50% of cases showed positive expression of PSMA.

However, the expression of anaplastic carcinoma thyroid is negative in all 4 cases involved in our study. In other studies done by Heitkotter et al [14], the expression is seen as positive in anaplastic carcinoma. As the number of cases is very less, hence more cases have to be involved to know the status of the expression.

Conclusion:

Our study demonstrates the immunohistochemical expression of prostate-specific membrane antigen (PSMA) in various malignant thyroid lesions. We found that PSMA expression was predominantly seen in the endothelial cells of blood vessels within the tumor. This expression pattern varied among different histological subtypes, with papillary carcinoma showing diffuse expression, follicular carcinoma showing focal expression, and anaplastic carcinoma showing negative expression.

The differential expression of PSMA among different malignant thyroid lesions suggests its potential utility as a diagnostic tool, particularly in cases where histological subtyping is challenging. Our findings also indicate a correlation between PSMA expression and tumor staging, with a higher proportion of positive expression observed in pT2 malignant tumors.

These results are helpful in exploring novel biomarkers such as PSMA in thyroid cancer diagnosis and management. Further research is warranted to validate these findings in larger cohort and to investigate the clinical implications of PSMA expression in guiding treatment planning and predicting patient outcomes.

Source of funding: Self-funded

Conflict of interest: None

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Tables and figures

Table 1: Distribution according to type of malignant thyroid nodules

		No of cases	**Percentage**
Malignant thyroid types	Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)	03	3.3
	Papillary carcinoma	13	43.3
	Follicular carcinoma	05	16.7
	Medullary carcinoma	05	16.7
	Anaplastic carcinoma	04	13.3
	Total	**30**	**100.0**

Table 2: Distribution of malignant thyroid lesions according to age group

	NIFTP	**Papillary carcinoma**	**Follicular carcinoma**	**Medullary carcinoma**	**Anaplastic carcinoma**

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Age group in years	<20	00	00	01	00	00
	21-40	03	08	02	03	00
	41-60	00	05	01	01	01
	> 60	00	00	01	01	03
	Total	**03**	**13**	**05**	**05**	**04**

Table 3: Distribution according to gender in malignant thyroid lesions

		NIFTP	**Papillary carcinoma**	**Follicular carcinoma**	**Medullary carcinoma**	**Anaplastic carcinoma**
Gender	Male	00	02	02	03	02
	Female	03	11	03	02	02
	Total	**03**	**13**	**05**	**05**	**04**

Table 4: Type of malignant thyroid nodule and its distribution according to TNM staging with PSMA expression

	NIFTP		**Papillary carcinoma**		**Follicular carcinoma**		**Medullary carcinoma**		**Anaplastic carcinoma**	
	+	-	+	-	+	-	+	-	+	-
T1	00	00	**04**	00	**01**	00	00	00	00	00
T2	**02**	**01**	**06**	00	**03**	00	**03**	**01**	00	00
T3	00	00	**03**	00	**01**	00	**01**	00	00	**04**
T4	00	00	00	00	00	00	00	00	00	00

Table 5: Expression of PSMA in malignant thyroid lesions

Intensity	**NIFTP**	**Papillary carcinoma**	**Follicular carcinoma**	**Medullary carcinoma**	**Anaplastic carcinoma**	**Total**	**P**
	No of cases	**No of cases**	**No of cases**	**No of cases**	**No of cases**		
Diffuse	01	13	00	02	00	**16**	0.02
Focal	01	00	05	02	00	**08**	
Negative	01	00	00	01	04	**06**	

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Total	**03**	**13**	**05**	**05**	**04**	**30**	