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PAPILLARY THYROID CARCINOMA SIZE;
ASSOCIATION WITH LYMPH NODE METASTASIS

Amjad Ali Khan[1], Abdul Shaheed Asghar[2], Muhammad Ishaq[3], Israr Ahmed Akhund[4]

1. MBBS, FCPS.
Assistant Professor of Pathology.
Jinnah Medical College, Peshawar.
2. MBBS, MPhil, PhD.
Professor of Pathology.
Jinnah Medical College, Peshawar.
3. MBBS, FCPS, FRCS.
Professor of Surgery.
Jinnah Medical College, Peshawar.
4. MBBS, MPhil.
Professor of Physiology.
Jinnah Medical College, Peshawar.

Correspondence Address:
Dr. Amjad Ali Khan
MBBS, FCPS.
Assistant Professor of Pathology.
Jinnah Medical College, Peshawar.
amjadalikhan52@hotmail.com

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ABSTRACT… Background: Papillary thyroid carcinoma (PTC) is the most common malignancy of thyroid gland. It constitutes about 90% of all well differentiated thyroid carcinomas and has an indolent course with excellent prognosis.[1,2,3] Death due to papillary thyroid carcinoma is rare and accounts for only 0.2% of cancer deaths in United States of America.[4] The prevalence of PTC has increased world over due to the wider use of ultrasonography and fine needle aspiration cytology (FNAC) in the routine diagnostic workup. Also papillary thyroid microcarcinomas (PTMC) are being increasingly diagnosed as incidental findings in thyroid gland removed for other thyroid pathologies, like follicular adenoma, multi-nodular goiter or diffuse goiter, etc. Due to uncertainty for this tumor to metastasize to the regional lymph nodes, it is usually not clear whether the surgeon should take the patient to the operating room and proceed with lymph node dissection or to wait and observe. **Study Design:** In this retrospective study from the year **Period:** January 2012 to January 2015, a total of 43 cases of total thyroidectomy with regional lymph node dissection and with histopathological diagnosis of papillary thyroid carcinoma were retrieved from archives of **Setting:** Charsada Teaching Hospital affiliated with Jinnah Medical College Peshawar. The slides and diagnoses of all the retrieved cases were reviewed. Information regarding primary tumor size, any metastasis in regional lymph nodes, patient's age and presence or absence of any associated thyroid disease was noted and analyzed. **Results:** The analysis of the 43 cases of PTC showed that papillary thyroid carcinoma was more common in females than males. It affected age groups between 10 and 80 years of age and was most common in the 4th decade of life. Cervical lymph node metastasis was directly related with the size of primary papillary thyroid carcinoma. The commonly associated thyroid diseases included Hashimoto's thyroiditis, followed by multinodular goiter and rarely Graves' disease. **Conclusions:** Papillary thyroid carcinoma is more common in females; it affects patients in their fourth decade of life and is commonly associated with Hashimoto's thyroiditis. Moreover the chances of cervical lymph node metastasis are directly proportional to the primary tumor size.

Key words: Papillary thyroid carcinoma, papillary thyroid microcarcinomas, Hashimoto's thyroiditis, cervical lymph node metastasis, multinodular goiter.

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INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy and is seen more commonly in young adult females. It constitutes 1% of all cancers, 75% to 80% of all thyroid malignancies, and 90% of all well differentiated thyroid carcinomas; however, death due to papillary thyroid carcinoma is rare and accounts for only 0.2% of cancer deaths in America.[2,3] Diagnosis of PTC depends mainly on the presence of universally accepted diagnostic nuclear features like: enlarged, oval, and crowded nuclei, frequent nuclear grooves, intranuclear cytoplasmic inclusions, and coarse granular chromatin along with other features like papillary architecture and psammoma bodies.[3,5,6] The purpose of this study is firstly to find the association of the size of the primary papillary thyroid carcinoma with the presence of metastasis in any of the cervical lymph node compartments; secondly, to find the most common age group affected by this tumor; and thirdly, to look for the commonest thyroid gland diseases associated with PTC.

METHODS

In this retrospective pathology laboratory-based study spanning over a period of three years (from January 2012 to January 2015), a total of

43 cases with histopathological diagnosis of papillary thyroid carcinoma diagnosed on total thyroidectomy specimens where regional lymph nodes were also removed were retrieved from the archives of Charsada Teaching Hospital affiliated with Jinnah Medical College Peshawar. The slides and diagnoses of all the retrieved cases were reviewed with regards to primary tumor size, metastasis in regional lymph nodes, patient's age, and presence or absence of any associated disease. Papillary thyroid microcarcinoma is defined according to American Joint Committee on Cancer as a subset of papillary thyroid carcinoma measuring ≤ 10 mm and that has not grown outside the thyroid.

RESULTS

On analyzing all the 43 cases of papillary thyroid carcinoma from the year 2012-2015, it was found that papillary thyroid carcinoma was more common in females (n=29) than males (n=14) with a male to female ratio of 1:2.1. Most of the patients were in their fourth decade of life (n= 23), though the age group affected ranged from 10 to 80 years (Table-I). The next commonly affected decades were 6th (n=5), 2nd and 5th decades (n=4, each). Papillary thyroid microcarcinomas (n=9) were not associated with any cervical lymph node metastasis. The chances of finding metastasis in ipsilateral cervical lymph nodes increased as the size of the primary PTC increased (Table-II). Hashimoto's thyroiditis was the most commonly associated thyroid disease (n=19), followed by multinodular goiter (n=10). Graves' disease was associated with only one case of papillary thyroid carcinoma. Thirteen (n=13) cases of PTC were not associated with any particular thyroid disease (Table-III).

Patient's Age in years	Number of Cases of PTC
11 – 20	4
21 – 30	3
31 – 40	23
41 – 50	4
51 – 60	5
61 – 70	1
71 – 80	3

Table-I. Age group affected by papillary thyroid carcinoma

S. No	Primary Tumor Size	Number of Patients	Metastatic Lymph nodes	%
1	0 — 1 cm	9	0	0
2	1.1 – 2 cm	13	3	23
3	2.1 – 3 cm	8	2	25
4	3.1 – 4 cm	6	3	50
5	4.1 – 5 cm	5	3	60
6	5.1 – 6 cm	1	1	100
7	6.1 –7 cm	0	0	0
8	7.1 – 8 cm	1	1	100

Table-II. Association of primary PTC size with presence of lymph node metastasis.

Patient's Age	Multi-nodular Goiter	Hashimotos's Thyroiditis	Graves' Disease	None
11 – 20	0	1	0	3
21 – 30	1	1	0	2
31 – 40	7	12	0	3
41 – 50	1	2	1	1
51 – 60	1	2	0	2
61 – 70	0	0	0	1
71 – 80	0	1	0	1
Total	10	19	1	13
Percent	23.3%	44.2%	2.3%	30.2%

Table-III. Commonest thyroid gland pathology associated with PTC

DISCUSSION

Papillary thyroid carcinoma is a common malignancy in young adults especially females. It is the commonest malignancy of thyroid and its prevalence has increased because of the wider use of ultrasonography and fine needle aspiration cytology (FNAC) in the routine diagnostic workup. PTC has an indolent course and excellent prognosis. Unlike follicular carcinoma, it has predilection for lymphatic spread; the sequence of spread being first to the central compartment (VI), then to the ipsilateral lateral compartments (II, III and IV), and later to the ipsilateral posterior triangle compartment (V), skip lesions however are encountered rarely.[7,8] The presence of cervical lymph node metastasis is a known predictor of loco-regional recurrence and therapeutic central lymph node dissection reduces the frequency of this loco-regional recurrences.[7,9] This relation of lymph node metastasis to loco-regional recurrence has now shifted the standard

of patient care from a focus on overall survival to a focus on recurrence free survival. Papillary thyroid microcarcinomas are being increasingly diagnosed as incidental findings in thyroidectomy specimens, where thyroid glands were removed for various reasons, like follicular adenoma, multi-nodular or diffuse goiter, etc. The long term recurrence rate for PTMC has been reported by Kim et al to be 12%.[10] In such instances of incidental PTMCs it is usually unclear whether the surgeon should take the patient again to the operating room and proceed with lymph node dissection or to wait and observe for lymphadenopathy.

In our study, papillary thyroid carcinoma was most commonly encountered in females as compared to males in a M:F ratio of 1:2.1. It was more commonly encountered in the 4th decade of life (Table-I). The distribution of the disease in the other decades like 2nd, 3rd, 5th, 6th and 8th decades was almost the same. No patient in the 1st decade of life was encountered, though it is the most commonly reported thyroid malignancy in this age group. PTC is reported to be present in all age groups, the mean age at initial diagnosis being usually 40 years.[3]

It was found that the presence of ipsilateral cervical lymph node metastases were directly proportional to the size of the primary papillary thyroid carcinoma (Table-II). For up to 1 mm primary tumor size, no metastases were seen in any of the cervical lymph nodes. Thereafter, as the size of the primary tumor increased, so did the chance of finding metastasis in the ipsilateral cervical lymph node. For primary tumor size above 5.1 cm, 100% of the ipsilateral cervical lymph nodes showed presence of metastasis. Kim et al reported in their study of 428 cases of papillary thyroid microcarcinoma that for primary tumors measuring $\leq$ 1 cm, central lymph node metastasis was significantly associated with primary tumor size, multifocality and extrathyroidal extension, whereas primary tumor size $>$ 0.5 cm was an independent predictor of central lymph node metastasis.[10,11] However on the contrary, El-Foll et al concluded in their study of 44 cases that primary tumor size does not affect the frequency of lymph node metastasis.[2]

Papillary thyroid carcinoma has been reported to be associated with various disease processes in the thyroid gland. In our study (Table-III), it was most commonly associated with Hashimoto's thyroiditis (n=19, 44.2%). The hypothesis for the development of cancer at the site of chronic inflammation was first proposed by Rudolf Virchow in 1863. This concept was later extended further to propose relationship between Hashimoto's thyroiditis and papillary thyroid carcinoma (PTC) by Dailey et al in 1955.[12] Konturek et al reported 23.5% prevalence of papillary thyroid carcinoma in patients of Hashimoto's thyroiditis.[12] Repplinger et al in a study of almost 1,200 patients found that 29% of patients with Hashimoto's thyroiditis exhibited papillary thyroid carcinoma.[13] Further in our study multinodular goiter was found as the background disease in ten (n=10, 23.3%) cases of papillary thyroid carcinoma. PTC in thirteen (n=13, 30.2%) patients was not associated with any other known thyroid disease. Hanumanthappa et al reported in their study a prevalence of 6 % for papillary thyroid carcinoma in multinodular goiter.[14] Prevalence of 1.9% has been reported by Rehman et al for papillary thyroid carcinoma in multinodular goiter.[15] In our study, all the associated diseases were found in a slightly higher percentage than reported by other investigators.

It is concluded that papillary thyroid carcinoma is more common in females; it commonly affects patients in 4th decade of life and is usually associated with Hashimoto's thyroiditis. Also size of the primary tumor is directly proportional to the presence of ipsilateral cervical lymph node metastasis. Therefore, it is recommended for incidental PTCs of more than 1 cm in size, to perform frozen section on the ipsilateral central compartment lymph nodes and if these are positive for metastasis then only should lateral compartments be dissected to reduce morbidity and possible complications. For PTCs less than 1 cm in size without enlarged cervical lymph nodes on clinical or radiological examination, only follow up is recommended.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Amjad Ali Khan	Concept & design, Data collection, analysis and interpretation, Manuscript drafting, Manuscript revision.	
2	Dr. Abdul Shaheed Asghar	Concept & design, Data collection, analysis and interpretation, Manuscript drafting, Manuscript revision.	
3	Dr. Muhammad Ishaq	Concept & design, Data collection & analysis, Manusctipr revision.	
4	Dr. Israr Ahmed Akhund	Concept & design, Data collection & analysis, Manusctipr revision	