IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 1 Ver. II (Jan. 2015), PP 61-64
www.iosrjournals.org

Mixed Medullary -Papillary Thyroid Carcinoma: A Case Report

Dr. Leena Gajare[1], Dr. Archana Joshi[2]
[1]*Assistant Lecturer,* [2]*Associate Professor, Department of Pathology, NKP Salve Institute of Medical Sciences, Nagpur 440019, Maharashtra, India*

Abstract: *Mixed medullary-papillary thyroid carcinoma is a rare thyroid malignancy accounting for less than 1% of all the thyroid malignancies. Here we report a case of 50-year-old female with complaints of gradually increasing thyroid swelling for last 2 years. Fine-needle aspiration was suggestive of follicular neoplasm. Serum calcitonin levels were elevated. The patient underwent total thyroidectomy with regional cervical lymph node excision. Histopathological diagnosis of mixed medullary-papillary carcinoma of the thyroid was given. The aim of presenting this case is to know about this entity for its prognostic implications and to prevent diagnostic dilemmas.*

Keywords: *Thyroid carcinoma, mixed medullary-papillary, calcitonin.*

I. Introduction

Thyroid carcinomas are divided in two major groups [1] depending on their embryogenic origin; those arising from the neuroectodermal derivation of the fourth branchial arch (parafollicular or medullary carcinoma), and those of foregut endodermal origin arising from the base of the tongue (follicular and papillary carcinomas).

Medullary thyroid carcinoma (MTC) accounts for 5-10 % of all the thyroid malignancies while papillary thyroid carcinoma (PTC) represents about 90% of the cases [1, 2]. It is also known to show many cytoarchitectural variations. Mixed medullary-papillary thyroid carcinoma, a variant of MTC is a rare malignancy and is known to represent less than 1 % of all thyroid malignancies [2]. Very few cases have been reported so far.

Classification of thyroid tumors by the World Health Organization (WHO) includes mixed medullary-follicular carcinoma [3]. It describes tumors showing morphological features of medullary carcinoma with immunoreactivity for calcitonin along with follicular (or papillary) carcinoma with immunoreactivity for thyroglobulin. Under this entity tumors showing mixed medullary and follicular components have been observed more often than medullary mixed with papillary carcinoma.

II. Case Presentation

A 50 year old female patient presented with painless palpable mass in lower part of right side of neck, increasing in size over 2 years. The patient had hoarseness of voice, but no symptoms of toxicity or hypothyroidism. Patient denied a family history of thyroid malignancy, radiation exposure or other endocrinopathies.

Physical examination showed well demarcated nodule moving with deglutination. It measured about 3.5 cm in its largest diameter. It was not adherent to any adjacent structure.

Serum levels of free triiodothyronine, free thyroxine, and thyrotrophin were within normal ranges, and anti-thyroperoxidase/anti-thyroglobulin autoantibodies and anti-thyroglobulin antibodies (anti Tg Ab) were negative. Preoperative serum calcitonin level was elevated (45.8 ng/L) (chemiluminescence immunometric assay kit with reference interval in adults: less than 11.5 ng/L for men and less than 4.6 ng/L for women) while the levels of serum calcium, phosphorous and parathyroid hormone were normal.

An ultrasound examination suggested thyroiditis with multinodular goiter. Fine needle aspiration (FNA) of the nodule suggested diagnosis of follicular neoplasm.

Urinary levels of vanyl mandelic acid and catecholamine were normal. The patient was screened negative for multiple endocrine neoplasia (MEN). A chest X-ray and abdomen ultrasound scan were unremarkable.

The patient underwent hemithyroidectomy with regional cervical lymph node dissection. The cut surface of the thyroid specimen is shown in Fig. 1. Surgical specimens of thyroid measured 3 cm x 2.5 cm x 2 cm. The cut surface of the thyroid specimen showed single greyish white nodule with areas of hemorrhage and adjacent thyroid tissue. Four lymph node measured 0.5 cm x 0.5 cm each.

Fig. 1. Gross- Thyroid specimen - cut surface showing white nodule and adjacent thyroid tissue.

The microscopic analysis of the tumor with low and high power view is shown in Fig. 2 to Fig. 6. Microscopically, tumor cells were arranged in nests separated by homogenous hyaline stroma as seen in Fig. 2. The tumor cells were polygonal to spindle shaped having pale eosinophilic cytoplasm and oval to spindle shaped nucleus as observed in Fig. 3. Mitotic activity was low, and no area of necrosis or hemorrhage was observed. The focus of tumor comprised of papillary fronds and fibrovascular core as seen in Fig. 4 and 5 respectively. These were lined by cuboidal cells having round to oval nuclei with nuclear clearing (ground glass appearance), overlapping and grooving (Fig. 6). Foci of PTC were not separated from MTC by unaffected thyroid parenchyma. Lymph nodes showed no metastasis.

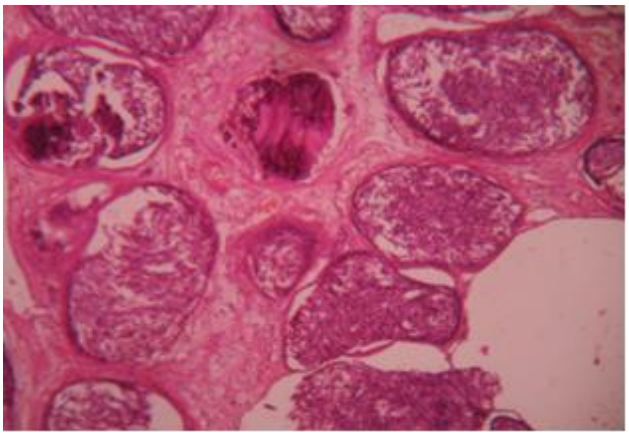

Fig. 2. Tumor cells arranged in nests separated by homogenous hyaline stroma.

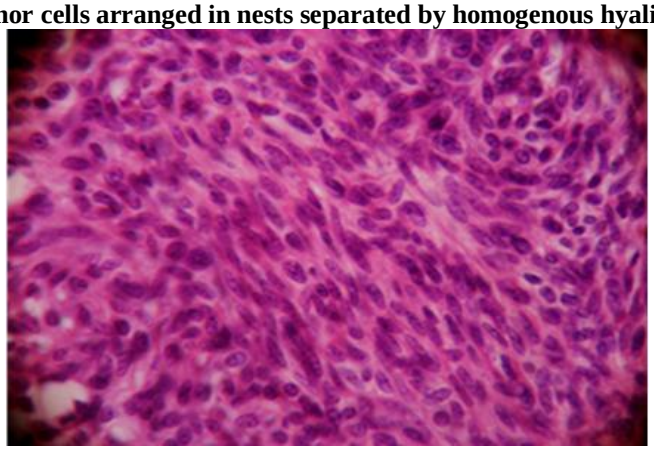

Fig. 3. Polygonal to spindle shaped tumor cells having pale eosinophilic cytoplasm and oval to spindly nucleus.

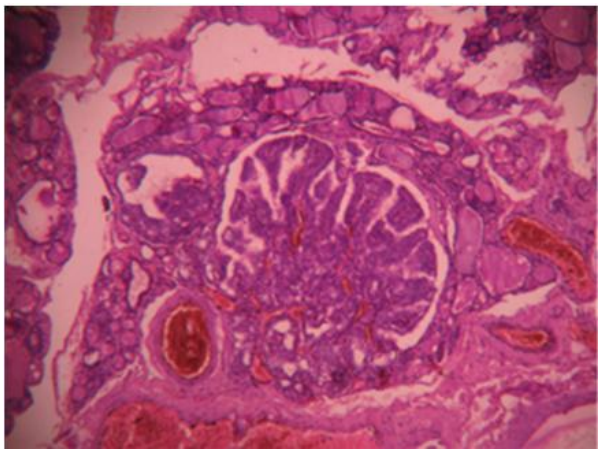

Fig. 4. Focus of tumor cells arranged in papillary pattern.

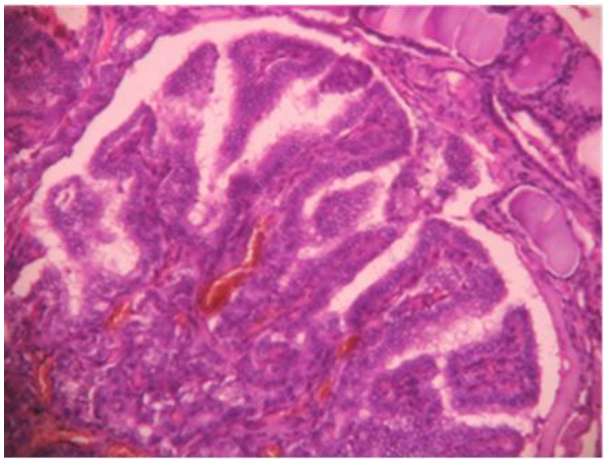

Fig. 5. Tumor cells arranged in papillary fronds with fibrovascular core.

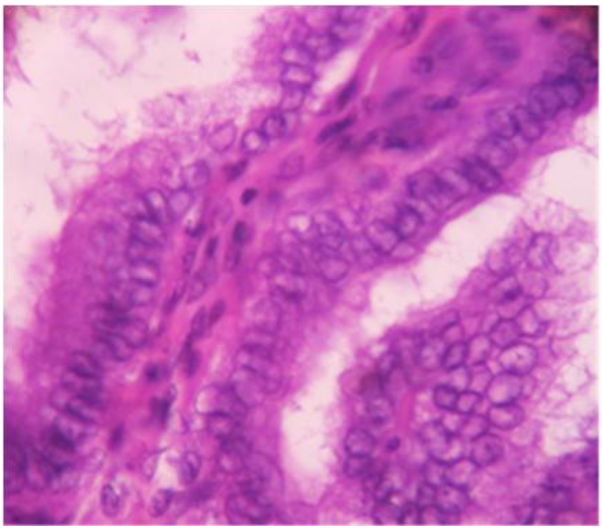

Fig. 6. Nucleus show typical ground glass appearance and nuclear grooving.

III. Discussion

The thyroid carcinomas are divided in two groups, based on the proposed cell of origin the groups are, 1. Follicular and papillary tumors arising from follicular cells; and 2. Medullary neoplasms arising from parafollicular cells [4]. The simultaneous occurrence of MTC and PTC in the same thyroid is a rare phenomenon that can occur as a mixed tumor showing dual differentiation [5] or a collision tumor (i.e., a tumor with two separate and different components) [4-6].

In the presented case, lesions with features of MTC and PTC were detected in same locations and were not separated by a normal thyroid tissue. Thus it is a case of a mixed tumor showing dual differentiation.

Albores-Saavedra et al. [7] reported two cases of mixed medullary-papillary carcinoma of the thyroid showing intimately admixed distinctive population of medullary and papillary carcinomas in which medullary component predominated.

Matias-Guiu et al. [8] described a case with two components of medullary and papillary carcinomas which merged imperceptively in some areas and were clearly separate in few other areas.

Gero et al. [4] reported a case of collision tumor of medullary and papillary thyroid carcinoma. The case showed predominantly a papillary component and a separate small firm white nodule grossly which demonstrated medullary carcinoma. Similar three cases were reported by Rossi et al. [2]

According to WHO [3], male to female ratio of mixed thyroid carcinoma is 1.3:1. Patients usually present with a "cold" thyroid nodule. Some of these mixed thyroid tumors have been shown to occur in kindreds with inherited MTC caused by germline RET mutation. With course of progression lymph nodes are involved. Distant metastasis to lung, liver, mediastinum or bone are also seen.

The cellular origin for the simultaneous occurrence of MTC and PTC carcinoma is not exactly established, yet histogenesis of our case may be explained by several hypothesis. One is of common stem cell origin, with the potentiality of dual differentiation of both C cell and follicular cell elements. The second hypothesis is divergent differentiation, in which, some cells of medullary carcinoma differentiate towards a follicular phenotype by the acquisition of additional molecular defects. The third is field effect hypothesis. In other words, a common oncogenetic factor stimulates neoplastic transformation of both C cells and follicular cells. The last hypothesis is that a separate conditional neoplastic transformation takes place in both C cell and follicular cells i.e. collision tumor. It may not be possible to speculate which hypothesis is dominantly operative in such cases [9].

A precise diagnosis of this uncommon variety of mixed thyroid carcinoma is fundamental for both adequate treatment of patient and genetic screening for excluding Multiple Endocrine Neoplasia 2 (MEN2) syndromes and familial medullary thyroid carcinoma (FMTC). Treatment of mixed medullary–follicular (or papillary) carcinoma is driven by medullary component, and early diagnosis is essential. It is difficult to comment upon the prognosis of such combined thyroid carcinomas as few cases have been reported [10]. Patients with papillary carcinoma have the highest relative survival of 10 years, while MTC is considered to have a worse prognosis, difficult to cure and more likely to recur [11]. However, according to WHO, prognosis of mixed medullary and follicular thyroid carcinoma depends upon the medullary component [3]. Hence, the presence of the medullary component makes the prognosis worse as compared to pure papillary carcinoma.

IV. Conclusion

A case of MTC and PTC mixed tumor showing dual differentiation is presented. Overall, mixed MTC-PTC is a rare clinical entity. Due to its prognostic implications, thorough sampling is important for accurate diagnosis of this type of tumor to avoid diagnostic dilemma.

References

[1] K. Akhtar, S.S. Ahmad, S. Zaheer, S.M. Vasenwala, Mixed medullary and follicular carcinoma of the thyroid - A rare entity, Medical Case Studies, 2(1), 2011, 12-14.

[2] S. Rossi, L. Fugazzola, De Pasquale L., P. Braidotti, V. Cirello, P. Beck-Peccoz, S. Bosari and A. Bastagli, Medullary and papillary carcinoma of the thyroid gland occurring as a collision tumour: report of three cases with molecular analysis and review of the literature, Endocrine Related Cancer, 12(2), 2005, 281-289.

[3] M. Papotti, G. Bussolati, P. Komminoth, X. Matias-Guiu and M. Volante, Mixed medullary and follicular cell carcinoma, in R.A. DeLellis, R.V. Lloyd, P.U. Heitz, C. Eng (Ed.), World Health Organization Classification of Tumors: Pathology and Genetics: Tumors of Endocrine Organs. (Lyon: IARC Press, 2004), 92-93.

[4] M.J. Gero, S. Lipper, A.E. Chernys and L. Silver, Medullary and papillary carcinomas occurring as a collision tumor: report of a case. Clinical Nuclear Medicine, 14(3), 1989, 171-174.

[5] D.J. Marsh, D.L. Learoyd, S.D. Andrew, L. Krishnan, R. Pojer, A.L. Richardson, L. Delbridge, C. Eng, B.G. Robinson, Somatic mutations in the RET proto-oncogene in sporadic medullary thyroid carcinoma, Clin Endocrinol (Oxf), 44(3), 1996, 249–257.

[6] M.S. Alavi, N. Azarpira, Medullary and papillary carcinoma of the thyroid gland occurring as a collision tumour with lymph node metastasis: A case report, Journal of medical case reports, 5(590), 2011, 1-4.

[7] J. Albores-Saavedra, T. Gorraez de la Mora, F. de la Torre-Rendon, E. Gould, Mixed medullary-papillary carcinoma of the thyroid: A previously unrecognized variant of thyroid carcinoma. Human Pathology, 21(11), 1990, 1151-1155.

[8] X. Matias-Guiu, A. Caixas, I. Costa, R. Cabezas, J. Prat, Compound medullary-papillary carcinoma of the thyroid: True mixed versus collision tumour [corrected], Histopathology, 25(2), 1994, 183-185.

[9] M. Shimizu, M. Hirokawa, V.A. Livolsi, Y. Mizukami, T. Harada, T. Itoh, T. Manabe, Combined "Mixed medullary - follicular" and "Papillary" carcinoma of the thyroid with lymph node metastasis. Endocrine pathology, 11(4), 2000, 353-358.

[10] S.F. Lax, A. Beham, D. Kronberger-Schönecker, W. Langsteger, H. Denk, Coexistence of papillary and medullary carcinoma of the thyroid gland-mixed or collision tumour? Clinicopathological analysis of three cases, Virchows Archive: An International Journal of Pathology, 424(4), 1994, 441-447.

[11] G. Dionigi, P. Castano, V. Bertolini, L. Boni, F. Rovera, M.L. Tanda, C. Capella, Luigi Bartalena and R. Dionigi, Simultaneous medullary and papillary thyroid cancer: Two case reports. Journal of Medical Case Reports, 1(133), 2007, 1-5.