Original Research Paper

Volume - 7 | Issue - 7 | July - 2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Pathology

RARE SEQUELAE OF HASHIMOTO THYROIDITIS: TWO CASE REPORTS OF MEDULLARY CARCINOMA AND POORLY DIFFERENTIATED CARCINOMA OF THYROID WITH HASHIMOTO THYROIDITIS.

Dr. Indroneel Bhattacharya	Junior Resident, NRS Medical College and Hospital, Kolkata 14
Dr. Moumita Maity	Assistant Professor, NRS Medical College and Hospital, Kolkata 14.
Dr. Neepamanjari Barman	Assistant Professor, NRS Medical College and Hospital, Kolkata 14.
Dr.Moumita Paul	Assistant Professor, NRS Medical College and Hospital, Kolkata 14.
Dr. Palas Bhattacharyya	Associate Professor, NRS Medical College and Hospital, Kolkata 14.

ABSTRACT Hashimoto thyroiditis (HT) is an autoimmune disease that leads to the destruction of thyroid gland with gradual and progressive hypothyroidism. Individuals suffering from Hashimoto thyroiditis are at an increased risk of developing different thyroid neoplasms. Most common being papillary carcinoma of thyroid, followed by extranodal marginal zone B-cell lymphoma of thyroid and Hurthle cell neoplasms. Incidence of medullary carcinoma (MC) and poorly differentiated thyroid carcinoma (PDTC) of thyroid, coexisting with Hashimoto thyroiditis are rare. According to international literature incidence of MC accounts for only 0.35% of all malignant neoplasms developing in a patient of HT. Whereas no formal statistics are available regarding the incidence of PDTC in patients with HT, which further accentuates the rarity of this unusual combination. Here we present two such rare case report of patients with histopathological features of MC and PDTC coexisting with long standing Hashimoto thyroiditis.

KEYWORDS : Hashimoto thyroiditis, Medullary carcinoma thyroid, Poorly differentiated carcinoma thyroid, Coexistence.

INTRODUCTION

Hashimoto's thyroiditis (HT) is an organ specific immune mediated inflammatory disorder generically designated as autoimmune thyroiditis [1]. Medullary thyroid carcinoma is a malignant tumour showing parafollicular C–cell differentiation. While the malignant neoplasms of thyroid gland arising from the follicular cells are traditionally classified as, well-differentiated type, and an undifferentiated or anaplastic type, a group of tumors that fall in between these two extremes, in terms of both morphologic appearance and behavior have been termed as poorly differentiated thyroid carcinoma or insular carcinoma, which on microscopy show a nesting or insular pattern of growth and is grossly invasive [2].

The association between HT with lymphoma, papillary carcinoma and Hurthle cell neoplasms of thyroid has been well documented [3]. But there are only a few reports depicting a co -existence of this condition with medullary carcinoma of thyroid. The prevalence of medullary carcinoma in a patient of long standing HT is 0.35% [4,5]. Incidence of HT with PDTC is yet to be established, which highlights the unusualness of this combination. Here two such exceptional cases are being reported.

CASE REPORT 1:

A 54-year-old female was diagnosed with Hashimoto thyroiditis six years back. Since last four months patient experienced rapid enlargement in her neck swelling.

Her thyroid hormonal status was as follows: T3–1.0 ng/ml (normal range 0.5 to 1.8 ng /ml), T4–6.7 µg /dL (normal range 4 to 11 µg/dL), TSH-6.04 µU/ml (normal range 0.39 to 6.16 µU/ml) and Anti-thyroid peroxidase antibodies (anti TPO Ab) 580 IU/ml (normal range <34 IU/ml).

She was advised for fine needle aspiration cytology (FNAC) of the thyroid swelling and the smear appeared markedly cellular with aggregates of follicular epithelial cells surrounded by a syncytial arrangement of round to polygonal cells with abundant granular eosinophilic cytoplasm resembling Hurthle cells. Few large cells with stippled chromatin inconspicuous nucleoli was noted along with a few multinucleated giant cells. The cytopathological features were suggestive of HT coexisting with a neoplastic process of thyroid. Patient subsequently underwent total thyroidectomy, following which, the specimen was sent for histopathological examination.

HISTOPATHOLOGY:

Grossly, the total thyroidectomy specimen consisted of both lobes of thyroid measuring 3.5 X 3 X 1.5 cm and 3 X 2 X 1.5 cm respectively**.** Cut section of the left lobe showed, irregular greyish-white lesion measuring 1 X 1 cm (Fig – 1a).

On microscopic examination of haematoxylin and eosin (H&E) stained sections histopathological features of round, polygonal and spindle shaped cells with amphiphilic cytoplasm and medium sized nucleus, along with intervening areas of fibrocollagenous stroma containing amyloid like material was noted (Fig – 1b). Which was confirmed by positive staining with Congo red (Fig – 1c). The above histological features were consistent with medullary carcinoma. Adjoining areas showed features of abundant lymphocytic aggregates, forming germinal centers, follicular cells with oncocytic changes confirming the coexistence of Hashimotos thyroiditis (Fig – 1d & 1e).

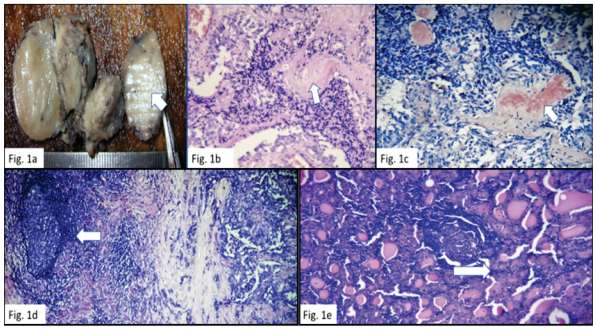

Fig. 1a: Cut section of the left lobe showed, irregular greyish-white lesion measuring 1 X 1 cm; Fig. 1b: Fibrocollagenous stroma containing amyloid like material was noted; Fig. 1c: Positive staining with Congo red; Fig. 1d: Germinal center formation; Fig. 1e: Follicular cells with oncocytic changes

CASE REPORT 2:

A 60-year-old female was diagnosed with Hashimoto thyroiditis five years back. Since last two months she experienced rapid and progressive enlargement in her neck swelling accompanied by mild tenderness and odynophagia.

Her thyroid hormonal status was as follows: T3–0.8 ng/ml (normal range 0.5 to 1.8 ng /ml), T4–3.8 µg /dL (normal range 4 to 11 µg/dL), TSH 6.9 µU/ml (normal range 0.39 to 6.16 µU/ml) and Anti-thyroid peroxidase antibodies (anti TPO Ab) titrated at 340 IU/ml (normal range <34 IU/ml).

On consultation, was advised for a fine needle aspiration cytology (FNAC) of the thyroid swelling. On FNAC the smear appeared bloody with scanty colloidal background and abundant follicular cells, arranged in three dimensional clusters, some forming trabeculae, rosettes and microfollicles. The follicular cells were found to possess bizarre nucleus. Mitosis was evident. The smear was suggestive of a follicular neoplasm, and the patient was advised for histopathological examination, of the thyroid swelling.

HISTOPATHOLOGY:

Grossly the total thyroidectomy specimen consisted of both lobes, measuring 16 X 10 X 6 cm. On cut section the gland was grossly occupied by a greyish white and partially encapsulated nodular mass (14 X 8 X 3 cm) with focal areas of hemorrhage and cystic degeneration.

On microscopic examination, haematoxylin and eosin (H&E) stained sections exhibited histopathological features of monomorphic cells arranged in solid nests, with a trabecular pattern (Fig – 2a). The cells were small exhibiting round, convoluted nucleus, open vesicular chromatin, occasionally distinct nucleoli, scanty pale eosinophilic cytoplasm. Few follicular cells were found, interspersed between these cells (Fig – 2b). Large areas of necrosis were appreciated and extensive vascular invasion was evident surrounding the cluster of neoplastic cells (Fig. – 2c). Brisk mitosis was evident with numerous atypical mitotic figures (Fig – 2d). The histopathological features were suggestive of PDTC. Adjoining areas exhibited intense lymphoplasmacytic infiltrate, germinal centers, and follicular epithelial cells with oncocytic changes, confirming coexistence of Hashimotos thyroiditis (Fig – 2e & 2f).

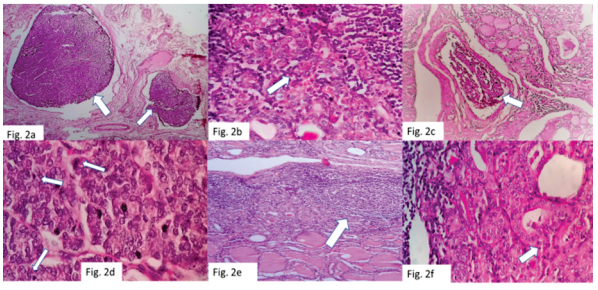

Fig. 2a: Cells arranged in solid nests and islands; Fig. 2b: Entrapped follicular epithelial cells; Fig. 2c: Vascular invasion; Fig. 2d: Brisk mitotic activity; Fig. 2e: Germinal center formation; Fig. 2f: Oncocytic changes in follicles

DISCUSSION

The development of thyroid carcinoma in a background of HT was first described by Dailey et al. [2]. followed by Okayasu in 1997 [6]. The incidence of association between HT and thyroid carcinoma is highly variable, the prevalence ranging from 0.5% to 38% [7]. The most common malignancy developing in thyroid with pre-existing HT, is papillary carcinoma, the prevalence being 36.6% of all thyroid carcinomas in a background of HT [8,9]. Pathogenetic process involved in the co-existence of Hashimoto's thyroiditis with neoplasms, is a matter of debate. It is controversial whether HT predisposes to carcinoma, or HT develops secondarily as an immune response to the malignancy. One of the study inferred that chronic stimulus of thyroid stimulating hormone (TSH) on thyroid tissue produced as a result of an autoimmune process and progressive hypo functioning of the gland, could be the main inciting factor leading to a subsequent neoplastic process. Studies show that elevated TSH levels play key role in the development of clinically detectable thyroid cancer, and LT4 treatment reduces risk of thyroid malignancy in patients with nodular thyroid disease [10]. Elevated titers of Anti thyroglobin antibody (TgAb) in HT, may have a tumorigenic effect and is closely associated with a specific tumorigenic inflammatory response [11].

The coexistence of medullary carcinoma of thyroid with Hashimotos thyroiditis is a rare condition, very few sporadic cases have been reported till date. The first well documented case of co–existence of these two entities was published in 1983 [12]. Since then, only few sporadic cases have been reported. Schuetz et al. reported an overall prevalence of medullary carcinoma of 0.35% in HT patients [5].

The coexistence of Poorly differentiated thyroid carcinoma with Hashimotos thyroiditis is an extremely rare combination. Thus, necessitating further investigations to determine a possible correlation between these two pathological entities. Only exhaustive studies, can determine whether combination of PDTC and HT is pathogenically related or a coincidental event.

Though association between thyroid carcinoma and Hashimoto's thyroiditis is rare, the occurrence of a malignancy should be kept in mind for patients with thyroiditis, who develop a thyroid nodule, complain of a sudden enlargement of a pre-existing neck swelling, tenderness and compression symptoms. Subsequently these patients should be advised for histopathological examination, to rule out malignant neoplasms in a background of long standing HT.

CONCLUSION

Association of a malignant neoplasm with long standing Hashimoto thyroiditis has been widely reported and studied, concluding the prevalence of malignancy with HT from 0.5 to 38%. Of all the possible malignant neoplasms, papillary thyroid carcinoma has been deemed to be most common with an incidence of 36.6%. Prevalence of other malignant neoplasms is albeit a rare presentation. Medullary thyroid carcinoma coexisting with HT has a prevalence of 0.35% only. Association of Poorly differentiated thyroid carcinoma or Insular carcinoma of thyroid with HT is a rare and extraordinary combination.

REFERENCES

[1] Rapoport B: Pathophysiology of Hashimoto's thyroiditis and hypothyroidism. Annu Rev Med 1991; 42:91-96.
[2] Carcangiu ML, Zampi G, Rosai J: Poorly differentiated ('insular') thyroid carcinoma. A reinterpretation of Langhans' 'wuchernde Struma'. Am J Surg Pathol 1984; 8:655-668
[3] Dailey ME, Lindsay S, Skahen R: Relation of thyroid neoplasms to Hashimoto's disease of the thyroid gland. Arch Surg 1955; 70:291-297.
[4] Gaskin D, Parai SK, Parai MR. Hashimoto's thyroiditis with medullary carcinoma. Can J Surg. 1992; 35:528-30.
[5] Schuetz M, Beheshti M, Oezer S, Novotny C, Paul M, Hofmann A, et al. Calcitonin measurements for early detection of medullary thyroid carcinoma or its premalignant conditions in Hashimoto's thyroiditis. Anticancer Res. 2006; 26:723-727.
[6] Okayasu I: The relationship of lymphocytic thyroiditis to the development of thyroid carcinoma. Endocr Pathol 1997; 8:225-230.
[7] Tamimi DM: The association between chronic lymphocytic thyroiditis and thyroid tumors. Int J Surg Pathol 2002; 10:141-146
[8] Nikiforova MN, Caudill CM, Biddinger P, Nikiforov YE: Prevalence of RET/PTC rearrangements in Hashimoto's thyroiditis and papillary thyroid carcinomas. Int J Surg Pathol 2001; 10:15-22
[9] Prasad ML, Huang Y, Pellegata NS, de la Chapelle A, Kloos RT: Hashimoto's thyroiditis with papillary thyroid carcinoma (PTC)-like nuclear alterations express molecular markers of PTC. Histopathology 2004; 45:39-46.
[10] Haymart MR, Repplinger DJ, Leverson GE, Elson DF, Sippel RS, Jaume JC & Chen H: Higher serum thyroid stimulating hormone level in thyroid nodule patients is associated with greater risks of differentiated thyroid cancer and advanced tumor stage. Journal of Clinical Endocrinology and Metabolism 2008; 93: 809–814
[11] Kim ES, Lim DJ, Baek KH, Lee JM, Kim MK, Kwon HS et al.: Thyroglobulin antibody is associated with increased cancer risk in thyroid nodules. Thyroid 2010; 20: 885–891.
[12] Weiss LM, Weinberg DS, Warhol MJ. Medullary carcinoma arising in a thyroid with Hashimoto's disease. Am J Clin Pathol. 1983; 80: 534-538.