Hemiagenesis of Thyroid Gland: A Case Report

Dr. Swapna A. Ambekar*, Dr. Priya P. Wattamwar**, Dr. Azhar A. Siddiqui*** & Dr. Hussain R. Zuberi**

* Associate professor, JIIU’S IIMSR, Warudi
** Assistant professor, JIIU’S IIMSR, Warudi
*** Professor and Head JIIU’S IIMSR, Warudi

Abstract- Thyroid is a highly vascular endocrine gland which is placed anteriorly in the neck. Thyroid hemiagenesis is a rare congenital anomaly in which one thyroid lobe with or without an isthmus fails to develop. We are presenting such a case detected accidentally during routine cadaveric dissection. This condition usually is undiagnosed as it leads to symptoms only when it is associated with other conditions. It is one of the contributing factors for hypothyroidism. It may develop as a sporadic case or familial or due to some genetic abnormalities. Four different genes were identified for development of thyroid but every case of hemiagenesis was not associated with mutations of these genes. Molecular mechanism of development of hemiagenesis needs to be explored.

Index Terms- Thyroid gland, Hemiagenesis, Hypothyroidism, Thyroid anlage, Transcription factors

I. INTRODUCTION

Thyroid is a highly vascular endocrine gland which is placed anteriorly in the neck. It extends from the C5 to T1 vertebrae. The gland is composed of two lateral lobes which are connected by a narrow median isthmus measuring 1.25 cm transversely and vertically. It corresponds to the second and the third tracheal rings.

Thyroid hemiagenesis (THG) is a rare congenital abnormality in which one thyroid lobe with or without an isthmus fails to develop [1]. The first case of thyroid hemiagenesis was described in 1866 by Hansfield Jones [2], since then approximately 285 cases have been reported in the literature till 2005 and so it is labeled as a rare condition [3].

Hemiagenesis as such is seldom responsible for the clinical presentation but it is usually associated with other conditions leading to symptoms; such as Hashimoto’s thyroiditis, multinodular goiter, hyperthyroidism, Grave’s Disease, hypothyroidism, adenoma, adenocarcinoma, chronic thyroiditis or subacute thyroiditis [1,3,4,5]. It is detected either accidentally during dissection or while investigating for any other associated pathological condition or during routine screening ultrasound of neck in school children [3].

II. AIM OF THE STUDY

Objective of the study is to discuss hemiagenesis of thyroid with
- to add a rare case to the literature

III. CASE REPORT

During routine cadaveric dissection in Department of Anatomy at JIIU’s IIMSR, Warudi, agenesis of left lobe of thyroid gland was noted in an old male cadaver. Right sided blood vessels were the sole supply of right lobe. The specimen was carefully dissected and photographed.

Further details about thyroid disease or medication were not available but histological study of right lobe revealed normal thyroid anatomy. There were no signs of any operation around neck.

IV. DISCUSSION

Hemi is a Greek word meaning half and agenesis is a Latin word meaning absence or lack or failure of development. We use hemiagenesis synonymously for the partially developed thyroid. It may be failure of right or left lobes with or without isthmus. The anomalies of the development of thyroid gland distort the morphology of the gland and may cause clinical functional disorders and various thyroid illnesses. About 5% of the world population is affected from various thyroid diseases [6].

Persistence of pyramidal lobe, thyroglossal cysts, agenesis of the thyroid gland and aberrant thyroid are the major developmental anomalies observed in the thyroid gland [7]. Though THG is rare, the exact prevalence cannot be postulated as the condition is usually accidently detected either during dissection or because of the clinical symptoms associated with such a variant. The prevalence was estimated between 1:1900 to 1:2675 (Shabana et al) [3]. It varies between 0.02 – 0.05 % as studied by various researchers. Interestingly, THG is more observed in girls than boys. The incidence of left to right is 4:1[7,8,9,10, and 11]. Absence of the left lobe occurs in 80% of THG and agenesis of the isthmus occurs in 50% of cases [7].

Morphogenesis of thyroid follicular cells is often disturbed in newborns, resulting in a set of conditions collectively known as thyroid dysgenesis (TD). TD is present in 85% of congenital hypothyroidism (CH), a condition that affects 1 of 3500 newborns worldwide [12]. Castanet et al [9] (2005) studied 22 patients with THG retrospectively. He noted normal hormonal levels in the majority of THG patients (59%), which could suggest that a single thyroid lobe was capable of covering hormone requirements. The probable explanation for left sided incidence is agenesis of paired organs is also more likely to occur on the left side.
Thyroid has an asymmetric shape, the right lobe being larger than the left, also the lobe size is reversed in patients with dextrocardia. Thyroid hemiagenesis, could, therefore be considered an exaggeration of this difference, producing an extreme asymmetry of the thyroid gland. THG is more frequent in the female sex, because of a selection bias due to the fact that thyroid diseases are more frequent in women.

Most of reported cases of THG were sporadic; a few were familial with genetic predisposition to hemiagenesis. Enzyme deficiencies associated with hemiagenesis were common causes of hypothyroidism.

A hypothesis put forward in 1949 incriminated congenital unilateral absence of the thyroid vasculature, but some patients with THG have been reported with normal vasculature. In contrast, vascular anomalies of the thyroid are reported in patients with normal bilobed gland. In our case, left sided superior and inferior thyroid arteries were absent.

Humoral or environmental factors controlling the descent and development of the thyroid gland may influence hemiagenesis; but there has to be genetically determined mechanisms.

Embryologically, thyroid is first endocrine gland to start developing in embryo. It begins to form about 24 days after fertilization, from a median endodermal thickening situated in the floor of the primitive pharynx near junction of first & second pharyngeal arches. Thickening lies between tuberculum impar and copula respectively. This thickening soon forms a small outpouching called thyroid primordium. As the tongue grows, the developing thyroid gland descends through the neck, passing ventral to the developing hyoid bone and laryngeal cartilages. At first the thyroid primordium is hollow but it soon becomes solid & divides into right and left lobes connected by the isthmus. Initially thyroid gland is connected to the tongue by a narrow tube (thyroglossal duct). With further development, this tube disappears by the end of 5th week and the isolated thyroid gland now consisting of lateral lobes connected by a well defined isthmus continues to descend. By 7th week, the gland reaches its destination and also assumes its definitive shape. Proximal opening of the thyroglossal duct persists as a small pit in midline of the tongue – the foramen caecum, near the junction of anterior 2/3 and posterior 1/3 of tongue. Molecular mechanisms involved in the translocation of the thyroid primordium have not been completely elucidated. Aberration in development can lead to various anomalies like persistence of thyroglossal duct, thyroglossal cysts, fistula, sinuses, ectopic thyroid tissue, and absence of a part or whole of the gland. These anomalies may be asymptomatic or may cause functional disorders and may be cause of surgical failures and complications.

Various theories have been proposed on the thyroid organogenesis. It has also been proposed that the lateral thyroid lobes derive contributions from caudal pharyngeal endoderm (4th and 5th branchial pouches). They arise later in the development than median component. The median and lateral thyroid components unite by complicated mechanisms. Conversely, recent literature states that thyroid rudiment is derived solely from the median thyroid anlage as mentioned above.

Congenital thyroid gland anomalies occur either as a result of failure of differentiation of the embryonic fields within normally located thyroid tissue or as a result of abnormal location of the thyroid gland in the midline of the neck along the thyroglossal tract (ectopic). The cause of unilateral agenesis of the thyroid gland is unknown but it may arise from the failure of the original analogue to become bilobed and spread out laterally to both sides. Congenital thyroid anomalies are associated more with hypofunction than with hyperfunction. Persistence of thyroglossal duct leads to formation of pyramidal lobe or levator glandulae thyroidae. High division of thyroglossal duct results in two independent thyroid lobes with no isthmus. Raffella Maiorana noted that patients of TGH have a pituitary thyroid axis set at a different level leading to higher frequency of hypothyroidism or other thyroid. It produces subtle abnormalities of thyroid function which may or may not be clinically relevant but it maintain patient in a situation of thyroid tissue overstimulation. Such patients are at high risk for goiter and hypothyroidism.

The occurrence of thyroid hemiagenesis among monozygotic twins, among sisters, or together with other thyroid malformations within one family suggests genetic predisposition. Several genes such as thyroid-specific transcription factors TTF-1 or Nkx2.1, TTF-2 or FOXE1, and Pax8 have been found to control thyroid descent, development and morphogenesis. Castanet observed four genes in thyroid gland development; three encode thyroid enlisted above and one encodes the TSH receptor gene. Analysis of the candidate gene Pax8 in his cohort found no mutations, suggesting that Pax8 may not be a key genetic factor in this disorder and that other genes may be involved.

Gangbo etal observed agenesis of isthmus of thyroid in a case of trisomy 22 and hence suggested that chromosome 22 could play a role in the thyroid development. According to Langman, in the developing embryo, establishment of body axes, anteroposterior, dorsoventral and left right takes place before and during the period of gastrulation. The primitive streak is initiated and maintained by expression of Nodal, a member of TGF-β family. HNF-3 β maintains node and induces regional specificity. Left – right sidedness is orchestrated by cascade of genes. FGF8 secreted exclusively by the cells of left side of node and primitive streak. PITX2 is a homeobox containing transcription factors responsible for left sidedness. FGF8 and LEFTY-2 upregulates PITX2. So any defect in this gene cascade may be responsible for THG on left side.

Mario De Felice studied genetics and molecular mechanisms of developing thyroid in patients with dysgenesis. He stated cell interactions are required for normal organogenesis. He suggested influence of the developing heart on thyroid organogenesis as the cardiac malformations represent the most frequent birth defects associated with TD. He noted morphological and biochemical changes in thyroid cell specification, making them clearly distinct from their neighbors. Many disorders appeared to be derived from alterations of initial morphogenetic events. He found transcription factors Foxe1, Pax8, and Hhex to be expressed both in mature thyroid cells and in their precursors. When the thyroid diverticulum begins to migrate, the expression of these factors was restricted to the thyroid primordium as they were never expressed in the thyroglossal duct. In the primitive pharynx, Tifl/Nkx2-1 was present exclusively in the thyroid anlage. Interestingly, he
identified Titf1/Nkx2-1 mRNA in parafollicular C cells and in the epithelial cells of the ultimobranchial body which are neuroectodermal in origin; end up in the thyroid gland in close proximity with the TFCs. He proved that Titf1/Nkx2-1 is an essential requirement for the survival of thyroid cell precursors to prevent apoptosis. According to him, Pax8 was not only required for the survival of the thyroid precursor cells but also holds a specific upper role in the genetic regulatory cascade, which controls thyroid development and functional differentiation. He revealed mutations in regulatory genes. Many cases of TD did not show mutations of TITF1/NKX2-1, FOXE1, PAX8. So he expressed the possibility of mutations of other genes controlled by these transcription factors. So, ultimately, the exact molecular mechanism of development of THG was not given and it needs further research.

V. CONCLUSION

Thyroid Hemiagenesis can be associated with other types of dysorganogenesis or variations in the neurovascular relations. This knowledge should be borne in mind during operations around this region for safe surgery and better prognosis.

Though the genes responsible for development of thyroid are known, the exact gene for hemiagenesis still needs exploration.

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AUTHORS

First Author – Dr. Swapna A. Ambekar - MBBS MS (anatomy), Associate professor, JIJI’S IIMSR, Warudi, Email – swapnabondekar@gmail.com
Second Author – Dr. Priya P. Wattamwar – MBBS MD (anatomy), Assistant professor, JIJI’S IIMSR, Warudi
Third Author – Dr. Azhar A. Siddiqui - MBBS MS (anatomy), Professor and Head JIJI’S IIMSR, Warudi, Email - drazharsiddiqui@gmail.com
Fourth Author – Dr. Hussain R. Zuberi MBBS MS (anatomy), Assistant professor, JIJI’S IIMSR, Warudi
Picture 1: Hemiagenesis of left lobe of thyroid gland

1 – RIGHT SUBMANDIBULAR GLAND
2 – INFRAHYOID MUSCLES
3 – THYROID CARTILAGE
4 – RIGHT SIDED THYROID GLAND
5 – TRACHEA
6 – RIGHT SUPERIOR THYROID ARTERY
7 – INFERIOR THYROID VEIN