DYSTHYROIDISM IN CHRONIC LIVER DISEASE

Thesis

Submitted in the partial Fulfillment of the M.D. Degree in Internal Medicine

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2010

Acknowledgement

I am greatly honored to express my thanks and gratitude to Dr. ***Khadiga El Ashmawy****, Professor of Internal Medicine, Cairo University who suggested the subject, set up the plan and carefully supervised the manuscripts. Professor Dr. Khadiga has always been there, for my professors, my colleagues and myself, whenever we needed her. I am also very grateful to her, without her support and continuous help this work would not be completed.*

I would also like to express my deepest gratitude and sincere appreciation to Dr. ***Mona Ameen,*** *Professor of Internal Medicine, Cairo University, for her valuable guidance, encouragement, keen supervision, and co-operation throughout this work.*

I am deeply grateful to Dr. ***Mona Salem,*** *Professor of chemical and clinical pathology, Cairo University, for her faithful helping in the laboratory studies in this work.*

My deepest thanks to Dr. ***Einas Hamdy****, lecturer of chemical and clinical pathology, Cairo University, for her co-operation and help in the laboratory studies in this work.*

Abstract

Patients with chronic liver disease may have thyroiditis, hyperthyroidism, or hypothyroidism ***(Richard, 2008).*** These facts encouraged us to study the relation between various chronic liver diseases and the thyroid functions.Our study included 80 subjects classified into 4 groups: group (A) included 20 patients with liver cirrhosis due to chronic hepatitis C, group (B) included 20 patients with liver cirrhosis due to other causes than hepatitis C, group (C) included 20 patients with fatty liver, and group (D) included 20 healthy controls. liver function tests, hepatitis markers, thyroid functions (FT3, FT4, TSH), anti-thyroid peroxidase antibodies(anti-TPO), anti-thyroglobulin antibodies(anti-Tg), liver and thyroid ultrasound were done. we found significant decrease in the FT3 and FT4 in patients with chronic hepatitis C and patients with liver cirrhosis due to other causes compared to patients with fatty liver and the control group, We also found significant increase in the TSH levels in patients with chronic hepatitis C and these findings significantly correlated with disease severity. we found statistically significant increase in anti-TPO and anti-Tg in patients in chronic hepatitis C patients when compared to patients in the other groups.

Key words: (chronic hepatitis C-cirrhosis-fatty liver-the thyroid gland)

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List of Abbreviations

THs: Thyroid hormones

TRH: Thyrotropin releasing hormone

TSH: Thyroid stimulating hormone

FT4: Free thyroxin

FT3: Free triiodothyronine

TSHr: Thyroid stimulating hormone receptor

TRs: Thyroid hormone receptor

TREs: Thyroid hormone response elements

TPO: Thyroid peroxidase

Tg: Thyroglobulin

AITD: Autoimmune thyroid disease

IIT: Interferon induced thyroiditis

HT: Hashimoto's thyroiditis

TABs: Thyroid autoantibodies

GD: Graves' disease

NAFLED: Non alcoholic fatty liver disease

MELD: Model of end stage liver disease

CTP: Child-Tuurcotte-Pugh

HBsAg: Hepatitis B surface antigen

HBIg: hepatitis B immunoglobulin

HBeAg: hepatitis B e antigen

anti-HBs: anti hepatitis B surface

anti HBc: anti hepatitis B core

anti HCV Ab: anti hepatitis C virus antibodies

Alb: albumin

AST: aspartate aminotransferase

ALT: alanine aminotransferase

PC%: prothrombin concentration

Bil: bilirubin

INTRODUCTION

Thyroxin and tri-iodothyronine are essential for normal organ growth, development and function. These hormone regulate the basal metabolic rate of all cells, including hepatocytes, and thereby modulate hepatic function; the liver in turn metabolizes the thyroid hormones and regulates their systemic endocrine effects. Thyroid dysfunction may perturb liver function, liver disease modulates thyroid hormone metabolism, and a variety if systemic diseases affect both organs ***(Malik and Hodgson, 2002).***

Most chronic illness defects which arise in thyroid hormone metabolism, resulting in the sick euthyroid syndrome. This is characterized by a normal total T4, normal or high free T4, low total T3, low free T3 and elevated rT3***(Leonard et al., 2000)***

In different types of liver disease, similar process may occur to those seen in the sick euthyroid syndrome, but in addition a number of changes specific to the type or stage of liver disease are also found ***(Malik and Hodgson, 2002).***

Latent autoimmune thyroiditis is more frequent in untreated patients with HCV chronic hepatitis ***(Ganne et al., 2000)***

Aim of work:

- To highlight the intricate relations between the thyroid gland and the liver in health and disease.
- To detect the thyroid abnormalities and its correlation with etiology of chronic liver diseases.

THE THYROID GLAND

Anatomy Of The Thyroid Gland

The Germans call the thyroid the "shield gland" (Schilddrüse), and the English name, derived from the Greek, means the same thing. Such a term gives a most erroneous impression of its shape. It is interesting, however, that in the Minoan culture, a shield was used that had a shape somewhat like that of the mammalian thyroid gland ***(Dumont et al., 2005).***

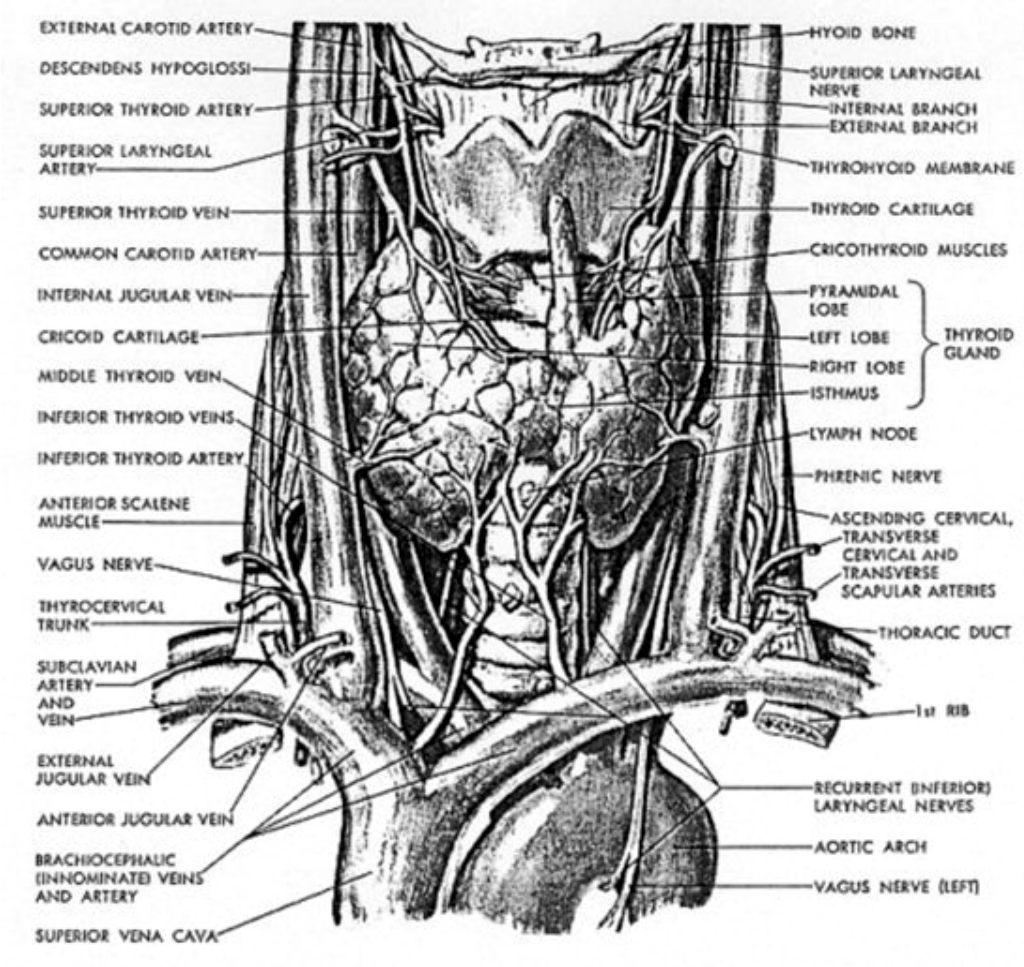

Fig. (1): Gross anatomy of the thyroid and surroundings

(From: Netter FH, 1965)

The thyroid is a brownish-red and highly vascular gland located anteriorly in the lower neck, extending from the level of the fifth cervical vertebra down to the first thoracic. The gland varies from an H to a U shape and is formed by 2 elongated lateral lobes with superior and inferior poles connected by a median isthmus (with an average height of 12-15 mm) overlying the second to fourth tracheal rings.Each lobe is 50-60 mm long, with the superior poles diverging laterally at the level of the oblique lines on the laminae of the thyroid cartilage. The lower poles diverge laterally at the level of the fifth tracheal cartilage. Thyroid weight varies but averages 25-30g in adults (slightly heavier in women). The gland enlarges during menstruation and pregnancy. Usually, 2 pairs of parathyroid glands lie in proximity to the thyroid gland (***David, 2005).***

Histology:

The lobules are composed of follicles, the structural units of the gland, consisting of a layer of simple epithelium enclosing a colloid-filled cavity; this colloid (pink on hematoxylin and eosin [H&E] stain) contains an iodinated glycoprotein, iodothyroglobulin, a precursor of thyroid hormones. Follicles vary in size, depending upon the degree of distention, and they are surrounded by dense plexuses of fenestrated capillaries, lymphatic vessels, and sympathetic nerves (***David, 2005).***

Epithelial cells are of 2 types: principal cells (ie, follicular) and parafollicular cells (ie, C, clear, light cells). Principal cells are responsible for formation of the colloid (iodothyroglobulin), whereas parafollicular cells produce the hormone calcitonin. Parafollicular cells lie adjacent to the follicles within the basal lamina (***David, 2005).***

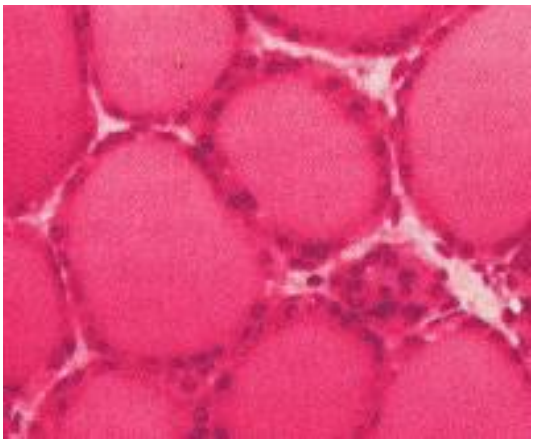

Fig. (2): Histology of the thyroid gland shows the structural units of the gland and the follicles, consisting of a layer of simple epithelium enclosing a colloid-filled cavity.

The arterial supply Comes from the superior and inferior thyroid arteries and, occasionally, the thyroidea ima artery. These arteries have abundant collateral anastomoses with each other, both ipsilaterally and contralaterally. The thyroid ima artery is a single vessel, which originates, when present, from the aortic arch or the innominate artery and enters the thyroid gland at the inferior border of the isthmus **(David, 2005).**

Anterior view **Posterior view**

Fig. (3): Distribution of thyroid arteries with associated laryngeal nerve *(David, 2005).*

Venous Drainage

Three pairs of veins provide venous drainage from the thyroid gland. The superior thyroid vein ascends along the superior thyroid artery and becomes a tributary of the internal jugular vein. The middle thyroid vein follows a direct course laterally to the internal jugular vein. The inferior thyroid veins follow different paths on each side. The right passes anterior to the innominate artery to the right brachiocephalic vein or anterior to the trachea to the left brachiocephalic vein. On the left side, drainage is to the left brachiocephalic vein. Occasionally, both inferior veins form a common trunk called the thyroid ima vein, which empties into the left brachiocephalic vein ***(David, 2005).***

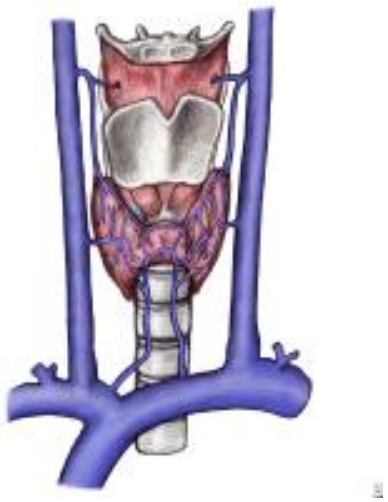

Fig. (4): Distribution of thyroid veins *(David, 2005).*

Lymphatic drainage of the thyroid gland is extensive and flows multidirectionally. Immediate lymphatic drainage courses to the periglandular nodes, to the prelaryngeal (Delphian), pretracheal, and paratracheal nodes along the recurrent laryngeal nerve, and then to mediastinal lymph nodes. Regional metastases of thyroid carcinoma can also be found laterally, higher in the neck along the internal jugular vein. This can be explained by tumor invasion of the pretracheal and

paratracheal nodes causing an obstruction of normal lymph flow ***(David, 2005).***

Innervation

Principal innervation of the thyroid gland derives from the autonomic nervous system. Parasympathetic fibers come from the vagus nerves, and sympathetic fibers are distributed from the superior, middle, and inferior ganglia of the sympathetic trunk. These small nerves enter the gland along with the blood vessels. Autonomic nervous regulation of the glandular secretion is not clearly understood, but most of the effect is postulated to be on blood vessels, hence the perfusion rates of the glands ***(David, 2005).***