Cryoglobulins in Thyrotoxicosis

Submitted for Partial Fulfilment of the M.Sc Degree
In Internal Medicine

By

Alaa Mohamed Abbas Abaid

(M.B., B.ch)

Supervised by

Prof. Dr. Moatassem Salah Amer

Prof. of Internal Medicine
Faculty of Medicine
Ain Shams University

Prof. Dr. Mohsen Mostafa Maher

Prof. of Internal Medicine
Faculty of Medicine
Ain Shams University

Dr. Manal Hashem

Lecturer of Clinical Pathology
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University

1996

Acknowledgement

*Firstly ultimated thanks to **ALLAH**.*

*It is a great honour to express my deep gratitude and appreciation to **Prof. Dr. Moatassem Salah Amer**, Professor Of Internal Medicine. I am very grateful for his whole hearted support expert advice and enthusiastic help shown to me while under his supervision.*

*I would also like to express my deep gratitude and respectful thanks to **Prof. Dr. Mohsen Mostafa Maher** Prof. Of Internal Medicine for his kind guidance and supervision which enabled me to accomplish this work.*

*I am deeply grateful to **Dr. Manal Hashem**, Lecturer of Clinical Pathology, from whom I received valuable assistance, encouragement helpful instructions and enthusiastic stimulation throughout the whole work.*

Last but not least, I would like to thank all members who shared in preparation, writing and revising this thesis.

بسم الله الرحمن الرحيم

Contents

List of Tables

INTRODUCTION
&
AIM OF THE WORK

Introduction

Cryoglobulins are a group of the proteins which are responsible for vascular and thrombotic manifestations. It is commonly present in the chronic inflammatory disorders and autoimmune syndromes.

Thyrotoxicosis is one of the common autoimmune endocrine syndromes which are characterized by various vascular and thrombotic manifestations.

To the best of our knowldge, no previous studies have been done about this subject.

The aim of the work :

Is to investigate the presence of cryoglobulins in the thyrotoxicosis or not and to see whether if they are related to complications of thyrotoxicosis or not.

THYROID GLAND

Study of Cryoglobulins in Thyrotoxicosis

Anatomy of the thyroid gland

This hihgly vascular endocrine gland clasps the upper part of the trachea and extends from 5th or 6th tracheal ring inferiorly to the side of thyroid cartilage superiorly. It is enclosed in a sheath of pretracheal fascia which is attached to the arch of cricoid cartilage, and the oblique line of the thyroid cartilage superiorly. The gland therefore moves with the larynx in all its movements. Intenal to the sheath, it is enclosed in its own fibrous capsule and between these lie the arteies and veins of the gland, it consists of a pair of lobes joined across median plane by a narrow isthmus.

Lobes : each lobe is conical in shape and has a convex superfacial surface which is covered by sternohyoid, sternothyroid, omohyoid muscles & is overlapped by the anterior border of sternomastoid. The medical surface is moulded inferiorly on the trachea & oesophagus with recurrent largngeal nerve between them, while superiorly it is fitted to the cricoid & thyroid cartilages, with the cricothyroid, inferior constrictor muscles, and external branch of the superior laryngeal nerve intervening .

Isthmus : this is a band of variable width which lies on the 2nd to 4th tracheal rings, under cover of the skin and fascia in the median line of the neck, it is nearer the lower than the upper ends of the lobes which it connects.

The pyramidal lobe is an elongated slender process which frequantly springs. From upper border of isthmus on one of other side of the median plane.

Blood supply :

a) Arteries : this is a very vascular gland. at the apex of each lobe, the superior thyroid artery divides into two or three branches, the inferior thyroid artery sends its branches to basal part and deep surface of the lobe, the various arteries anastmose freely on the surface of the lobe.

b) Veins : three pairs of veins drain the venous network of the superfacial surface of the gland but the main tributaries emerge from its substance through its deep surface, the superior thyroid vein arises near the upper ends of the lobe, the middle thyroid vein is very short and arises near the lower end of the lobe, the inferior thyroid vein arises from the network on the isthmus.

Nerve supply :

It is supplied by branches from the cervical ganglia of the sympathetic trunk and from the cardiac and laryngeal branches of the vagus. **(Raomanes G.J. 1979)**.

Histology of the thyroid gland :

The thyroid gland is formed of two lobes connected to each other by the isthmus, the gland is formed of a connective tissue (C.T.) stroma and a parenchyma of endocrine cells.

The stroma : it includes

1. the capsule.
2. the trabeculae and
3. the reticular C.T.

1- The capsule : The thyroid has two capsules :

a) an outer capsule that is continuous with the pretracheal fascia.

b) the inner true capsule which is formed of C.T. cells and fibres. It is a fiberoelastic firmly adherent to the gland.

2- The trabeculae : they are very thin, formed of C.T. cells and fibres descending from the true capsule. and they carry the blood vessels, nerves and lymphatics.

3- Reticular C.T. : they form a fine network around the thyroid follicles which are surrounded by fenestrated blood vessels.

The parenchyma : it includes

1. Thyrod follicles.
2. Interfollicular tissue.

1. Thyroid follicles : they are the structural units of the thyroid gland, each follicle may be oval or rounded in shape, lined with simple cubical epithelium with a thin basement membrane, two types of cells are present in thyoid follicle :

a) the principle folliclar cells.

b) the parafollicular cells.

a) The principal follicular cells :

These constitute about 98% of the follicular epithelium, they are usually cuboidal but may change into columnar cells in hyperthyroidism or simple squamous in hypothyroidism, these cells lie on delicate basement membrane and their apical parts reach the follicular cavity, they have basophilic cytoplasm and central rounded nuclei, the cells are adherent to each other by functional complexes, the apical portions of the follicular cells have short irregular microvilli.

With electron microscope; they show elongated mitochondria with various shapes, Golgy apparatus is present between the nucleus and the luminal surface of the cell. Free ribosomes and many lysosomes are also present in the cytoplasm, these cells secrete thyriod hormone.

b) The parafollicular cells (C.Cells) :

They are present on the outer aspect of the thyroid follicles, they may be present in the follicular wall but don't reach the follicular cavity. They may be present also in the interfollicular C.T., they are larger and with paler cytoplasm than principal follicular cells.

The C-cells secretes thyrocalcitonin hormone which can lower blood calcium level, it is considered as antiparathyroid hormone.

2- Interfollicular tissue : in between the thyroid follicles there is a network of C.T., fenestrated blood capillaires, occasionally C-cells and interfollicular cells which are tangentially cut thyroid follicles. **(Worwick & Williams, 1973)**.

Phsiology of the thyroid gland :

The thyroid gland secretes thyroxine, 3,5,3,5, tetraiodothyronine (T4) and small amount of 3,5,3 tri-iodothyronine (T3). Iodine accounts for 65% of the weight of T4, since this relatively trace element in the earthys crust, mechanisms are present in the thyroid cells to allow it to concentrate and conserve idoine **(Reed Larsen P. 1982)**.

Iodine mechanism :

Extrathyroid compartment : The daily intake of iodine in man varies in different areas of the world, it ranges from extremly low levels (20) Ug to as high as 600 Ug per day in certain areas **(Reed Larsen P., 1982)**.

The ingested iodine is rapidly reduced to iodide in the upper intestine, and approximalely 90% is absorbed in the 1st 60 minutes (min.) after ingestion. Once iodide reaches the blood, it is distributed as an extracellular ion in a pool similar to the chloride space. The plasma concentration of iodine fluctuates between 0.1 and 0.5 Ug/dl. depending mostly on ingestion. Iodide leaves this compartment (plasma) throught thyriod uptake, and urinary excretion. A small amount of plasma iodide is concentrated by the salivary glands and gastric mucosa. This quantity soon enters the diagestive tract and re-cycled rather than lost **(John Harbert, 1986)**.

Under normal plasma concentration, the thyriod clearance of Iodide is 5 to 40 ml per min, in chronic iodine deficiency, thyroid clearance can increase to 100 ml per min, while with excess iodine, it may fall as low as 2 to 5 ml per min.

Thyroid Compartment :

Iodide trapped and organified by the thyroid gland is utilized in the synthesis of thyroid hormones. Iodide also is liberated by intrathyroidal deiodination of amino acids not utilized in hormone production.

Iodide trapping :

Iodide is trapped by means of high energy metabolic process known as the thyroid pump, which permits intracellular concentration 25 to 500 times plasma concentration depending on the thyroid functional state. The trapping mechanism depends on oxidative phosphorylation and is inhibited by anoxia, cyanides, dinitrophenal, and hypothermia, Iodide trapping can occur by several monovalent anions, including the halids e.g. Br., peroxy anions e.g. TCo4, Complex anions such as perchlorate and tetrafluoroborate.

Organification :

Once iodide has been incorporated into the cell, it is rapidly oxidized by enzymatic action. Iodide is oxidized to hypodide, the only form of iodide that can be utilized by the cells, soon after oxidation, idoine is complexed by tyrosine forming monoiodotyrosine (MIT) and diodotyrosine (DIT) which are bound to thyroglobuline. The organification of the iodine occur within the follicle lumen, it is stimulated by TSH and are blocked by thiourea. Thyroglobulin is a large glycoprotein, composed of 5000 amino acids and is stored in the follicular lumen.

Coupling :

Following organification, coupling of MIT and DIT occurs by intermolecular re arrangement or by inter molecular transfer to form T3 and T4. Most evidences suggest that the coupling occurs while tyrosine is bound to thyroglobulin is catalyzed by thyroid peroxidase (TPO), the coupling is stimlated by TSH.

Storage and release :

Microscopic section through the thyriod gland reveals the most prominent feature, the colloid-filled spherical sacs (acini), colloid consists mostly of thyroglobulin, the normal thyroid contains at least one month supply of hormone. The thyroglobulin doesn't enter the blood stream. The release of thyroid hormone is stimulated by TSH. Which act upon the thyriod cell membrane leading to activation of adenyl cyclase and prompt rise in cyclic adenosine monophosphate c(AMP), hydrolysis of thyroglobuin, and release of T3 and T4 they are bound to thyroid proteins, Thyroid Binding Globulin (TBG), Thyroid Binding PreAlbumin (TBPA), and Albumin Binding of T4 and TBG is strong 10 to 15 times as For T3. Binding to TBP is weak for both hormones **(John Harbert, 1986)**.