Thyroid Involvement In Different Rheumatic Diseases

Essay

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Physical medicine, Rheumatololgy and Rehabilitation

By

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بسم الله الرحمن الرحيم

وقُلِاعْمَلُوافَسَيَرَىاللَّهُعَمَلَكُمْورَسُولُهُوالْمُؤْمِنُونَ

صدق الله العظيم

سورةالتوبة آية (105)

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Ola Soliman Ahmed

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The List of Abbreviations

18F-FDG-PET: F18fluorodeoxyglucose -PET
ACPA : Anti-citrullinated peptide antibodies
AMA : Anti-microsomal Antibodies
ANA : Antinuclear antibodies
ANCA : Anti-neutrophil cytoplasmic antibodies
APL : Anti- phospholipid antibodies
APS : Anti- phospholipid Syndrome
ARF : Acute Rheumatic Fever
ARFI : Acoustic Radiation Force Impulse elastography
BMD : Bone Mineral Density
CASPAR : Classification Criteria for Psoriatic Arthritis
CD : Crohn's disease
CD4 : Cluster of Differentiation4
CD8 : Cluster of Differentiation 8
CRCD : Chronic Rheumatic Cardiac Disease
CRP : C-reactive Protein
CT : Computed Tomography
DAS28 : Disease Activity Score 28
DC : Dendritic Cells
DEMS : Dry Eye and Mouth Syndrome
DIP : Distal Interphalengial
DLco : Diffusing Capacity carbon monoxide
DM : Dermatomyocytis
dSSc : Diffuse cuteanos systemic seclerosis
ELISA : Enzyme-linked Immuno Sorbent Assay
ERK1/2 : Extracellular-signal-Regulated Kinases1/2
FM : Fibromyalgia
GCA : Giant Cell Arteritis
GFD : Glutine Free Diet
HLA-DR15: Humane Leukocytic Antigen-DR15
IBD : Inflammatory bowel disease
IGF-I : Insulin Growth Factor-1
IgG : Immunoglobulin G
IIM : *Idiopathic Inflammatory Myositis*

The List of Abbreviations (Cont.)

IL-2R : Interleukin -2 Receptor
IMA : Immuno-metric Assay
INF : Interferon
Issc : limited cutaneous systemic sclerosis
JIA : Juvenile Idiopathic Arthritis
LDL : Low density lipoproteins
LN : Lymph nodes
MCT8 : Monocarboxylate transporter 8
MMI : Methimazole
MOP (ANCA) : Myeloperoxidase ANCA
MRI : Magnetic Resonance Imaging
mRNA : Messenger Ribonucleic Acid
MSCT : Multi-slice CT
NHE : Na/H Exchanger
NIS : Na/I (sodium/Iodine) symporter
NK : Natural Killer
NO : Nitric Oxide
NSAIDs : Non-Steroidal Anti-Inflammatory Drugs
OATP14 : Organic-anion-transporting-polypeptide 14
OATP1c1: Organic-anion-transporting-polypeptide 1c1
OM : Overlap myositis
OP : Osteoporosis
PET : Positron Emission Tomography
PI3K : Phosphatidylinositol 3-kinase
PKC : Protein kinase C
PsA : Psoriatic Arthritis
pSS : Primary Sjogren Syndrome
PTU : Propylthiouracil
Q02 : O2 consumption
RA : Rheumatoid Arthritis
RHD : Rheumatic Heart Disease
RIA : Radio-immuno assay
RMS : Rheumatic Mitral Stenosis
RPM : Rheumatic Polymyalgia

The List of Abbreviations (Cont.)

s-IBM : Sporadic inclusion body myositis
SLE : Systemic lupus erythematosus
SPECT : Single-Photon Emission Computed Tomography
SS : Sjogren Syndrome
SSc : Systemic Seclerosis
T4 : Thyroxin T3: Triiodothyronin
TBAb : Thyroid Blocking Antibodies
TBG : Thyroid Biding Globulin
Tg : Thyroglobulin
TgAb : Thyroglobulin Autoantibodies
TH : Thyroid hormone
Th1 : T helper1 lymphocyte
THBR : Thyroid Hormone Biding Ratio
TNFR-1 : Tumor Necrosis Factor Receptor-1
TNF-α : Tumor Necrosis Factor-α
TPoAb : Thyroid Peroxidase Autoantibodies
TRAb : TSH Receptor Autoantibodies
TREs : TH response elements
TRH : Thyrotropin-Releasing Hormone
TRIAC : Triiodo-thyroaceticacid (natural thyroid hormone analogue)
TRMRA : Time-Resolved MR Angiography
TRs : Thyroid Receptors (isoformsTRα1, α2, -β1, -β2, and -β3)
TSAb : Thyroid Stimulating Antibodies
TSH : Thyroid stimulating hormone
TSHR : Thyroid-stimulating Hormone Receptor
TSHrAb : Thyrotropin receptor Antibodies
tTG.IgA : tissue TransGlutaminase Immunoglobuline A
UC : Ulcerative Colitis
US : Ultrasonography

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Introduction

Familial autoimmunity is a frequently seen condition. Further study of familial autoimmunity will help to decipher the common mechanisms of autoimmunity (**Cardenas-Roldan et al., 2013).**

Coincidence of autoimmune disorders is well known, as reported by **Magrey et al., (2013**) Fibromyalgia syndrome-associated pain and fatigue are significantly more frequent in patients with Poriatic arthritis (PsA) compared to controls.

Autoimmune thyroid disease (AITD) is a term used to bring together a group of pathologies that has thyroid dysfunction and an autoimmune response against this endocrine organ as its hallmark (**Eschler et al., 2011**).

As organ specific autoimmune diseases, (AITD) is a group of pathologies exhibits an autoantibody profile that may be composed of:

(1) Antibodies directed against the thyroperoxidase enzyme (TPOAb).
(2) Antibodies directed against thyroglobulin protein (TgAb).
(3) Antibodies directed against thyrotropin receptor (TSHrAb).

In this last case, the antibodies can either block or enhance the receptor's activity. Furthermore, there is a T or B lymphocytic response that prevails and, ultimately, this will define the pathology that becomes manifest. Generally, T

lymphocytes are the main cell type infiltrating the gland in Hashimoto's thyroiditis while a B response predominates and determines the presence of Grave's disease (**Shin et al., 2009**).

An organ-specific and non-specific polyclonal immune response is likely to exist in patients with AITD (**Atzeni et al., 2008**).

Patients with autoimmune thyroid disorders, more often Hashimoto's thyroiditis and also Graves' disease, often have rheumatic manifestations including a mild non-erosive variety of arthritis, polyarthralgia (multiple joints affected), myalgia (muscle pain), and sicca syndrome without a true Sjogren's syndrome (**Moor, 2009**).

Tagoe et al., (2013) concluded that Rheumatic manifestations frequently occur in patients with chronic lymphocytic thyroiditis (CLT) in the absence of overt thyroid dysfunction and mimic the presentation of the well-defined connective tissue diseases.

Regarding pathogenesis, the following hypotheses have been raised: participation of autoantibodies; overlapping of AITD and some AIDs; and systemic inflammatory reaction associated with thyroiditis. Most findings are limited to the occurrence of anti-thyroid antibodies and subclinical alterations (**Robazzi and Adan, 2012**).

Aim of The Work

In this study we aim to review thyroid gland abnormality in different rheumatic diseases in order to detect the impact of thyroid disease on the rheumatic disease morbidity, clinical course and management.

Anatomy and physiology of thyroid gland

1) Thyroid Gland Anatomy :

Thyroid gland is a butterfly-shaped organ and is composed of two cone-like lobes or wings, lobusdexter (right lobe) and lobus sinister (left lobe), connected via the isthmus. The organ is situated on the anterior side of the neck, lying against and around the larynx and trachea, reaching posteriorly the oesophagus and carotid sheath. It starts cranially at the oblique line on the thyroid cartilage (just below the laryngeal prominence, or 'Adam's Apple'), and extends inferiorly to approximately the fifth or sixth tracheal ring. It is difficult to demarcate the gland's upper and lower border with vertebral levels because it moves during swallowing (**YalçinandOzan, 2006).**

The thyroid gland is covered by a fibrous sheath, the capsulaglandulaethyroidea, composed of an internal and external layer. The external layer is anteriorly continuous with the lamina pretrachealis fasciae cervicalis and posterolaterally continuous with the carotid sheath. The gland is covered anteriorly with infrahyoid muscles and laterally with the sternocleidomastoid muscle (figre-1).

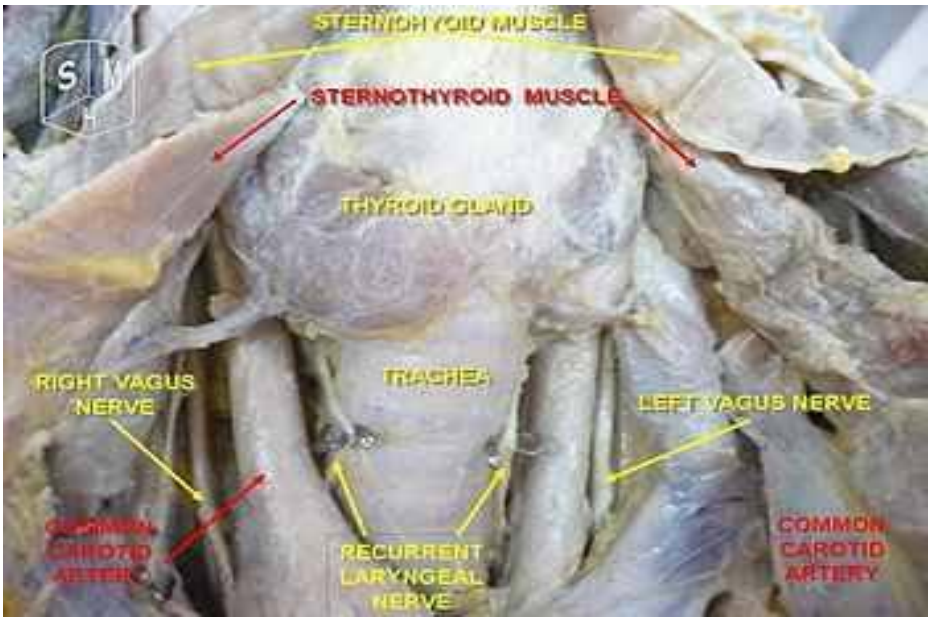

Figure (1): Relations of thyroid gland (**Wikimedia commons, 2011)**

On the posterior side, the gland is fixed to the cricoid and tracheal cartilage and cricopharyngeus muscle by a thickening of the fascia to form the posterior suspensory ligament of Berry.The thyroid gland's firm attachment to the underlying trachea is the reason behind its movement with swallowing **(Kamath, 2010).**

Between the two layers of the capsule and on the posterior side of the lobes, there are two parathyroid glandson each side.The thyroid isthmus is variable in presence and size, can change shape and size, and can encompass a cranially extending pyramid lobe, remnant of the thyroglossal duct. The thyroid is one of the larger endocrine glands, weighing 2-3

grams in neonates and 18-60 grams in adults, and is increased in pregnancy (**Lemaire and David, 2005**).

Blood supply of thyroid:

The thyroid is supplied with arterial blood from the superior thyroid artery, a branch of the external carotid artery, and the inferior thyroid artery, a branch of the thyrocervical trunk, and sometimes by the thyroid ima artery, branching directly from the brachiocephalic trunk.

Embryological development:

In the fetus at 3–4 weeks of gestation, the thyroid gland appears as an epithelial proliferation in the floor of the pharynx at the base of the tongue between the tuberculumimpar and the copula linguae at a point later indicated by the foramen cecum. The thyroid then descends in front of the pharyngeal gut as a bilobed diverticulum through the thyroglossal duct. Over the next few weeks, it migrates to the base of the neck, passing anterior to the hyoid bone. During migration, the thyroid remains connected to the tongue by a narrow canal, the thyroglossalduct (**Eugster and Pescovitz, 2004**).

Thyrotropin-releasing hormone (TRH) and thyroid-stimulating hormone (TSH) start being secreted from the fetal hypothalamus and pituitary at 18-20 weeks of gestation, and

fetal production of thyroxine (T4) reach a clinically significant level at 18–20 weeks. Fetal triiodothyronine (T3) remains low (less than 15 ng/dL) until 30 weeks of gestation, and increases to 50 ng/dL at term. Fetal self-sufficiency of thyroid hormones protects the fetus against brain development abnormalities caused by maternal hypothyroidism (**Zoeller, 2003**).

The portion of the thyroid containing the parafollicular C cells, those responsible for the production of calcitonin, are derived from the neural crest. This is first seen as the ultimobranchial body, which joins the primordial thyroid gland during its descent to its final location in the anterior neck **(Berbel et al., 2010).**

2) Physiology:

Action of Thyroid Hormones:

Thyroid hormones (TH) are required for the normal function of most tissues of the body, playing essential roles in growth, development, differentiation, and metabolism, with major effects on 02 consumption (Q02) and metabolic rate **(Videla, 2000).**

At least six major steps are required for secreted thyroid hormone (TH) to exert its action on target tissues **(Refetoff and Dumitrescu, 2007).**