Inflammatory myopathy:clinicalvaraiant and therapeutic interventions

Athesis by

Mohamed nasreldin Mahmoud ismail

M.B.B.CH.

Faculty of medicine -Ain shams university

Prof.Taha kamel alloush

Professor of neurology

Faculty of Medicine- Ain Shams University

Prof.Nagia Ali Fahmy

Professor of neurology

Faculty of Medicine – Ain Shams University

Prof.Dalia Fayez Mohamed

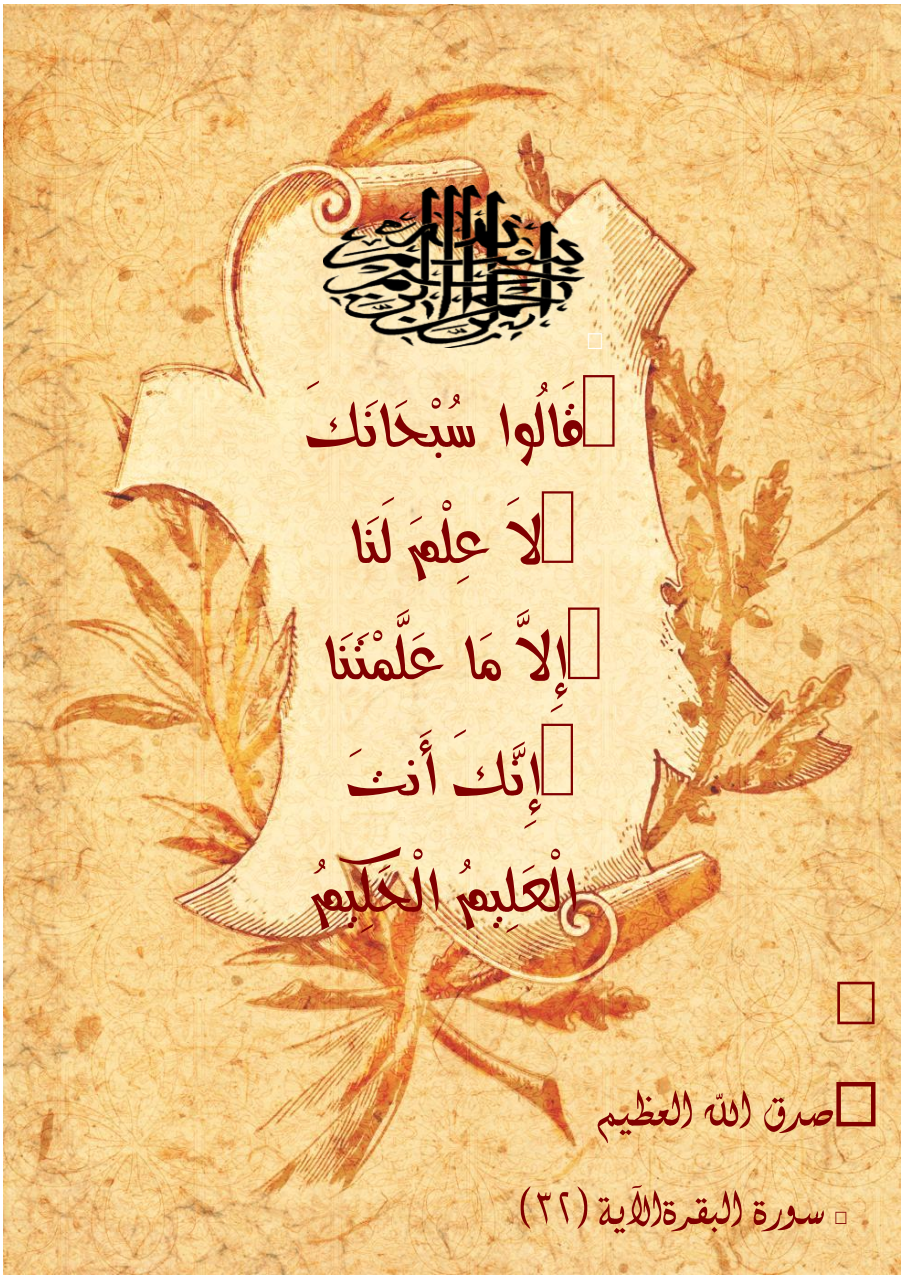
Professor of Internal Medicine and Rheumatology

Faculty of Medicine-Ain Shams University

Faculty of Medicine

Ain Shams University

2017


قَالُوا سُبْحَانَكَ
لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا
إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ
صدق الله العظيم
سورة البقرة الآية (٣٢)

Contents

List of tables

List of Abbreviations

ADM
amyopathic dermatomyositis
ALT
alanine aminotransferase
AST
aspartate aminotransferase
ATP
adenosine triphosphate
ATPase
adenosine triphosphatase
AZA
Azathioprine

CD
cluster of differentiation
CK
creatine kinase
COX
cytochrome oxidase
DC
dendritic cell
DM
dermatomyositis
EMG
electromyography
ENMC
European Neuromuscular Center
GGT
γ-glutamyltranspeptidase
H&E
hematoxylin and eosin
HIF-1α
hypoxia-inducible factor-1α
HLA
human leukocyte antigen

HMGCR
high-mobility group protein 1
3-hydroxy-3-methylglutaryl-coenzyme A reductase
IFN
interferon
IIM
idiopathic inflammatory myopathy
IL
interleukin
ILD
interstitial lung disease
IMNM
immune-mediated necrotizing myopathy
IVIg
intravenous immunoglobulin

JDM
juvenile dermatomyositis
MAA
myositis-associated autoantibody
MAC
Membrane attack complex
MDA5
melanoma differentiation
MHC
major histocompatibility complex
MSA
myositis-specific autoantibody
MUAP
motor unit action potential
MxA
myxovirus resistance protein A
RNAD-TR
reduced nicotinamide adenine dinucleotide
NF-κB
nuclear factor
NT5C1A
cytosolic 5-nucleotidase 1A

PAS
periodic acid
PDC
plasmacytoid dendritic cell
PM
polymyositis
SDH
succinate dehydrogenase
sIBM
sporadic inclusion-body myositis
snRNP
small nuclear ribonucleoprotein
SRP
signal recognition particle
STIR
short-tau inversion recovery
SUMO-1
small ubiquitinlike modifier
TGF-β
tumor growth factor-beta
TIF
transcriptional intermediary factor
TNF
tumor necrosis factor
Treg
T regulatory

Introduction

Inflammatory myopathy is a group of acquired muscle disease that include dermatomyositis and inclusion body myositis (Joushua et al , 2011).

Manifestations other than those involving skeletal muscles are very common including cardiac involvement and pulmonary involvement . Interstitial lung disease is a recognized complication for a long time that may be the most common (Marie et al , 2005) .

Although the overall incidence of inflammatory myopathies ranges from 6 to 10 per 1,000,000 population , the incidence of anti-jo-1 positivity ranges from 1.2 to 2.5 per million , with a reported prevalence of 1.5 per 100,000population . In one study of anti-jo-1-positive patients , Interstitial lung disease was found to be more severe in African – Americans than in whites . There is an association between certain HLAS and polymyositis , among anti-jo-1 positive patients ,91 % are positive for HLA-DR3 and 80% are positive for HLA-DQ2 (Mileti et al , 2009).

There are two types of autoantibodies detected in the sera of polymyositis and dermatomyositis patients . They include myositis associated and myositis specific antibodies (Targof and Reichilin 1985).

Myositis specific antibodies include antibodies directed against component of a nucleosome remodeling complex (anti mi 2), macromolecular complex involved in RNA degradation and processing (anti pm/scl), ribonucleoprotein

involved in protein synthesis (anti aminoacyl TRNA synthetase antibodies) and ribonucleoprotein involved in translational transport (antisignal recognition particles) (Mahler et al , 2005).

Antisynthetase syndrome recently described in both polymyositis and dermatomyositis patients consists of presence of the antisynthetase antibodies , interstitial pneumonia , myositis and other features including fever , arthlagia and raunauds phenomenon (Joushua et al , 2011).

Autoantibodies are antibodies directed against the cytoplasmic antisynthetase enzymes , there are multiple subtypes and the most common is aminoacyl –TRNA autoantibodies that are found in 20% of idiopathic inflammatory myositis patients (Mimori et al , 2007).

Inaddition , patients can have dermatomyositis skin lesions such gottron papule and heliotrope rash (Matsushita et al , 2007).

Prevalence of interstitial pneumonia in antisynthetase syndrome is as high as 95% (Yoshifuji et al , 2006) .

The sera of 5 % of inflammatory myositis patients are positive for signal recognition particle autoantibodies , such patients are positive for signal recognition paticles autoantibodies .Those patients may have significantly elevated muscle enzymes , dysphagia refractory to standard treatment , as well as cardiac involvement (Miller et al , 2002).

Antimi 2 are found in 20% of dermatomyositis patients and 9 % of myositis patients overall (Targoff and Reichilin 1989).

Such patients may have milder muscle involvement and lower risk of interstitial pneumonia (Miller et al , 2002).

Myositis associated autoantibodies are many types and they include anti –u-1-rnp , anti-u3-rnp , anti-pm-scl (Harsha et al , 2009).

Anti-u1-rnp autobodies occur in patients with mixed connective tissue disease , systemic sclerosis , systemic lupus erythematosis and other ill defined connective tissue diseases , yet immunoglobulin M (IGM) anti-u1 rnp antibodies occur predominantly in patients with systemic lupus erythematosis (Vlachoyainnopoulos et al , 1996).

Aim of the work

1-Describe various clinical variant of inflammatory myopathy patients referred to ain shams university hospital .

2-To measure different autoantibodies in different types of inflammatory myopathy .

3-To diagnose patients with antisynthetase syndrome and their response to various therapeutic interventions.

Epidemiology&Clinical variant of Inflammatory myopathy

The idiopathic inflammatory myopathies are a group of muscle disease characterized by chronic inflammation and weakness of skeletal muscles (Dalakas ,Hohfeld , 2003) .

Idiopathic inflammatory myopathies are classified into polymyositis and dermatomyositis and inclusion body myositis ,Idiopathic inflammatory myopathy subtypes differ from each other in clinical , laboratory, histopathology , prognosis and response to treatment (Dalakas , Hohfeld , 2003).

Each syndrome of the previously mentioned syndromes is associated with different autoantibodies (*Dimachkie , Barohn* ,2013)10.

Epidemiology:

There are multiple studies revealed that incidence rates of Idiopathic inflammatory myopathy patients vary between 4.27 and 7.89 per 100,000 person and prevalence rates range from 9.54 and 32.74 per 100,000 individual (*Furst et all, 2012*) .

Dermatomyositis and polymyositis occur more in women and african american , also Dermatomyositis affects both

children and adult equally , but polymyositis affect mainly adult persons (*Amato And Barohn , 2009).*

There is also another study revealed that incidence ofIdiopathic inflammatory myopathies ranges from 0.5-8.4 cases per milion population in the united states of america. The same study revealed that Polymyositis is more common within the black population , it was estimated that polymyositis is 5 times more common black patients and dermatomyositis is 3 times more common in black patients , Yet polymyositis is less common among japanese (Ramesh et al, 2016).

Polymyositis and dermatomyositis are twice more common in women , while inclusion body myositis is twice more common in men (Ramesh et al, 2016).

Polymyositis usually affects adultbetween 45-60 years.

The age of onset of polymyositis with another collagen vascular disease is related to the associated condition (Ramesh et al ,2016).

Dermatomyositis is primarily a disease of adults but it could also be seen in children usually those between 5 - 14 years. Inclusion body myositis occur commonly in patients older than 50 years (Ramesh et al ,2016).

risk factors:

Myositis has been associated with haplotypes A1,B8 and DR3 which also increase the risk of autoimmune disease (Ramesh et al, 2016).

There is alot of Enviromental agents that increase the risk for myositis and these include coxsachevirus B1 , Hiv , HTLV-1, Hepatitis B , Influenza , Echovirus and adenovirus (Ramesh et al, 2016) .

.Many drugs may cause myopathy such as hydroxychloroquine and colchicine , these drugs mostly cause myositis through immune mediated mechanism as muscle biobsy from these patients showed evidence of chronic inflammatory changes. these drugs include D-penicillamine , angiotensin converting enzyme inhibitor and statin (Ramesh et al, 2016).

Clinical features :

Dermatomyositis and polymyositis are characterized mainly by progressive symmetric proximal muscle weakness that develop over weeks to months , yet no sensory loss or ptosis with sparing of extraocular muscles , however , distal muscle weakness may occur early in inclusion body myositis (*Griggs et al ,1995).*

Deep tendon reflexes are normal except in severely weakened muscles such as respiratory and trunk muscles. *(Slobodin et al ,2005)* .

Respiratory muscle weakness may occur necessitating the need for assisted ventilation *(Marie et al ,2001)* .

Pharyngeal muscle weakness may occur in advanced cases of idiopathic inflammatory myositis causing dysphagia , nasal speech , hoarseness of voice and nasal regurgitation of food (*Ebert , 2010).*

Idiopathic inflammatory myositis mimic anumber of diseases in clinical picture including limb girdle dystrophy and fascioscapulohumeral dystrophy , metabolic , mitochondrial , endocrine and drug induced myopathy *(Greenberg , 2008).*

The presence of certain physical signs such as waddling gait , extraocular muscle weakness , scapular winging and calf hypertrophy should raise the suspicion of another aetiology (Greenberg , 2008) .

Polymyositis:

The differential diagnosis of polymyositis is very wide and includes inclusion body myositis, dermatomyositis , overlap syndrome associated with aconnective tissue