Autoinflammatory Periodic Fever Syndromes in Children

Essay

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By

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متلازمات الحمى الدورية ذاتية الالتهاب في الأطفال

رسالة
للحصول علي درجه الماجستير في طبالاطفال

مقدمه من
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✍*Ahmed Mohammed Hassan Al-brahmy*

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List of ABBREVIATION

ASC	**apoptotic speck protein**
BBD	B-box domain
BS	Blau syndrome
CAPS	Cryopyrin-associated periodic syndromes
CARD15	Caspase recruitment domain-containing protein 15
CARDs	Caspase activation and recruitment domains
CCD	Coiled-coil domain
CD2BP1	CD2 binding protein 1
CINCA	Chronic Infantile Neurological Cutaneous and Articular syndrome
CRDs	Cysteine-rich domains
CRP	C-reactive protein
ELE	Erysipelas-like erythema
ER	Endoplasmic reticulum
FCAS	Familial Cold Autoinflammatory Syndrome
FMF	Familial Mediterranean Fever
HIDS	Hyperimmunoglobulin D Syndrome
HSP	Henoch-Schonleinpurpura
IFN-α	Interferon alpha
Il-1RA	Interleukin-1 receptor Antagonist
IL1RN	Interleukin 1 receptor antagonist gene
IL-1β	Interleukin-1beta
JRA	Juvenile rheumatoid arthritis
MCP	Metacarpophalangeal
MEFV gene	Mediterranean Fever gene
MIM	Mendelian inheritance in man
MKD	Mevalonate Kinase Deficiency
MTP	Metatarsophalangeal
MVA	Mevalonicaciduria

MVK	Mevalonate kinase
MWS	Muckle-Wells Syndrome
NF-κB	nuclear factor kappa-light-chain-enhancer of activated B cells
NLRP3	NACHT, LRR and PYD domains-containing protein 3
NOD2	Nucleotide-binding oligomerization domain-containing protein 2
NOD-LRR	Nucleotide-binding oligomerization domain-leucine rich repeat
NOMID	Neonatal Onset Multisystem Inflammatory Disease
NSAIDs	Non steroidal anti-inflammatory drugs
PAMPs	Pathogen-associated molecular patterns
PAN	Polyarteritisnodosa
PAPA	Pyogenic arthritis, pyodermagangrenosum and acne
PCR	Polymerase chain reaction
PFAPA	Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Cervical Adenitis
PFMS	Protracted febrile myalgia syndrome
PFSs	Periodic fever syndromes
PGE2	Prostaglandin E2
PRRs	Pattern recognition receptors
PSTPIP	Proline, serine, threonine, phosphatase interactive protein
PSTPIP1	Proline-serine-threonine phosphatase interacting protein 1
PYD	Pyrin domain
SAA	Serum amyloid A
SAA	Serum amyloid A
sTNFR1	Soluble type 1 Tumor-Necrosis-Factor receptor
TLRs	Toll-like receptors

TNF	Tumor-Necrosis-Factor
TNFR1	Type 1 TNF receptor
TNFRSF1A	TNF receptor superfamily 1A
TRAPS	Tumor necrosis factor receptor-associated periodic syndrome
UPR	Unfolded protein response

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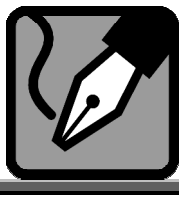

INTRODUCTION

Introduction

Periodic fever syndromes (PFSs) present with recurrent or fluctuating degrees of inflammatory symptoms, fever and an acute phase response. They mainly occur in the absence of infection or autoimmune reaction. Although the name suggests otherwise, the inflammatory attacks occur without intrinsic periodicity, usually at irregular intervals and therefore the name recurrent is to be preferred over periodic ***(Majeed, 2000).***

Hereditary periodic fever syndromes differ from autoimmune diseases in the absence of high levels of autoantibodies and autoreactive T cells. Disturbances in the innate immune response seem to be central to their pathogenesis, and usually no clear cause for an individual inflammatory attack can be identified. Therefore the name autoinflammatorysyndromes has become widely used for these rare disorders ***(Padeh, 2005).***

The innate immune system provides the first immunologic line of defense against many microbes and uses pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs) to recognize a limited number of widely expressed viral and bacterial molecular structures known as pathogen-associatedmolecular patterns (PAMPs). These pattern recognition receptors stimulate inflammation by activating intracellular proteins (also known as intracellular sensors), which mediate the regulation of nuclear factor-κB (NF-κB), cell apoptosis, and interleukin-1β (IL-1β) through cross-regulated and common signaling pathways. Mutations in these intracellular proteins lead to increased production and secretion of IL-1β, resulting in clinical signs and symptoms***(Gedalia, 2011).***

PFSs include: familial Mediterranean fever (FMF), tumour necrosis factor receptor-associated periodic syndrome (TRAPS), mevalonate kinase deficiency [MKD – previously known as hyperimmunoglobulin D (HIDS)], blau syndrome, deficiency of the interleukin (IL)-1-receptor antagonist (DIRA), pyogenic arthritis, pyodermagangrenosum and acne syndrome (PAPA syndrome), diseases of uncertain genetic aetiology including periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis (PFAPA) syndrome, the cryopyrin-associated periodic syndromes (CAPS) which include: familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disease (NOMID) [also called chronic infantile neurological cutaneous and articular syndrome (CINCA)]***(Lachmann, 2011).***

All these iseases are characterized by recurrent flares of systemic inflammation, presenting sudden fever episodes associated with elevation of acute phase reactants and with a number of clinical manifestations that might include inflammation of serosal surfaces and joints, skin rashes of unknown origin, lymphadenopathy, arthritis, as well as the involvement of other organs such as muscles and the central nervous system. Rheumatic manifestations are extremely common and highly variable in their presentation and course in PFSs***(Touitou&Koné-Paut, 2008).***

Aim of the work

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The aim of this work is to provide an up-to-date overview of periodic autoinflammatoryfever syndromes in children and their management.

Review of literature