Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection (PANDAS) – Review

An Essay
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In Neuropsychiatry
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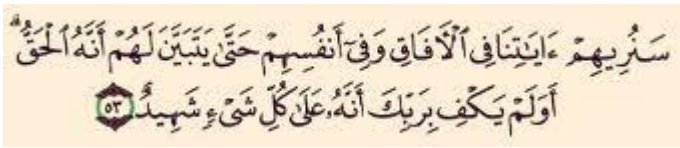
بسم اللہ الرحمن الرحیم


سَنُرِيهِمْ ءَايَٰتِنَا فِى ٱلْءَافَاقِ وَفِىٓ أَنفُسِهِمْ حَتَّىٰ يَتَبَيَّنَ لَهُمْ أَنَّهُ ٱلْحَقُّ ۗ
أَوَلَمْ يَكْفِ بِرَبِّكَ أَنَّهُۥ عَلَىٰ كُلِّ شَىْءٍ شَهِيدٌ ﴿٥٣﴾

فصلت - ۵۳

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Contents

List of Abbreviations

ABGA : Anti-Basal Ganglia Antibody

ADEM : Acute Disseminated Encephalo-Myelitis

ADHD : Attention Deficit Hyperactivity Disorder

AN : Anorexia Nervosa

ANA : Anti-Nuclear Antibody

ANCAs : Anti-Neutrophil Cytoplasmic Antibodies

ANNA-1 : Anti-Neuronal Nuclear Antibodies type-1

Anti-LKM : Anti-Liver-Kidney Microsome antibodies

Anti-RNP : Anti- Ribo-Nucleo-Protein antibodies

Anti-TPO : Anti-Thyroid Peroxidase antibodies

ASO : Anti-Streptolysin O

ASOT : Anti-Streptolysin O Test

CaM : Calcium-calmodulin dependent protein

CBT : Cognitive Behavioral Therapy

CMV : Cyto-Megalo Virus

CNS : Central Nervous System

CT : Computed Tomography

CY-BOCS : Children's Yale-Brown Obsessive Compulsive Scale

DNA : Deoxyribo-Nucleic Acid

DSM-III-R : Diagnostic & Statistical Manual of Mental Disorders–3rd Edition – Revised

DSM-IV : Diagnostic & Statistical Manual of Mental Disorders–4th Edition

EBV : Epstein - Barr Virus

ECG : Electro-Cardio-Graphy

ED : Eating Disorder

ELISA : Enzyme-Linked Immuno-Sorbent Assay

FDA : Food and Drug Administration

fMRI : Functional Magnetic Resonance Imaging

GABHS : Group A Beta-Hemolytic Streptococci

HBV : Hepatitis B Virus

HCV : Hepatitis C Virus

HIV : Human Immunodeficiency Virus

HLA : Human Leukocyte Antigen

HSV : Herpes Simplex Virus

HTLV : Human T-Lymphotropic Virus

HV : Healthy Volunteer

IFA : Immuno-Flourescent Assay

IVIG : Intra-Venous Immuno-Globulin

MDD : Major Depressive Disorder

MINI- Kid test: Mini International Neuropsychiatric Interview for children and adolescents

MRI : Magnetic Resonance Imaging

NIMH : National Institute of Mental Health

OCD : Obsessive-Compulsive Disorder

ODD : Oppositional Defiant Disorder

OSAS : Obstructive Sleep Apnoea Syndrome

PANDAS : Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection

PCR : Polymerase Chain Reaction

PET : Positron Emission Tomography

PITANDs : Pediatric Infection-Triggered Autoimmune Neuropsychiatric Disorders

RA : Rheumatic Arthritis

RF : Rheumatic Fever

RHD : Rheumatic Heart Disease

RT : Response Time

SC : Sydenham Chorea

SSRI : Selective Serotonin Reuptake Inhibitors

TD : Tic Disorder

TS : Tourette Syndrome

URI's : Upper Respiratory tract Infections

VH : Virus Herpes

VSG : Variant Surface Glygoprotein

Introduction

Introduction

Streptococcal infection in children is usually benign and self-limited. However, in a small percentage of children, prominent neurologic and/or psychiatric sequelae can occur **(Pavone et al., 2006)**. Previous studies suggested a link between Group A Beta-Hemolytic Streptococcal (GABHS) infections and the onset or worsening of pediatric Obsessive-Compulsive Disorder (OCD), Tourette Syndrome (TS), and tic disorder **(Douglas et al., 2008)**.

PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection) is a well-defined syndrome in which tics (motor and/or vocal) and/or OCD consistently exacerbate in temporal correlation to a GABHS infection **(Pavone et al., 2006)**.

The central hypothesis of PANDAS derives from the observations of neurobehavioral disturbance accompanying Sydenham chorea (SC) [the best defined, best recognized and most common neurological sequel of GABHS infection, and the neurological manifestation of Rheumatic Fever **(Segarra and Murphy, 2008)**]. Many studies associate SC with OCD as a result of basal ganglia autoimmune inflammation **(Boileau, 2011)**. An immune response to GABHS infections purportedly leads to cross reactivity with, and inflammation of, basal ganglia, with a distinct neurobehavioral syndrome that includes OCD, tics, and perhaps hyperactivity **(AACAP Official Action**, **2012**).

Karla and Swedo, 2009 examined the role of neuro-immune dysfunction in pediatric OCD. As stated, antibody formation may trigger an inflammatory reaction in the basal ganglia following GABHS, as well as possibly other micro-organisms such as viruses, borrelia, and mycoplasma.

Much behavioral overlap exists between SC and PANDAS. It is the absence of chorea and carditis that primarily differentiates PANDAS from SC. Evidence of cardiac abnormalities in patients believed to have PANDAS would suggest that the SC was missed. Nonetheless, some

clinicians may be faced with uncertainty as to how best to evaluate these children to ensure that RF is not missed **(Segarra and Murphy, 2008)**.

A common clinical picture of PANDAS is TS, which is a neuro-developmental disorder of childhood that is often associated with various psychiatric morbidities and can significantly impact psychosocial functioning. These morbidities may be a major source of disability, and may determine ultimate prognosis, although most children will experience significant improvement or resolution of symptoms by adulthood. Additional management considerations must be made in those with TS symptoms persisting into adulthood. The mainstay of therapy remains dopamine receptor blocking drugs, but new therapies are emerging **(Joohi Jimenez-Shahed, 2009)**.

Preliminary results suggest that the PANDAS spectrum might be enlarged to include Attention Deficit/Hyperactivity Disorder (ADHD). Although a number of immunological biomarkers have been proposed as markers of PANDAS variant, at present, none of these has been conclusively proved useful to diagnose and monitor disease course in children with a suspicion of PANDAS **(David et al., 2009)**.

Finally, diagnosis and treatment of the PANDAS variant of TS and OCD are still controversial issues. Despite their empirical use in community settings, we still lack conclusive, evidence-based data regarding the usefulness of antibiotic and immunomodulatory treatments in children with PANDAS. Given the relevance of this topic for general pediatric health, additional research efforts to solve all the pending issues and the hottest points of debate are warranted **(David et al., 2009)**.

RATIONALE OF THE SYUDY

PANDAS is a well-defined syndrome among children, proven by several studies, to be linked to streptococcal infection. It is worth to highlight such disorder, its clinical picture, assessment, management and the possible prevention.

HYPOTHESIS

Although PANDAS is a well-defined syndrome, yet it is still underestimated in Egypt, and efforts are needed to be done to draw the attention of both psychiatrists and pediatricians to the importance and prevalence of such a syndrome.

AIM OF THE WORK

1. To review previous epidemiological studies of PANDAS, as well as the diagnosing criteria, assessment techniques and treatment.

2. To highlight the updates in the understanding of the disorder.

METHODOLOGY

In order to fulfill the aim of the work, a review of literature on PANDAS, in addition to all available Egyptian studies on PANDAS will be done. Computerized literature searches will be conducted under the key words “PANDAS”, “Tourette disorder” and “OCD”, and the database in all the available data sources will be explored.