The Diagnostic Value of Antiribosomal P Antibodies in the Detection of Cerebral Lupus in Childhood

Thesis

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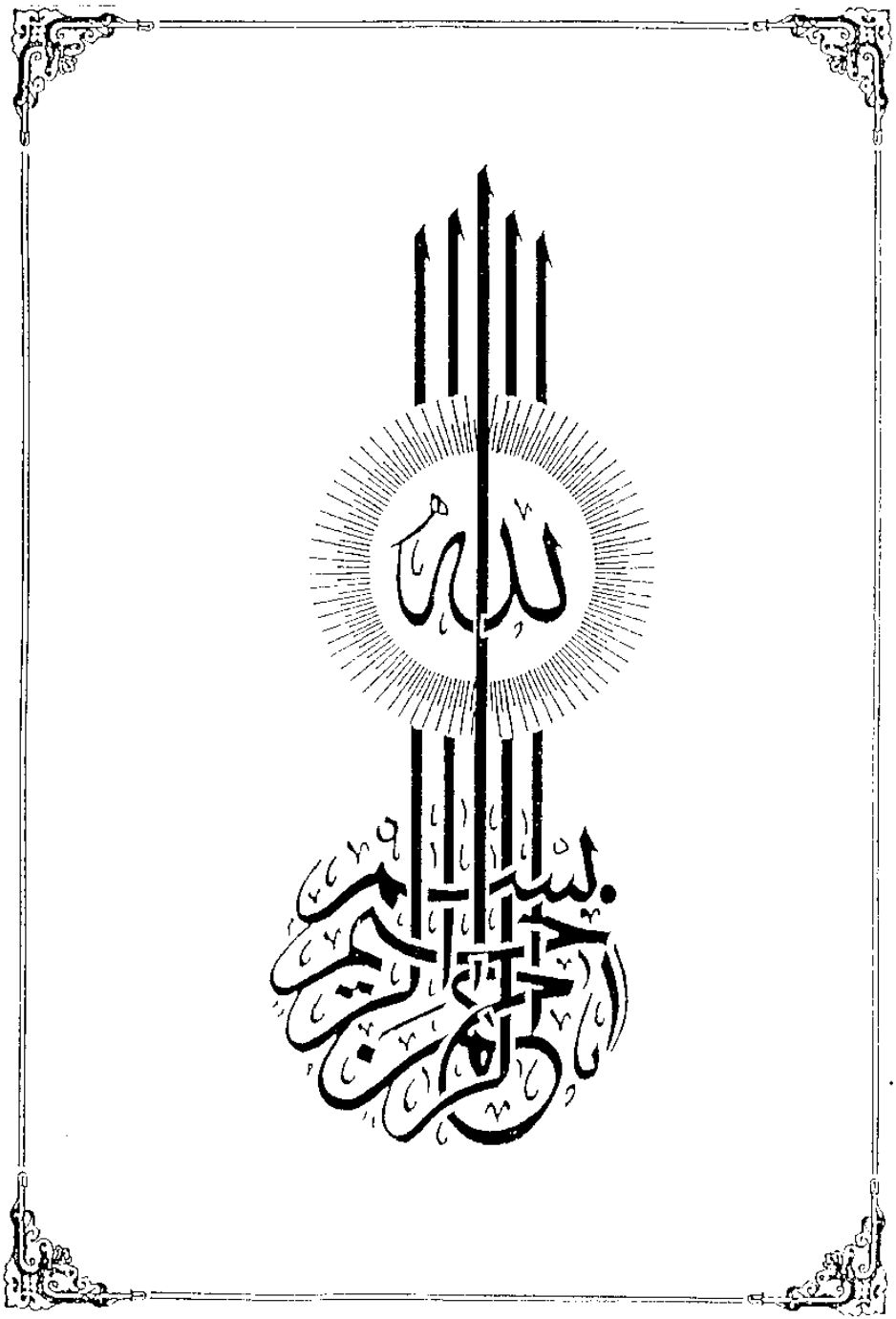

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LIST OF ABBREVIATIONS

ACR	American College of Rheumatism
ANA	Anti-nuclear antibody
Anti-DNP	Anti-deoxyribonucleic protein
Anti-RNP	Anti-ribonucleic protein
Anti-RP	Anti-ribosomal P
APF	Anti-perinuclear factors
ARA	Anti-ribosomal antibody
CBC	Complete blood count
CNS	Central nervous system
DNA	Deoxyribonucleic acid
ELISA	Enzyme-linked immunosorbant assay
ESR	Erythrocyte sedimentation rate
HLA	Human leucocytic antigen
Ig	Immunoglobulin
LE	Lupus erythematosus
MCTD	Mixed connective tissue disease
MHC	Major histocompatibility complex
n-DNA	Native deoxyribonucleic acid
NP	Neuro-psychiatric
NS-	Non-significant
NSAID	Non-steroidal anti-inflammatory drug
RA	Rheumatoid arthritis
RF	Rheumatoid factor
RNA	Ribonucleic acid
SD	Standard deviation
SLE	Systemic lupus erythematosus
Sm	Smooth muscle
SPECT	Single photon emission computed tomography
VLA	Very late activity

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INTRODUCTION

Connective tissue diseases affect almost all systems of the body and lead to a high frequency of morbidity and mortality. Neurological manifestations may develop as a consequence of the general pathogenesis of the disease or secondary to complications affecting other systems during the course of the disease *(West et al., 1995)*. Neurological lesions due to ischemia and occlusion of the arterial supply of the nervous system in the form of infarction, transient ischemic attacks and ischemia of the peripheral nervous system have been reported to occur in vasculitis associated with autoimmune diseases *(Belmont et al., 1994)*.

Manifestations of cerebral involvement may occur in up to 70% of all patients with SLE at some time during their disease course, depending on the criteria one uses to diagnose this complication of SLE. A wide variety of symptoms ranging from global cerebral dysfunction to focal abnormalities has been attributed to cerebral lupus *(Nossent et al., 1991)*, but the pathophysiologic mechanisms involved are still undetermined *(West et al., 1995)*.

Psychiatric features are a common CNS manifestation and may present as behavioural abnormalities including affective disorders and psychosis. The diagnosis of lupus psychosis often may be difficult and other processes including metabolic encephalopathy, steroid–induced psychosis or infection must be excluded *(Kovacs et al., 1993)*.

It has been reported that adult patients with SLE demonstrate an association between anti–RP antibodies and

CNS involvement. These antibodies were found to increase in titer in SLE patients with active disease and were detected more frequently in patients with severe behavioural disturbances specially those with affective disorders *(Arnett et al., 1996)*.

AIM OF THE WORK

The purpose of this study is to assess the value of anti RP antibodies as a diagnostic marker for cerebral affection in sera of children with SLE and to correlate the level of these antibodies with the severity of the disease.

Review of Literature

I. HISTORICAL ASPECT AND DEFINITION

The term "lupus", derived from the Latin word for "wolf", was originally used in medicine from the 13th to the 19th centuries to describe a dermatitis characterized by recurrent florid facial ulcerations. The acute and chronic types of the skin disease were first differentiated by *Kaposi* in 1872. In 1895, *Osler* recognized the systemic nature of this disease, its characteristic exacerbations and remissions and he suggested that "erythema exudativum" was a form of vasculitis. Cardiac involvement was described in detail by *Libman and Sacks* in 1924 and by *Gross* in 1940. The clinical features of SLE as recognized today, however, were first delineated by *Baehr, Klemperer and Schifrin* in 1935. These authors emphasized that characteristic visceral involvement could occur in the absence of the typical cutaneous lesions. In 1948, the description of the lupus erythematosus (LE) cell by *Hargraves, Richmond and Morton* at the Mayo Clinic represented a major advance in interest and knowledge of this disease. It became possible to recognize a broader spectrum of patients with SLE (***Cassidy and Petty, 1990***).

Later, the discovery of antinuclear antibodies (ANAs), and the clinical application of the technique of indirect fluorescence microscopy in routine diagnostic laboratories led to a more accurate diagnosis (***Klippel, 1994***).

II. EPIDEMIOLOGY

Data suggest that childhood SLE is very uncommon, but these data date from the era when children with mild SLE were unrecognized. The incidence of SLE in childhood is much higher than previously suspected, but precise numbers that reflect the improved recognition of mild cases are not available (***Lehman, 1995***).

The prevalence of SLE has been estimated to be between 4 and 250 per 100,000 population, being more common in urban than in rural areas (***Schur, 1993***).

The peak age of onset of the first symptom is between 15 and 25 years. About 90% of the patients are females, but a higher percentage of males is affected among children and elderly SLE patients (***Rothfield, 1993***). Over the age of 10 years, SLE becomes more common among girls because of the synergetic effect of female sex hormones (***Lehman, 1993***). However, in children younger than 10 years of age, the ratio of girls to boys is 4:3. After the age of 10, girls are affected five times more frequently by SLE than boys, and the peak age seems to be just prior to or in early puberty (***Celejamer et al. 1984***).

Regarding the race, the incidence of SLE in the 10 to 20-year-old age group varies from 4.4 per 100,000 white females to 3 per 100,000 oriental females and 19.86 per 100,000 black females. This variation may be related to a variety of genetic factors including differences in estrogen expression and its impact on the immune system (***Rothfield, 1993***).

III. AETIOLOGY

SLE may be the expression of a common pathogenic mechanism initiated by a variety of factors. It may not be a single disease but rather a constellation of signs and symptoms produced by many aetiological factors (***Schur, 1993***). It seems that the causing factors initiate the disease in an already predisposed person and that separate mechanisms then perpetuate the disease and maintain the pathogenic process (*Horwitz, 1993*).

1. Infectious Agents

Evidence is accumulating suggesting the possible role of a chronic or latent virus infection in the initiation of autoimmunity and the immune complex processes that are seen in SLE patients. EBV, cytomegalovirus, herpes zoster, herpes simplex and endogenous retroviruses have been suspected (*Cooper et al., 1998*).

2. Hormonal Factors

Females are affected at least 5 to 9 times more frequently than males. As data suggest, this may be due to an estrogen-mediated immune hyperactivity. SLE may appear to be exacerbated during pregnancy or in the immediate postpartum period (*Cooper et al., 1998*). Klinefelter's syndrome in males is associated with the development of SLE (*Fram et al., 1980*).

3. Environmental Factors

Some children develop acute SLE or have an exacerbation of an established disease precipitated by excessive exposure to sunlight, drug sensitivity reaction, infection or severe physical or emotional stress. Ultraviolet irradiation results in