Clinical presentation of rheumatic fever in developing countries

Thesis

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Abstract

Rheumatic fever (RF) is an illness that occurs as a complication of untreated or inadequately treated streptococcal throat infection. Diagnosis depends on modified Jones criteria. This study included 64 patients with RF admitted to Cairo university pediatric hospital from April 2006 to march 2007 they were undergone analytical study. Male to female ratio was 1 (32 patients for each. Their ages ranged between 4 and 14 years with a mean of 9.78±2.89 years.57.8% were from rural areas. History of previous attack of RF was found in 37.5%.

Key Words :

Aortic regurge – Left ventricle – Mitral regarge .

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ABBREVIATIONS

ADHD: Attention deficit hyperactive disorder.
AHA: American heart association.
Anti-DNase: anti-deoxyribonuclease B.
APR: acute phase reactants.
AR: Aortic regurge
ARF: acute rheumatic fever
ASO: anti-streptolysin O
BPG: benzathine penicillin G
CHF: congestive heart failure.
CRP: C-reactive protein
ECG: electrocardiogram
ECHO: echocardiography
ESR: erythrocyte sedimentation rate
GAS: group A streptococcus
GABHS: group A beta hemolytic streptococci.
GRAB: G-related alpha (2)-macroglobulin-binding
HLA: human leukocyte antigen
IVIG: intravenous immunoglobulin
LV: left ventricle.
M R: Mitral regurge.
MVP: mitral valve prolapse
MV: mitral valve.
NSAIDs: non-steroidal anti-inflammatory drugs
OCD: Obsessive compulsive disorder
PANDAS: pediatric auto-immune neuropsychiatry disorders associated with streptococcal infections.
PSRA: Poststreptococcal reactive arthritis
RF: rheumatic fever.
RHD: rheumatic heart disease.
SA: septic arthritis
SCPA: streptococcal C5a peptidase
sfb1: streptococcal Fibronectin-binding protein 1
SLE: Systemic lupus erythematosus.
TNF: tumor necrosis factor.
TLC: Total leukocytic count
URT: Upper respiratory tract.
WHO: World health organization.

Introduction and aim of work

Rheumatic fever is a multisystem, immunologically mediated inflammatory disease, that occurs as a delayed sequel to group A streptococcal (GAS) infection. Its subsequent complication, chronic rheumatic heart disease (RHD), remains a major public health problem in developing countries**. (Binotto et al, 2002)**

Acute rheumatic fever (ARF) is an inflammatory process occurring as a delayed sequel to group A streptococcal pharyngitis due to certain group A streptococcal types. ARF is extremely variable in its manifestations and remains a clinical syndrome for which no specific diagnostic test exists. Persons who have experienced an episode of ARF are particularly predisposed to recurrent episodes following subsequent specific (rheumatogenic) types of group A streptococcal infections. (Lutwick and Ravishankar, 2005)

Rheumatic valvular heart disease, an important sequel to rheumatic fever, is the most common acquired heart disease world wide and is the major cause of cardiovascular death during the first 5 decades of life in developing countries. (Nordet, 1993)

Rheumatic valvular heart diseases are associated with severe incapacitating haemodynamic disturbances in young adults and children. (Bavdekar et al, 1999)

Acute rheumatic fever can mimic many other diseases and because the diagnosis is based on clinical criteria, it is still under-diagnosed or overdiagnosed in different settings. (Da Silva and Pereira, 1997)

Rheumatic fever and rheumatic heart disease remain a significant cause of cardiovascular morbidity and mortality in countries around the globe even into the 21st century; it is a medical and public health problem which needs a solution**.** (Kaplan, 2005)

Prevention of chronic rheumatic heart disease is feasible and cost effective if secondary prophylaxis is started and maintained regularly. (Nordet, 1993)

Aim of work

In the present study we aimed at describing the clinical profile of acute rheumatic fever in Egypt which is one of the developing countries, to increase the awareness of practitioners involved in the health care of young children. Identifying the different signs, symptoms and the atypical presentation that lead to difficulty in diagnosis. And assessing the role of laboratory investigation and echocardiography in diagnosis, and hence try to avoid missing cases which preclude the proper treatment and adequate prevention of this disease.

Review of literature

Historical background

Rheumatic fever causes chronic progressive damage to the heart and its valves. Until 1960, it was a leading cause of death in children and a common cause of structural heart disease. The disease has been known for many centuries. Baillou (1538-1616) first distinguished acute arthritis from gout. Sydenham (1624-1668) described chorea but did not associate it with acute rheumatic fever (ARF). In 1812, Charles Wells associated rheumatism with carditis and provided the first description of the subcutaneous nodules. In 1889, Walter Cheadle published classic works on the subject.

The association between sore throat and rheumatic fever was not made until 1880. The connection with scarlet fever was made in the early 1900s. In 1944, the Jones criteria were formulated to assist disease identification. These criteria, with some modification, remain in use today. The introduction of antibiotics in the late 1940s allowed for the development of treatment and preventive strategies. The dramatic decline in the incidence of rheumatic fever is thought to be largely owing to antibiotic treatment of streptococcal infection.

(Parillo and Parillo, 2005)

Epidemiology

The epidemiology of acute rheumatic fever is that of an infectious disease; group A streptococcal infection of the upper respiratory tract (Kaplan, 1992).

Outbreaks of rheumatic fever closely follow epidemics of streptococcal pharyngitis. Adequate treatment of a documented infection markedly reduces the incidence of acute rheumatic fever. Appropriate antimicrobial prophylaxis prevents the recurrence of the disease in patients with rheumatic fever. If the sera of these patients were tested, most would have elevated antibody titers to three antistreptococcal antibodies: streptolysin O, hyaluronidase, and streptokinase. (Gibofsky, 1998)

Low income, poor living, and substandard housing (especially crowding) are risk factors associated with outbreaks of the disease (Zamman,et al 1997).

Climatic factors such as cold and humidity are implicated in the incidence of acute rheumatic fever, which may be important in the spread of the infection with Streptococcus. In addition, high altitude may contribute to a poor prognosis. (Da Silva and Periera,1997)

Acute rheumatic fever has become much less common since the beginning of the 21st Century than it was 50 years ago. A great decline in acute rheumatic fever incidence has been noticeable in the United States, Japan, and most European countries between 1950 and 1980. By the end of the 1970s, acute rheumatic fever had become a rare disease in most areas of the United States. The reasons for this decline have been speculated; several factors have been mentioned, but by themselves do not appear sufficient to explain the phenomenon. Improvement in the general standard of living, such as socioeconomic conditions and housing, is a factor. In addition, the use of antibiotics to treat and prevent the disease played a significant role in the decline of acute rheumatic fever
incidence. Another possible explanation is that group A streptococcal strains vary in their capability of inducing the disease**.** (Rullan and Sigal, 2001)

However, in many developing countries, streptococcal infection, rheumatic fever, and rheumatic heart disease remain significant public

health problems and are the leading causes of heart disease among children and adults. (Stollerman, 1997).

The incidence of rheumatic fever in Egypt is less than adequately reported. ARF and RHD incidence among school children dropped from 563/100,000 in 1982 to 126/100,000 in1990 (Kassem et al, 1995)

In 1994 a prospective study on more than 5000 school children in Alexandria estimated the incidence at 110/100,000. (Abdel Moula et al, 1998).

The prevalence of RHD has also been estimated in surveys, mainly of school-age children. The surveys results showed there was wide variation between countries, ranging from 0.2 per 1000 schoolchildren in Havana, Cuba, to 77.8 per 1000 in Samoa (Table 1). (WHO, 2004)

In a study done by Mahmoud and El-Karaksy (1995) in primary school in Cairo, they found that the prevalence rate of RHD was 2.06 per thousand among all the 1939 school children examined.

Age:

RF is principally a disease of childhood, with a median age of 10 years; however, RF also occurs in adults (20% of cases) (Chin et al, 2006).
Acute rheumatic fever most often occurs in children, with a peak age-related incidence between 5 and 18 years. In adults, most initial attacks occur at the end of the second and beginning of the third decades, with rare initial attacks occurring as late as the fourth decade. (Fauci et al, 1998)

A recent study revealed that approximately 5% of children with RF were younger than 5 years at diagnosis. Compared with older patients, children who presented before 5 years of age were more likely to have moderate to severe carditis and to present with arthritis or the rash of erythema marginatum and were less likely to have chorea. (Tani et al, 2003)

Sex:
RF occurs in equal numbers in males and females. Females with RF fare worse than males and have a slightly higher incidence of chorea. (Chin et al, 2006)

Table (1): Examples of reported prevalence of RHD in school children in different countries (WHO, 2004)

WHO Region (country, city)	Year	Rate (per 1000 population)
Africa		
Kenya (Nairobi)	1994	2.7
Zambia (Lusaka)	1986	12.5
Ethiopia (Addis Ababa)	1999	6.4
Conakry (Republic of Guinea)	1992	3.9
DR Congo (Kinshasa)	1998	14.3
Americas		
Cuba (Havana, Santiago, P. del Rio)	1987	0.2–2.9
Bolivia (La Paz)	1986–1990	7.9
Eastern Mediterranean		
Morocco	1989	3.3–10.5
Egypt (Cairo)	1986–1990	5.1
Sudan (Khartoum)	1986–1990	10.2
Saudi Arabia	1990	2.8
Tunisia	1990	3.0–6.0
South-East Asia		
Northern India	1992–1993	1.9–4.8
India	1984–1995	1.0–5.4
Nepal (Kathmandu)	1997	1.2
Sri Lanka	1998	6
Western Pacific		
Cook Islands	1982	18.6
French Polynesia	1985	8.0
New Zealand (Hamilton)	1983	6.5 (Maoris) 0.9 (non-Maoris)
Samoa	1999	77.8
Australia (Northern Territory)	1989–1993	9.6

Race:

No race or ethnic group, is intrinsically resistant or unusually susceptible (Stollerman, 2001)

Race (when controlled for socioeconomic variables) has not been documented to influence the disease incidence. (Chin et al, 2006)

Season:

RF is more common in winter and spring, seasonal variation similar to that of streptococcal pharingitis. (EL-Said, 1990)

Mortality/Morbidity:

Morbidity from ARF is directly proportional to the rate of streptococcal infections. Infections that are not treated adequately are most likely to cause the major sequelae noted in the list of Jones criteria. Morbidity also is related to the care that the patient receives. The mortality rate has declined steadily over the last 3 decades. A partial explanation for the decrease in mortality rate may be the increase in antibiotic use. In developing nations and lower socioeconomic areas where rheumatic fever is more prevalent, ARF is a major cause of death and disability in children and adolescents. Cardiac involvement is the major cause of long-term morbidity. Valvular vegetations (endocarditis) are the cause of mitral valve regurgitation, the end result being LV dilation and CHF. Migratory polyarthritis occurs early in the disease course and is a common complaint for patients with rheumatic fever. Joint involvement ranges from arthralgia without objective findings to overt arthritis with warmth, swelling, redness, and exquisite tenderness. The larger joints are involved most frequently, such as the knees, ankles, elbows, and wrists. An inverse relationship between severity of joint involvement and risk of carditis appears to exist in approximately 75% of cases, the acute attack lasts only6 weeks. Ninety percent of cases resolve in 12 weeks or less. Fewer than 5% of patients have symptoms that persist for 6 months or more. (Parrillo and Parrillo, 2005)

Group A streptococcal infections

Beta-haemolytic streptococci can be divided into a number of serological groups on the basis of their cell-wall polysaccharide antigen. Those in serological group A (Streptococcus pyogenes) can be further subdivided into more than 130 distinct M types, and are responsible for the vast majority of infections in humans. (Shullman et al, 2000).

Furthermore, only pharyngitis caused by group A streptococci has been linked with the etiopathogenesis of RF and RHD. Other streptococcal groups (e.g. B, C, G and F) have been isolated from human subjects and are sometimes associated with infection; and streptococci in groups C and G can produce extracellular antigens (Including streptolysin-O) with similar characteristics to that produced by group A streptococci. (Kotb et al, 1993).

Nevertheless, the available evidence does not link streptococci in non-group A types with the pathogenesis of RF and RHD, although further