

Cardioembolic Strokes in Eastern Iran and the Importance of Rheumatic Valvular Disease

Kavian GHANDEHARI¹
Zahra IZADI MOOD²

Background: Rheumatic valvular disease is a common complication of rheumatic fever in children in developing countries. Later in life, rheumatic valvular disease becomes an important modifiable risk factor of stroke. The incidence of rheumatic valvular disease and its complications are unknown in Iran.

Materials and Methods: This is a prospective study of 302 consecutive patients admitted to a tertiary care hospital in Iran with a diagnosis of non-hemorrhagic stroke from June 2003 to June 2005. All patients underwent diagnostic work-up to determine stroke etiology according to clinical indications. Diagnosis and classification of stroke were made according to World Health Organization (WHO) criteria.

Results: In 302 patients with stroke (mean age 66.78, SD: 14.36), 60 (20%) patients (mean age 65.61, SD: 17.48) had cardiac source of embolism (CSE). Rheumatic mitral stenosis was present in 28 (28/60; 46.6%) of these cardioembolic stroke patients. Atrial fibrillation was documented in 19 (67.8%) patients with mitral stenosis. The remaining 32 (32/60; 53.3%) cardioembolic stroke patients had other CSE. Among the latter group, 8 (25%) patients had non-valvular atrial fibrillation. In the entire group of CSE, there were a total of 30 patients who were candidates for anticoagulation, and among those, 14 (14/30; 46.6%) were anticoagulated, but only 6 (6/30; 20%) were within therapeutic range at the time of their stroke.

Conclusions: Rheumatic valvular disease seems to be the most common CSE in Iran. Many patients with rheumatic or non-rheumatic CSE are not adequately managed for prevention of cardioembolic stroke.

Key Words: Cardioembolic, stroke, rheumatic

¹ Department of Neurology,
Faculty of Medicine,
Mashhad University of Medical
Sciences, Mashhad - IRAN

² Department of Emergency Medicine,
Faculty of Medicine,
Southern Khorasan University of
Medical Sciences, Birjand - IRAN

Doğu İran'da Kardiyolojik Embolik İnme ve Romatizmal Kapak Hastalığının Önemi

Giriş-Amaç: Romatizmal kapak hastalıkları özellikle gelişmekte olan ülkelerde çocukların romatizmal ateş hastalığının en sık komplikasyonudur. Yaşamın sonraki evrelerinde, romatizmal kapak hastalıkları inme için en önemli değiştirilebilir risk faktörüdür. İranda romatizmal kapak hastalığı insidansı ve komplikasyonları tam olarak bilinmemektedir.

Yöntem ve Gereç: Bu çalışma İranda hemorajik olmayan inme tanısıyla üçüncül bir referans hastanesine başvuran 302 hasta üzerinde yapılmış prospektif bir çalışmadır. Hastaların tümü klinik endikasyonlara uygun olarak inme etyolojisini saptamaya yönelik testlere tabii tutuldu. İnme tanısı ve sınıflaması Dünya Sağlık Örgütü kriterlerine göre yapıldı.

Bulgular: İnme olduğu saptanan ortalama yaşı 66.8(14) olan 302 hastanın ortalama yaşı 65.6(17.5) olan 60'ında (%20) emboli kardiyak kaynaklı idi(CSE). Bu kardiyolojik inme olan hastaların 28'inde (28/60) romatizmal mitral darlığı mevcuttu. Kalan 32 hasta (%53)da diğer kardiyak nedenler mevcuttu. Bu son gruptaki hastaların 8'inde (%25) valvüler olmayan atriyal fibrilasyon mevcuttu. CSE grubundaki hastaların 30'u antikoagülasyona adaydı ve bunların da 14'ü antikoagülen alıyordu ancak inme anında bunların sadece 6'sı tedavi edici dozlarda ilaç almaktaydı.

Sonuç: İranda en sık görülen CSE romatizmal kapak hastalıklarıdır. İster romatizmal ister romatizmal olmayan nedenlerle olsun hastaların çoğu kardiyolojik inmeleri önlemeye yönelik uygun tedavi almamaktadır.

Anahtar Sözcükler: Kardiyolojik emboli, İnme, Romatizma

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Correspondence

Kavian GHANDEHARI
Department of Neurology ,
Ghaem Hospital,
Ahmadabad Street, Mashhad,
Khorasan - IRAN

kavianghandehari@yahoo.com

Introduction

While one-fourth of strokes are cardioembolic, cardiac source of embolism (CSE) is considered as a modifiable risk factor of stroke. The distribution of cardiac pathology as the cause of embolic stroke varies among countries. While in the developed countries non-valvular atrial fibrillation is the most prevalent, in developing countries rheumatic valvular disease continues to prevail as the most common cause of CSE (1). Data regarding the incidence and prevalence of rheumatic heart disease in developing countries are lacking (2). Adequate anticoagulation offers stroke prevention in patients with rheumatic valvular disease or other potential CSE.

In developing countries, prevention of rheumatic valvular disease and its complications is inadequate (2). The incidence of stroke complicating rheumatic valvular disease is in the range of 1.5% to 4.7% (3). Unfortunately, epidemiologic studies on rheumatic valvular disease and its complications are lacking in Iran. However, many tertiary care centers are involved with managing the complications of this preventable childhood disease. Herein we present our experience with CSE in a tertiary care center in Iran.

Materials and Methods

Valie-Asr hospital is a tertiary care university hospital in Khorasan, Iran, and it serves a population of 400,000. From June 2003 to June 2005, all consecutive patients admitted to this hospital with a diagnosis of non-hemorrhagic stroke were included into this prospective observational study.

All of the patients were seen by a stroke specialist. Stroke was defined and classified according to World Health Organization (WHO) criteria (4,5). Patients underwent a standard battery of diagnostic investigations, including brain computed tomography (CT), ECG, blood electrolytes, blood count and differential, coagulation profile, carotid Doppler, trans-thoracic echocardiogram, fasting blood glucose and lipid profile. Trans-esophageal echocardiogram was obtained in patients in whom trans-thoracic echocardiogram was non-diagnostic despite high suspicion of CSE. A 24-hour Holter monitoring was obtained in patients with history of syncope and/or palpitation or high suspicion of CSE with non-diagnostic echocardiography and ECG. Three serial blood cultures were requested for any stroke

patient with fever and heart murmur or valvular vegetation detected by echocardiography. Data on patient demographics, clinical presentation, and diagnostic work-up were recorded in a database.

Statistical methods: Results were expressed as mean with standard deviation for quantitative variables and number with percentage for qualitative variables. Univariate analysis was done by using independent sample t-test, Mann-Whitney U test, and Pearson chi-square test, whenever appropriate. P-value less than 0.05 was considered as statistically significant.

Results

From June 2003 to June 2005, non-hemorrhagic stroke was diagnosed in 302 patients (159 female, 143 male). CSE was diagnosed in 60 (19.8%) of these patients, and 37 (61.6%) of them were female. Mean age of the group with CSE was 65.61; SD: 17.48. The mean age of female patients was 64.59; SD: 2.80, and of male patients was 67.26; SD: 3.83.

Among patients with cardioembolic stroke, rheumatic valvular disease was detected in 28 (28/60; 46.6%), and of those, 19 (19/28; 67.8%) had atrial fibrillation. The remaining 32 (32/60; 53.3%) cardioembolic stroke patients had other types of CSE. In the latter group, 8 (8/32; 25%) patients had non-valvular atrial fibrillation. The frequency rate of various CSE in our 60 cardioembolic stroke patients is illustrated in Table.

In the rheumatic valvular disease group, there were significantly more female patients (OR = 2.34, CI = 0.97-6.24, P-value = 0.036). Gender was not a significant factor in the non-rheumatic CSE group (OR = 1.02, CI = 0.46-2.26, P-value = 0.89). The average age of female patients in the rheumatic valvular disease group was 59.30, SD: 16.6, and of male patients was 61.12, SD: 17.54, with no significant difference between the two genders (P = 0.899). The average age of female patients in the non-rheumatic CSE group was 70.82, SD: 15.82, and of male patients was 70.53; SD: 18.59, with no significant difference between the two genders (P = 0.894). There was no significant difference in the number of patients referred from urban or rural dwellings in the rheumatic CSE group; OR = 1.0, CI = 0.45-2.31, P = 0.96.

Table. Cardiac source of emboli in 60 cardioembolic stroke patients.

Cardiac Disorders	Female	Male	Total
Valvular Atrial Fibrillation (VAF)	12	7	19
Non-valvular Atrial Fibrillation (NVAF)	4	4	8
Mechanical Mitral Valve (1 with VAF)	1	-	1
Mitral Annular Calcification	2	-	2
Rheumatic Mitral Stenosis (18 with VAF)	7	1	8
Mitral Valve Prolapse	7	2	9
Nonbacterial Endocarditis	1	1	2
Left Ventricular Thrombus	-	1	1
Acute Myocardial Infarction (1 with NVAF)	-	1	1
Left Ventricular Aneurysm	-	1	1
Left Ventricular Akinetic Segment	-	1	1
Congestive Heart Failure (1 with NVAF)	2	4	6
Patent Foramen Ovale	1	-	1
All Cardiac Sources of Emboli	37	23	60

In the rheumatic valvular disease group, 24 patients were candidates for anticoagulation; however, only 11 (11/24; 45.8%) were anticoagulated, and among those only 5 patients (5/24; 20.8%) had international normalized ratio (INR) within therapeutic range. Among the non-rheumatic patients, 6 were candidates for anticoagulation; however, only 3 (3/6; 50%) were anticoagulated, and only 1 (1/6; 16.6%) was within therapeutic range. In the entire group of CSE, there were total of 30 patients who were candidates for anticoagulation, and among those, 14 (14/30; 46.6%) were anticoagulated, but only 6 (6/30; 20%) were within therapeutic range.

Discussion

The incidence of CSE in our stroke patients was 19.8%. Cardioembolic strokes represented 14% of the Stroke Data Bank (6) and 20% of the Lausanne Stroke Registry (7). Almost half of the cardioembolic strokes in developed countries are secondary to non-valvular atrial fibrillation and 7.6% of CSE is due to rheumatic heart disease (8). Rheumatic heart disease is an important cause of mitral and aortic valve disease in developing countries (9,10,11). Rheumatic valvular disease was present in 46.6% of CSE in our cardioembolic stroke patients and in 70.3% of the atrial fibrillations. Cardiac disease was found in 23% of Ethiopian stroke patients and valvular heart disease accounted for 40% of all

heart disease in the stroke patients (12). Rheumatic valvular disease was found in 44.8% of the patients with cardioembolic stroke and in 63.5% of fibrillating stroke patients in the Khorasan stroke registry (13). The incidence of rheumatic valvular disease in our stroke patients was 9.3% (28/302), and was significantly higher in females. This is in agreement with previous reports (14,15). The cause of this gender discrepancy is unknown (14,15). In Iran, epidemiologic studies on rheumatic heart disease are lacking. Therefore, data on early diagnosis and management of streptococcal throat infection and its complications are not available. Further improvement in the quality of the manufacturing and storage of antibiotics is recommended in developing countries (2). Clear indications for anticoagulant therapy are identified in patients with CSE (16,17); however, adequate anticoagulation was achieved in 20% of our patients who were candidates for this treatment. The reasons for this inadequate management of CSE are unknown, though inadequacies in logistics and infrastructure may be among the contributing factors.

Through our study we opened only a small window to evaluate rheumatic valvular disease as a public health concern. Much work is required with respect to the epidemiology and prevention of rheumatic valvular disease and its complications in Iran and other developing countries.

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