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Complex Aortic Arch Atheromas: A New Potential Source of Brain Embolism, Frequency, Risk Factors And Management.

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Abstract:
Background: *Significant aortic arcliatheromas (>4mm thick) have been identified as one of the most powerflil independent risk factors for ischemic strokes in western patients >60 years of age, but there is little published literature on frequency of aortic atheromas in Indian population.*
Material and Methods: *The current study was aimed at assessing the frequency and risk factors of significant aortic arch atheroma in stroke patients attending a tertiary care center in south India, whose stroke mechanism was not clear even after detailed clinical assessment, and investigations including Carotid Doppler, Magnetic resonance imaging and 2D Transthoracic echocardiography.*
Results: *Out of 297 consecutive patients of ischemic stroke, seen between 1st January 2001 and 31st December 2001, Transesophageal Echocardiography (TEE) was performed in 85 patients with stroke of unknown mechanism. Eighteen patients (21%) were discovered to have significant and complex aortic arch atherosclerosis as the underlying cause of their stroke. The men: women ratio was 15:3 and the mean age was 54.28±12.41. Four were protruding but immobile, whereas 14 were mobile atheromas. Two patients had superadded ulcerations. Nine (50%) had hypertension, 6 (33%) had diabetes, 4 (22%) had history of smoking and 1 (5%) had alcoholism. There was no significant difference between the frequency of these risk factors between aorto-embolic and other stroke subtypes. Regarding the clinical features, 6 patients had left hemiparesis, 6 had right hemiparesis, 2 had ataxia, 2 had dementia and 1 had hemianopia.*
Conclusions: *To conclude, aortic arch atherosclerosis was found to contribute to a significant number of stroke patients in a south Indian tertiary care center. All stroke patients with unknown mechanism should be subjected to TEE to detect aortic atheroma as this has therapeutic implications.*
Key words: *Aortic Arch, Atheromas, Embolism, Stroke.*

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I. Introduction

There has been a growing awareness about the cerebro-embolic potential of aortic atheromas in the last decade. [1, 2] Large atheromas (>4mm thick) have been identified as one of the most powerful independent risk factors for ischemic strokes in patients >60 years of age[3, 4] Whether high-risk population should be routinely screened for the presence of aortic atheromas would depend on the prevalence of such complex lesions in patients of ischemic stroke in a given population. Data regarding aortic atheroma and stroke have been derived almost exclusively from white populations and little is known about the frequency of aortic atheromas in Indian population. This is relevant, as ethnic differences are known to determine the distribution of atherosclerotic lesions in the vascular tree. [5] The current study was aimed at assessing the frequency and risk factors leading to aortic arch atheroma in stroke patients attending a tertiary care center in south India.

II. Subjects and Methods

The study material consisted of 297 consecutive patients of ischemic stroke enrolled in the Stroke Data Bank of Nizam's Institute of Medical Sciences, Hyderabad, between 1st January 2001 to 31st December 2001. This hospital is a major neurological centre in Telangana region of Andhra Pradesh state in India, where patients are either referred by practising physicians or can get registered themselves. The patient population is fairly representative of the disease pattern in this region. Stroke Data Bank of Nizam's Institute of medical Sciences is

an ongoing, prospective observational project aimed at consecutively collecting, clinical, imageological and laboratory and follow-up data on all cases of fully investigated acute strokes.

Each patient with acute stroke was examined by a Senior Resident in Neurology, specifically trained in stroke diagnosis, and the findings confirmed by a qualified stroke neurologist within a week of onset of stroke. Information was collected on each patient concerning details of risk factors, past history, general and neurological examination. Each patient was investigated according to a fixed protocol, with the aim of delineating the causal mechanism and identifying the risk factors on the pattern practiced in the standard Stroke Data Banks in USA, Europe and Oriental countries [6-8] Thus, all patients were required to have a basic minimum of CT scan of brain, extra cranial carotid duplex examination and a 2D- Echocardiography. [6-8]

If the stroke mechanism was still not clear, then the patients, depending on the clinical suspicion, were subjected to one or more of additional investigations which included, magnetic resonance angiography (MRA), transcranial color-coded duplex (TCCD) study and hematological investigations like estimation of protein C, S and antithrombin III deficiency, homocyteine and collagen profile. Trans esophageal Echocardiography (TEE) was performed, if the above tests failed to delineate the stroke mechanism or if clinical features were suggestive of cardiac source of embolism. Before the procedure, patient was explained the nature and purpose of the TEE test and consent was taken.

Transesophageal echocardiographic examination (TEE) was performed in a standard and systematic fashion (11) with a biplane or multiplane transducer. The aortic arch was defined as the portion of aorta between the curve at the end of ascending portion and the takeoff of the left subclavian artery. The aortic arch was examined for the presence and degree of protruding atheroma. The patients with grade 1, 2 or 3 disease were classified as having mild to moderate disease with intimal thickening but without protruding atheromas (sessile atheroma extending <5mm into the aortic lumen). Patients with grade 4 or 5 disease were classified as having atheromas protruding > 5mm into the aortic lumen (grade5 with mobile components). [9]

At the time of discharge, or sometimes during follow up , a diagnosis was determined , according to TOAST criteria , taking into account all the available data. [10] A classification for diagnosis was designed to characterize each stroke by its causal mechanism. This classification took into account the neurological and medical history, neurological symptoms and signs, head CT scan, findings from carotid and transcranial duplex sonography, magnetic resonance angiography, electrocardiography and TEE. Ischemic strokes were classified into following categories: 1) large-artery disease, either intracranial or extracranial 2) small artery disease (lacune) 3) cardio embolism 4) aortoembolism 4) stroke of other determined etiology, and 5) stroke of undetermined etiology.

Statistical analysis

The chi square test was employed to find the difference in the frequency of risk factors between aortoembolic stroke and large artery, small artery disease (lacune), cardio embolic and stroke of undetermined etiology.

III. Results

Out of a total of 297 patients with ischemic stroke, there were 236 men and 61 women. The mean age was 55.04+24. The underlying mechanism was identified as significant intracranial atherosclerosis in 118 (40%), extracranial atherosclerosis in 26 (9%), cardio- embolic in 40 (13%), Aortoembolic in 18 (6%), Lacunar in 67(23%), other determined etiologies 7 (2%) and unknown mechanism in 67 (23%) patients. Among the 18 patients discovered to have aorto-embolic stroke, the men: women ratio was 15:3 and the mean age was 54.28+12.41. Out of 18 patients, 4 were protruding but immobile, whereas 14 were mobile atheromas. Two patients had superadded ulcerations. All the significant atheromas were located in arch of aorta along with insignificant atherosclerotic lesions in the ascending aorta. Eleven patients were found to have grade 1 to 3 aortic atherosclerosis, but these were not used for analysis (table 1). Regarding the risk factors 9 (50%) had hypertension, 6 (33%) had diabetes, 4 (22%) had history of smoking and 1 (5%) had alcoholism. There was no significant difference between the frequency of these risk factors between aorto-embolic and other stroke subtypes (table 2). Regarding the clinical features, 6 patients had left hemiparesis, 6 had right hemiparesis, 2 had ataxia, 2 had dementia and 1 had hemianopia. All the patients showed reasonable recovery and were discharged within a week on oral anticoagulants (table 3).

IV. Discussion

Several studies have clearly established the role of aortic atheromas in stroke causation, but the data is limited to western studies. Similar frequency of large atheromas has been reported in whites, blacks and hispanic patients [11] It must be noted however, that although aortic atherosclerosis in general, is a common concomitant of aging, and is known to be associated with coronary artery disease, [12-14] it is the complex aortic atheromas (> 4mm protruding into lumen, mobile, immobile or ulcerated) ,which have been shown to have a very high risk of stroke. Thrombi, fibrinous material and cholesterol crvstalsmav dislodge from a complex

ulcerated atherosclerotic plaque within span of Indians is at least 10 years less than that of western population [8]and aortic atherosclerosis increases steeply with advancing age. Interestingly, while western studies have emphasized the occurrence of significant aortic atherosclerosis above the age of 60 years, the mean age of our patients with aorto-embolic stroke was only 55 years, almost a decade less than that reported from west. Hence the threshold of age of patient, at which to suspect atheroma and subject patients to transesophageal echocardiography, should be lower in India. It is recommended that all strokes due to unknown mechanisms should undergo TEE to rule out aortic arch atherosclerosis.

It is interesting to find that all 18 patients with aortoembolic strokes were discharged home and there was no death. This is a significant observation, as out of all the stroke subtypes, cardioembolic strokes have been reported to have the worst outcome. Based on our earlier experience [15] and the experience during the present study, it seems that aorto- embolic strokes have a milder clinical picture than other cardioembolic strokes. Although there are no other studies to confirm this observation, it is possible that there are different clinical subtypes even within the category of cardioembolic strokes. It is known that there are different sizes of cardiogenic emboli depending on the fibrin content, and it has been suggested that the smaller emboli may be associated with minor cerebral events [16] The current knowledge about clinical features of cardioembolic strokes is based on previous studies where atrial fibrillation was the most frequent underlying cardio-embolic source. Atrial fibrillation is known to be associated with heavy red clots and could have strongly influenced the conclusions of those studies. [17-20]

Since none of the 18 patients in the present study had atrial fibrillation, their course was mild. The major risk factors, were increasing age, male sex, hypertension, and diabetes, and the frequency of these risk factors was not significantly more than in other stroke subtypes (tablc2). The best therapeutic and preventive options for patients with stroke with aortic arch atheromas are not known at present. As there is no data based on prospective double-blind randomized trials to address this issue, the treatment has been largely empiric. Although systemic anticoagulation is controversial because of the potential of inducing plaque hemorrhage and subsequent rupture and embolization, its use has usually been advocated in the case of complex lesions with superimposed mobile components, which have been shown to be thrombotic material in some studies .[21, 22]In one of the practice surveys done in a University hospital, it was found that even in the absence of clear guidelines to prevent recurrent cerebral events, many clinicians favoured long-term anticoagulation over aspirin, possibly based on the limited data available. [23]

Table 1: Grades of Aortic atherosclerotic plaque as measured by Trans-esophageal echocardiography

	HTN	P Value	DM	P Value	Smoking	P Value	Mean	P value
AES	9		6		6		54.4	
n=18								
IAS	85	0.733	42	0.512	34	0.935	54.9	0.467
n=l 18								
EAS	12	0.0613	7	0.889	6	1.031	54.19	0.0972
n=26								
CES	21	0.924	11	0.094	5	0.365	50.87	0.361
n=40								
LS	48	0.0769	32	0.819	21 '	0.778	54.87	0.493
n=67								
Unknown	44	1.021	20	1.163	20	0.201	50.17	0.907
n=67								

Table 2

No	Age/Sex	Clinical features	Location of infarct	Outcome	Treatment
1	72/M	Lt hemianopia	Infarct in Rt Occipital area.	DIS	Acit,Rami,Alor j
2	63/M	Rt hemiperesis	Lt Parietal inf	DIS	Clop, Rami, Ator
3	60/M	Ataxia	Infarcts in Rt cerebellum & Thalamus	DIS	Clop, Rami, Ator
4	67/M	Lt hemiperesis	infarct in Rt Parieto Occipital area	DIS	Acit, Eco, Rami,
5	61/M	Lt hemianopia, Hemianesthesia	Infarcts in Rt Occipital & Thalamus	DIS	Acit, Eco, Rami,
6	69/M	Ataxia	Infarct in Rt Pons & Cerebellum	DIS	Eco, Rami, Ator
7	60/M	Dementia	Infarcts in Bil Sub cortical white matter	DIS	Eco, Rami,Ator :
8	60/M	Dementia	Bil Multiple Lacunar infarcts	DIS	Acit, Eco, Rami,
9	72/F	Rt hemiperesis	Infarct in Lt Pons	DIS	Acit, Eco, Rami,
10	70/F	Lt hemiperesis	Rt Parietal inf	DIS	Aci,Eco,Rami,Ator
11	62/M	Rt hemiperesis, Hemianopia	Infarct in Lt Tempero Parietal area	DIS	Eco, Rami,Ator

V. Conclusion

Like western population, Aortic arch atherosclerosis contributes to a significant number of stroke patients in Indian patients also, although Indian patients are about a decade younger than their western

counterparts. It could account for cerebral infarction in patients, whose stroke mechanism remains unknown even after carotid Doppler, MRA and 2D Echocardiography. All such patients should be subjected to Transesophageal echocardiography, which is an accurate, safe and well-tolerated technology for examining the aortic arch.

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