Atherosclerotic Aortic Arch Plaques in Acute Ischemic Stroke

Abstract

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Background: Atherosclerotic aortic arch plaques (AAP) have been linked to an increased risk of thrombo-embolic events as a cause of acute ischemic stroke of undetermined etiology.

Objectives: To find out the presence of atherosclerotic plaques in aortic arch and their potential role as a source of embolism in cerebral infarction of undetermined etiology.

Methods: We performed trans-esophageal echocardiography (TEE) and multislice computerized tomography (MSCT) of the aortic arch on 30 patients with acute ischemic stroke of undetermined cause from a total series of 150 non-selected patients with acute ischemic stroke studied prospectively by clinical evaluation, laboratory investigations, cranial computed tomography ,color coded duplex ultrasonography of the carotid arteries and transcranial Doppler (TCD).

Results: Using trans-esophageal echocardiography eight patients (29.6%) had atherosclerotic aortic arch plaques, while using multislice computerized tomography atherosclerotic aortic arch plaques were revealed in twelve patients (40%). Atherosclerotic aortic arch plaques were significantly related to older age, male gender, hypertension, ischemic heart disease and low-grade atherosclerotic carotid lesions. Multislice computerized tomography of the aortic arch was more sensitive than trans-esophageal echocardiography in detecting the site, size and characters of atherosclerotic aortic arch plaques.

Conclusion: Atherosclerotic aortic arch plaques are a frequent finding in patients with acute ischemic stroke of undetermined cause supporting the hypothesis that aortic plaques have embolic potential. In addition, multislice computerized tomography is more sensitive than trans-esophageal echocardiography in detecting atherosclerotic aortic arch plaques and better characterization of these plaques especially relevant one.

Keywords: Aorta, Atherosclerotic plaques, Echocardiography, Multislice Computerized Tomography, Stroke.

Introduction

The origin of cerebral infarction is undetermined in up to 40% of patients and an embolic origin is suspected in approximately 60%.[1,2] In the last few years, several studies have found a close link between protruding plaques in the aortic arch and the risk of ischemic stroke as well as other recurrent vascular events.[3-7] Patients older than 60 with plaques in the proximal aorta ≥4 mm thickness are especially at risk.[3,5,8]

Varying criteria have been used in selecting patients and in defining significant lesions, and this may explain the differences found in relevant plaque prevalence (from 23 to 61%).[9]

The aim of this study was to find out the presence, extent, and morphology of relevant atherosclerotic plaques in the aortic arch, and their potential role as a source of embolism in patients with acute cerebral infarction of undetermined etiology.

Subjects and Methods

Out of 150 consecutive acute ischemic stroke patients admitted in the Neurology department and Stroke unit at Cairo University

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Table 1: Demographic and clinical characteristics, risk factors and ultrasound findings in stroke patients with undetermined etiology.

	Patients with AAP (n =12)	Patients without AAP (n = 18)
Age, year (mean ± S.D)	69.30 ± 9.10**	54.20 ± 13.20
Sex, male (19)	9 (75.00%)*	10 (55.56%)
Current smoking (12)	5 (41.67%)	7 (38.89%)
Diabetes mellitus (7)	3 (25.00%)	4 (22.22%)
Hypertension (13)	7 (58.33%)*	6 (33.33%)
Ischemic heart disease (4)	3 (25.00%)*	1 (5.56%)
Hyperlipidemia (10)	4 (33.30%)	6 (33.33%)
Carotid artery plaques (‹50%) on duplex examination (10)	6 (50.33%)*	4 (22.22%)

**P‹0.001 = highly significant, *P‹0.05 = significant

Hospital over an 18 month period between 2007 and 2008. We studied thirty stroke patients of undermined etiology within the first 72 hours of the onset of their symptoms.

All acute ischemic stroke patients were subjected to thorough medical history to record potential vascular risk factors, general clinical and neuro-vascular examination, blood and coagulation tests. Twelve-lead electrocardiogram (ECG), non-contrast computed tomography (CT) scan, colour-coded duplex ultra sonography of the carotid, transcranial Doppler (TCD) and transthoracic echocardiography (TTE).

Stroke of undetermined etiology was diagnosed if no potential cause of cerebral infarction was found. Patients without carotid or intracranial arterial stenosis ›50%, and patients not meeting the criteria for cardioembolic stroke (by clinical and ECG criteria) were classified as having stroke of undetermined etiology.[10]

Aortic arch were studied in stroke patients with undetermined etiology using both trans-esophageal echocardiography (TEE) and multislice computerized tomography (MSCT).

Trans-esophageal echocardiography (TEE) protocol

A Phillips S72 Omni ultrasound equipment was used to perform TEE. Before TEE evaluation, all patients were submitted to a complete transthoracic examination performed by experienced cardiologist who were blinded to the results of the other diagnostic procedures. The echoscope was entered into the esophagus and the tip was tilted to permit a clear image of the atrial septum at the level of the fossa ovalis. After cardiac structure examination the transducer was gradually withdrawn to proceed with the examination of the thoracic aorta in search of atherosclerotic aortic plaques (AAP) or thrombus as possible sources of emboli. Plaques of 4 mm thickness or greater located in the ascending aorta or proximal arch were considered.

Multislice computerized tomography (MSCT) protocol

Using 64 channel multi-detector row CT scanner. After patient laboratory data were initially revised especially the results of renal functions, patients were instructed to stop food and fluid intake for 6-8 hours prior to examination and positioned supine on the CT table with the arms resting comfortably above the head. CT angiography was performed following target injection of 120-150 ml of contrast medium (Omnipaque) at a flow rate 3-4 ml/sec.

Results

One hundred and fifty admitted patients, thirty of whom (20%) had acute ischemic stroke of undetermined etiology (mean age 62.63 ± 12.27, sex 19 male/11 female) were included in this study.

Thirteen patients (43.3%) were suffering from hypertension, 5 patients (16.6%) had previous history of TIAs, smoking in 12 (40%), D.M. in 7 (23.3%), ischemic heart disease in 4 patients (13.3%) and hyper-lipidemia in 10 patients (33.3%). On CT examination, 15 patients (50%) showed lacunar cerebral infarction, small sized infarction in 11 patients (36.6%), medium sized in 3 (10%) and large sized in one patient (3.3%). Using carotid duplex low-grade atherosclerotic lesions (stenosis ‹50%) in the carotid arteries were found in 10 patients (33.3%).

TEE was successfully carried out on 27 (90%) patients with stroke of undetermined etiology. One patient showed poor insonation condition for the examination to be performed and 2 patients did not tolerated the procedure.

Table 2: TEE and MSCT results in stroke patients of undetermined etiology.

	TEE (n = 27)	MSCT (n = 30)
Positive	8 (29.61%)	12 (40.00%)
Number		
Multiple	4 (14.80%)	6 (20.00%)
Single	4 (14.80%)	6 (20.00%)
Site:		
Arch	8 (29.61%)	7 (23.30%)
Others	0 (0.00%)	5 (16.70%)**
Size:		
‹4-mm	7 (25.90%)	7 (23.30%)
≥4-mm	1 (3.70%)	5 (16.70%)**
Character:		
Homogeneous	7 (25.90%)	6 (20.00%)
Heterogeneous	1 (3.70%)	6 (20.00%)
**P‹0.01 = highly significant		

On TEE examination, atherosclerotic aortic plaques (AAP) were observed in 8 patients (29.6%) which were multiple in 4 patients (14.8%) and single in the remaining 4 (14.8%). Plaques were ‹4 mm thick in 7 patients (25.9%), and in one patient (3.7%) it was ≥4 mm thick. All plaques observed were in the arch of the aorta (29.6%). Plaques were heterogeneous in 7 patients (25.9%) and homogenous in only one patient (3.7%). Ulcerated plaques were not found in any case.

MSCT of the aortic arch was successfully performed for all selected stroke patients. AAP were observed in 12 patients (40%). They were multiple in 6 patients (20%) and single in the remaining 6 (20%) patients. Plaques were ‹4 mm thick in 7 patients (23.3%) and in 5 patients (16.7%),they were ≥4 mm thick. Plaques were found in the arch in 7 patients (23.3%), at the left subclavian ostium in 2 (6.6%), at the left common carotid artery ostium in one (3.3%), both in left CCA ostium and distal arch in one (3.3%) and in the ascending and distal arch in one (3.3%). AAP were calcified in 6 patients (20%), while in the other 6 patients (20%) they were hypodense [one of them was penetrating the wall of the arch (3.3%)].

Factors which are potentially associated with AAP were illustrated in Table (1) which revealed that the older the patients the greater the prevalence of plaques, and the frequency of AAP was significantly higher in men. AAP was significantly associated with hypertension, presence of atherosclerotic lesions (stenosis ›50%) in carotid arteries, and showed a trend of greater frequency in patients with coronary heart disease, but no significant relationship was found with other vascular risk factors.

Small sized cerebral infarctions were significantly common in patients with AAP [6 in TEE +ve patients (75%), and 9 in MSCT positive patients (75%)]. However, AAP were not significantly associated either with the side or site of the cerebral infarction.

Four out of 12 patients (33.3%) with positive MSCT results showed no lesion in TEE. All AAP were in arch of aorta in TEE, while MSCT showed AAP in other sites (ascending aorta and ostia of great vessels). 2 patients with single AAP on TEE showed multiple lesions of MSCT (both in the arch ostium, and left common carotid A). Among 7 patients with AAP ‹4 mm thick in TEE, 3 patients showed AAP ≥4 mm thick in MSCT. Again, 3 patients out of 7 patients with heterogeneous plaques with TEE showed hypodense plaques in MSCT.

The comparison of the results of TEE and MSCT (Table 2) revealed a significantly higher sensitivity of MSCT over TEE in detecting the site, size and characters of AAP (P‹0.01).

Discussion

Few studies have focused on strokes of undetermined etiology where AAP may have an important role as a cause of ischemic events.[3-5,11-13] Amarenco et al.[3,14,15] found in both autopsy and clinical studies of individuals older than 60, a higher prevalence of relevant plaques in the aortic arch in patients with cryptogenic stroke. In their study of 78 patients with cryptogenic stroke, 28% showed plaques greater than or equal to 4 mm thickness as compared with 14.4% of the 250 patients with defined stroke etiology, and just 2% of their control group. In contrast, 3 other reports have failed to find significant differences in the prevalence of atherosclerotic aortic arch lesions between patients

with undetermined strokes and those with strokes of determined origin.[4,9,16]

In this study, AAP using TEE and MSCT was observed in 8/27 patients (29.6%), and 12/30 patients (30%) respectively a figure which is less than that reported by Castellanous et al.[2] (46.9%). Only one relevant AAP (≥4 mm thick) was revealed by TEE (3.7%), a figure which is much less than all previously recorded figures (10.2%-50%).[2-4,9-14] On the other hand five relevant AAP(16.7%)were revealed using MSCT , a figure which is slightly more than that of Castellanos et al.[2] (10.2%) but much less than others.[3,4,9,14,16]

Several factors may explain the difference between our results and that of others. Firstly, we have studied a non-selected population taken from all age groups, it is likely that the presence of younger patients accounts for the lower proportion of relevant plaques, as these lesions are much more frequent in older patients.[3,4,6,15,16] In fact, no patients under 60 had plaques greater than 4 mm thickness. Secondly, we excluded patients with intracranial stenosis from the stroke of undetermined etiology group and these patients will often suffer from severe atherosclerosis and as such are more likely to have a higher frequency of AAP.

The association between aortic plaques and ischemic stroke is particularly strong when the plaques are ≥4 mm in thickness.[2,4,8,14] These studies were applied to a large scale of patients that could not be applied to the current study because of small sample size.

Some stroke risk factors were significantly associated with AAP. A finding that concurs with many other reports. As expected, advanced age (more than 60 years old),[7,17-19] Hypertension[17,20] and other manifestations of atherosclerosis such as ischemic heart disease[21] and low grade atherosclerotic carotid lesions were significantly more in patients with AAP.

As reported by Otsubo et al.[22] size of brain infarction in aortogenic brain embolism was smaller than that in cardiogenic brain embolism this was in agreement with the our findings where small sized infarctions were the most frequent, while large-sized one were not related to AAP.

Using MSCT , plaques sites were in accordance with Amarenco et al.[14] where the lesions detected by TEE were in proximal arch but in contrast to Hueb et al.[20] where atheromas were located in the proximal descending aorta. Lesions in either the ascending aorta or aortic arch were less frequent finding using TEE.

This distinction between the distal and proximal locations is important because lesions located more frequently in the distal part of the arch (distal to the ostium of the left subclavian artery) than in the proximal part of the arch and the lesions in the distal part of the arch were less likely to give rise to cerebral emboli but there was no difference in the hemispheric lateralization of the infarctions.[3] This was in accordance with the results of the current study where there is a lack of correlation between aortic atheroma and side of hemispheric affection. However, Tunick et al.[23] reported that left hemisphere events are more common than right hemisphere events.

Out of positive lesions detected by MSCT, atheromatous plaques in two patients were detected at the Lt. subclavian ostium. This may be due to the retrograde and rotational blood flow in the thoracic aorta that probably exists in all patients with systemic emboli and mobile protruding aortic atheromas therefore, retrograde cerebral embolism from distal aortic plaques is possible[24] or the presence of these APP may be an index of generalized atherosclerosis rather than a source of embolization.[25]

The difference between TEE and MSCT regarding the site of lesions may be due to the fact that distal part of the ascending aorta and the branches of the aortic arch cannot be adequately evaluated by TEE.[26] Also this difference may accounts for the difference in the number of lesions detected by both tools as lesions in the ostia of large arteries were not properly seen by TEE.[26] Interference by the trachea and the left main bronchus produces a blind spot which may be a very limiting factor for visualization of aortic plaques by TEE.[3] While in MSCT this area could be visualized adequately with proper assessment of aortic branches.[27]

Comparing both TEE and MSCT in examining the size of lesions, MSCT detected larger number of patients with lesions more than 4 mm thickness, but there is no single study comparing both tools regarding the size of lesions. A study on TEE explained that the thickness of an intimal plaque and superimposed mobile thrombi can be measured on trans-esophageal echocardiography and that measurement of wall thickness is less accurate in the longitudinal plane.[28]

Demonstrating plaque composition is important as ulcerated and non-calcified aortic plaques had a significantly higher correlation with ischemic stroke.[29,30]

Similar to results observed in studying coronary plaques.[31,32] MSCT achieves a good differentiation regarding the composition, consistency and characterization of AAP. In an area, where TEE is extremely less sensitive. The sensitivity of TEE for detecting small ulcerations has been reported to be less than optimal (74%) when compared to pathology data. Therefore, the frequency of ulcerated atheromas may be under estimated.[33] Initially, TEE may fail to identify the aortic ulcer and may reveal only intramural hematoma from a tiny aortic "ulcer mouth".[34] While in MSCT, Hayashi et al.[35] considered that its use had largely replaced angiography that was previously the standard of reference for the diagnosis of many aortic diseases, this is due to the early detection of penetrating ulcers that were often associated with thickening or enhancement of the aortic wall.

AAP is more frequent in stroke patients of undetermined etiology so it is implicated that aortic plaques have embolic potential. MSCT is more sensitive than TEE in detecting AAP especially relevant one moreover; it is significantly sensitive in detecting the site, size and character of these plaques.

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