Dolichoectasia - A Posterior Circulation, Large Vessel Vasculopathy with Unique Clinical and Radiologic Features

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Abstract

Aim: To determine the frequency and clinicoradiologic features of patients with dolichoectasia in large vessel ischemic cerebrovascular disease in a tertiary referral based stroke population.

Methods: A standardized prospective investigative protocol including brain imaging, angiography and sonography was applied to all cerebrovascular patients (n=1292). Retrospective analysis was performed in patients with stroke or transient ischemic attack with radiological features of dolichoectasia. Comparison was made between large vessel atherosclerotic (LVA) vasculopathies (n=355) and large vessel dolichoectasia (LVDE).

Results: Within the stroke registry, LVDE comprised of 50/1292 (3.9%) with strokes and 10/223 (4.5%) presented with TIA's (p=NS). Risk factor comparison between LVA and LVDE was not significant for gender, age, hypertension, hyperlipidemia, smoking, alcohol excess, ischemic heart disease and diabetes mellitus. Clinical stroke presentation differed significantly for total anterior circulation (TAC) (p=0.002) and partial anterior circulation (PAC) (p=-0.001) being more numerous in LVA. In the LVDE group posterior circulation (POC) ischemia was more numerous (p=<0.0001). Most frequent isolated symptoms in the LVDE group included vertigo (17/60; 28%), ataxia (13/60; 22%), facial weakness (12/60; 20%), diplopia (6/60; 10%). Quantitative neurological deficit by Canadian Neurological Scale (CNS) and disability (Rankin) did not differ significantly between LVDE and LVA. Angiographic abnormalities involved the basilar artery in 47/50 (94%) of the stroke subgroup and 9/10 (90%) of the TIA subgroup of the LVDE group. Posterior circulation lesions were seen in 33/50 (67%) of LVDE and 64/355 (18%) of LVA (p=0.0001). During a 7 year follow up period (mean 4.5 years), recurrent stroke or TIA occurred in 10/50 (20%) in the LVDE as opposed to 8/355 (2.3%) in the LVA group (p=<0.0001). No further sequele occurred in the LVDE group treated with anticoagulation (n=9/10) as opposed to antiplatelet therapy (1 died of myocardial infarct) in a 2.5 year follow up period.

Conclusion: 1. LVDE differs significantly from LVA disease in terms of posterior circulation symptoms, stroke syndromes, brain parenchymal and angiographic features. 2. Recurrent stroke or TIA may be more frequent in LVDE and anticoagulation may be required more often in this subgroup.

Background

Most drug interventions in acute stroke have been negative [1,2]. Those recently published, that are beneficial, have shown a disappointingly small benefit ratio [3-5] implying subgroups in the stroke population may have a differential response. Identification of more precise mechanisms of stroke is necessary.
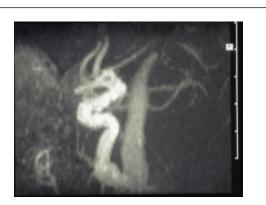
Note the diameter of the basilar is approximately 2.5 times that of the internal carotid arteries (arrows).

Elongation and tortuousity (megadolichoectasia) of the basal intracranial vessels is known to cause cerebral ischemia and infarction, compressive cranial neuropathies, hydrocephalus and a variety of brainstem symptoms [6,7] (Figure 1A and Figure 1B). No distinct clinical syndrome is recognized, probably leading to under diagnosis [6]. The reported incidence is 0.06-5.8% (autopsy and clinical data) but varying criteria have been applied [8,9]. Newer imaging procedures can facilitate the non invasive diagnosis. The entity has not been subject to prospective analysis [6]. The prospective Durban Stroke Data Bank specifically included this as a predefined entity and the results to date are presented.

Methods

Recruitment

All patients with stroke or transient ischemia between October 1992 and October 1998 admitted to a metropolitan acute stroke unit, in Durban South Africa and clinical and investigative data entered into a digitized stroke registry. The protocol was reviewed and sanctioned by the Institutional Review Board of the University of Natal. The definition of stroke was that of the WHO definition of stroke [10] but in addition with appropriate brain scan (CT, MRI or SPECT) changes consistent with stroke were entered into a digitized registry. A transient ischemic attack (TIA) was defined as a sudden onset neurological deficit, reversible within 24 hours with migraine, seizures, cerebral mass lesions and metabolic causes excluded clinically and by appropriate investigations.
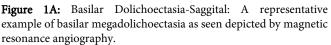
Figure 1A: Basilar Dolichoectasia-Saggital: A representative example of basilar megadolichoectasia as seen depicted by magnetic resonance angiography.

Figure 1B: Basilar Dolichoectasia- Coronal: A representative example of basilar megadolichoectasia as seen depicted by magnetic resonance angiography.

Investigations

The minimum work up included basic stroke relevant blood tests (complete blood count, platelets, serum electrolytes, urea, creatinine, lipogram, erythrocyte sedimentation rate, serum glucose, international normalized ratio (INR), partial thromplastin time (PTT), computed tomography (CT) or magnetic resonance imaging (MRI) brain scan, chest radiograph, electrocardiogram, transcranial Doppler TCD), duplex Doppler sonography, MR angiography and catheter cerebral angiography in selected patients with MR contraindications or appropriate clinical need. Depending on clinical circumstances additional tests included the single photon emission computed tomography (SPECT) scanning, prothrombotic tests, cerebrospinal fluid analysis, Holter monitoring, trans-esophageal cardiac echo and neuropsychological assessment, A category of seldom required tests, included examination for rare, often inherited disorders such as genetic and metabolic causes of stroke and brain biopsy for the diagnosis of suspected cerebral vasculitis.

Radiological dolichoectasia criteria

Basilar dolichoectasia was defined as $\geq$ 4.5 mm diameter of the basilar artery and the position of the artery lying lateral to the margin of the clivus in the cerebellopontine angle or above the level of the suprasellar cistern [11,12]. All radiological diagnoses were corroborated by board certified radiologists. Ectasia of anterior vessels such as the middle and anterior cerebral vessels was arbitrarily defined as at least double the normal diameter of 3 millimeters. The definition of large vessel disease was in accordance with the TOAST classification. Briefly this entailed 50% or more stenosis of an intracranial or cervicocephalic artery by catheter angiography or magnetic resonance angiography.

Standardized Quantifiable Scales

Standardized scales were incorporated into the registry protocol including clinical stroke scale; the Oxfordshire Community Stroke Project Score (OCSP) divided into total anterior circulation (TAC), partial anterior circulation (PAC), lacunar (LAC) and posterior circulation (POC), a neurological deficit scale; the Canadian Neurological Scale (CNS), a handicap scale; the Rankin Disability Scale (R) and an expanded etiopathogenetic (TOAST) classification with categories for large vessel disease, small vessel disease, cardiogenic, undetermined and other. In the "other" category were included probable or presumed causes of stroke after the investigative protocol failed to determine another cause of stroke. Comorbidity was also documented. The other category included strokes in association with; vasculitides, cervicocephalic dissection, aortic arch atheroma, metabolic strokes, drug induced strokes, prothrombotic states, migraine, Moya Moya syndrome, cerebral venous thrombosis and dolichoectasia.

Statistics

For proportions, a univariate analysis was done using Chi-square tests of association. For continuous variables, the t-test was used for significance of means, and the non-parametric median test for judging the significance of differences in median values.

Results

Clinical features

Within the stroke registry (n=1515) stroke (n=1292), TIA (n=223), large vessel dolichoectasia (LVDE) comprised of 50/1292 (3.9%) with strokes and in 10/223 (4.5%) presented with TIA's (p=NS). Risk factor comparison between large vessel atherosclerosis (LVA) and LVDE was not significant for age, gender, hypertension, hyperlipidaemia, smoking, alcohol excess, ischemic heart disease and diabetes mellitus (Table 1).

	LVA (%)	LVDE (%)	P-value
Demographics			
Men	207 (58)	40 (67)	NS
Women	150 (42)	20 (33)	NS
Age (mean)	60.4	62.1	NS
Risk factors			

Hypertension	205 (57)	21 (47)	NS
Hyperlipidaemia	43 (12)	4 (7)	NS
Smoking	129 (36)	20 (33)	NS
Alcohol Excess	31 (8)	5 (8)	NS
Ischemic Heart Disease	95 (26)	11 (18)	NS
Diabetes Mellitus	75 (21)	8 (13)	NS
Clinical Stroke Syndromes			
TAC (total anterior circulation)	62 (17)	1 (2)	0.002
PAC (partial anterior circulation)	201 (56)	17 (34)	0.001
LAC (lacunar)	31 (9)	4 (8)	NS
POC (posterior circulation)	63 (18)	28 (56)	<0.0001
Total	357 (100)	50 (100)	

Table 1: Clinical features–continued

Clinical stroke, as determined by OCSP presentation differed significantly in that TAC (p=0.002) and PAC (p=0.001) were more numerous in LVA. In the LVDE group POC was more numerous (p=<0.0001) (Table 1). The most frequent isolated symptoms in the LVDE group included vertigo (17/60; 28%), ataxia (13/60; 22%), facial weakness (12/60; 20%), diplopia (6/60;10%) with significant differences when compared with the LVA group. Comorbidity with cardiac, small vessel disease and other vasculopathies was established in 12% of the LVA group and 7% of the LVDE group which was not statistically different. Quantitative neurological deficit by the Canadian Neurological Scale (mean score: LVA 10.3, LVDE 10.7) and disability by the Rankin Scale (mean score: LVA 1.9, LVDE 1.7) did not differ significantly (Table 2).

Symptoms/signs (stroke or TIA)			
Vertigo	56 (15)	17 (28)	0.02
Ataxia	25 (7)	13 (22)	0.001
Facial weakness	56 (15)	12 (20)	NS
Diplopia	13 (4)	6 (10)	0.04
Etiology and co-morbidity			
TOAST classification			
Cardiac/SVD/Other	44 (12)	4 (7)	NS
Quantifiable deficit and handicap			
CNS (mean)	10.3	10.7	NS
Rankin Scale (mean)	1.9	1.7	NS

Table 2: Clinical features-continued

Neuroimaging

Angiographic abnormalities of dolichoectasia involved the basilar artery in 47/50 (94%) of the stroke subgroup and 9/10 (90%) of the TIA subgroup of the LVDE group. Posterior circulation lesions were seen on anatomical brain imaging in 33/50 (67%) of LVDE and 64/355 (18%) of LVA (p=0.0001) (Table 3).

	LVA (%)	LVDE (%)	P-value
Anatomical imaging			
Brainstem	15 (4)	19 (38)	<0.0001
Cerebellum	18 (5)	4 (8)	NS
Thalamus	15 (4)	5 (10)	0.08
Occipital regions	28 (8)	3 (6)	NS
Subcortical	106 (30)	106 (30)	NS
Anterior circulation and other	175 (49)	3 (6)	<0.0001
Angiography (MRA or catheter angiography) – vessel dolichoectasia			
Arterial territories			
Basilar artery	-	56 (93)	-
Vertebral artery	-	2 (3)	-
Ant. circulation - carotid	-	1 (2)	-
Ant. circulation - MCA	-	1 (2)	-

Table 3: Neuroimaging

Prognosis and treatment

During a 7 year follow up period (mean 4.5 years), frequency of review occurred 6 monthly, recurrent stroke or TIA occurred in 10/50 (20%) in the LVDE as opposed to 8/355 (2.3%) in the LVA group (p≤0.0001). All were treated with antiplatelet or combination antiplatelet therapy. In a subgroup of LVDE patients, no further sequelae occurred in 9/10 treated with anticoagulation because of recurrent posterior circulation events, as opposed to antiplatelet therapy (1 died of myocardial infarct) in the 2.5 year follow up period.

Discussion

This study represents one of the largest series to date of prospectively evaluated, retrospectively analyzed, dolichoectasia subtype cerebrovascular disease of the cerebral arteries, allowing delineation of the frequencies of different stroke syndromes associated

with LVDE as well as follow up. The diagnosis can easily be made in most cases within the first tier (CT brain or MRI brain scanning) of the investigative protocol with invasive studies rarely required. This is underscored by the fact that the majority of these patients present with posterior circulation ischemia or stroke, a syndrome in which invasive angiography is associated with a significant morbidity and mortality. Although the DSDB is a hospital based registry, the frequency of 3.8% of basilar dolichoectasia is remarkably similar to the only population based study of this entity, namely the 3.1% of the Rochester MN group [13]. The clinical features such as risk factor profile and preponderance of posterior circulation stroke were similar to the only other large study published to date [14].

With respect to the postulated biological mechanism as proposed by Hegedues, Sahlbeck et al and Schwartz et al [6,15-20], the increase in vessel diameter with dilatation, blood flow velocity is reduced and may show a plug of inversion or even zero flow near the vessel wall by transcranial Doppler evidence [6]. Ring shaped layering of thrombus formation occurs with a smaller patent lumen and thrombus may enter origin of small penetrating vessels of 200-800 micrometers and give rise to thrombotic occlusion and lacunar infarction in the setting of large vessel (dolichoectatic) rather than small vessel disease. Embolism to more distal vascular territories is also thought to occur from the layered thrombus in the dilated arteries. Embolism to more distal cortical posterior circulation territories occurred infrequently (6%). Both represent different causes of cerebral infarction due to large artery disease mostly in the context of long standing hypertension which is typically associated with small vessel cerebrovascular disease.

Patients with posterior circulation ischemia or infarction should be evaluated for the presence of dolichoectasia, as this can be done non invasively and secondary preventative treatment is an option with at least Class III evidence as per American Academy of Neurology Practice Parameters [21] of benefit from Coumadin or Aspirin. As most patients in this series were relatively minimally disabled (CNS mean score of 10.7, normal is 11.5 and maximal impairment 0, the opportunity to avoid further strokes by identification of the correct stroke mechanistic diagnosis becomes all the more important. This does not detract from the rare possibility of dissection of the basilar with poor outcome as was seen in one patient. Notwithstanding the limitations of the present study, recurrent stroke appeared more frequently in the LVDE. In a subgroup with recurrent symptoms subsequent anticoagulation patients appeared to thwart events over a 2.5 year follow up, a finding that would need corroboration with randomization and larger numbers in both groups.

More recent clinical reviews revealed similar incidences and associated clinical findings as well as posterior circulation predilection of dilated arteropathies [22-24]. A recent meta-analysis of studies to date confirmed the persistent uncertainty with regards to optimum treatment, whether anti-platelet agents or anticoagulants [23] underscoring the need for a randomized controlled trial in this subgroup of stroke mechanisms.

Conclusion

1. LVDE differs significantly from LVA disease in terms of posterior circulation symptoms, stroke syndromes, brain parenchymal and angiographic features.

2. Recurrent stroke or TIA may be more frequent in LVDE and anticoagulation may be required more often in this subgroup.

References

1. Blecic S, Bogousslavsky J (1995) General management of patients with ischaemic stroke: clinical features and epidemiology. Curr Opin Neurol 8: 30-37.

2. [No authors listed] (1989) Stroke--1989. Recommendations on stroke prevention, diagnosis, and therapy. Report of the WHO Task Force on Stroke and other Cerebrovascular Disorders. Stroke 20: 1407-1431.

3. The International Stroke Trial (IST) (1997) a randomized trial of Aspirin, subcutaneous Heparin, both, or neither among 19435 patients with acute ischemic stroke. International Stroke Trial Collaborative Group. Lancet 349: 1569-1581.

4. [No authors listed] (1997) CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke. CAST (Chinese Acute Stroke Trial) Collaborative Group. Lancet 349: 1641-1649.

5. [No authors listed] (1995) Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med 333: 1581-1587.

6. Schwartz A, Rautenberg W, Hennerici M (1993) Dolichoectatic Intracranial Arteries: Review of Selected Aspects. Cerebrovasc Dis 3: 273-279.

7. Aichner F, Felber S, Birbamer G, Posch A (1993) Magnetic Resonance Imaging and Magnetic Resonance Angiography of Vertebrobasilar Dolichoectasia. Cerebrovasc Dis 3: 280-284.

8. Yu YL, Moseley IF, Pullicino P, McDonald WI (1982) The clinical picture of ectasia of the intracerebral arteries. J Neurol Neurosurg Psychiatry 45: 29-36.

9. Resta M, Gentile MA, Di Cuonzo F, Vinjau E, Brindicci D, et al. (1984) Clinical-angiographic correlations in 132 patients with megadolichovertebrobasilar anomaly. Neuroradiology 26: 213-216.

10. Hatano S (1976) Experience from a multicentre stroke register: a preliminary report. Bull World Health Organ 54: 541-553.

11. Smoker WRK, Price MJ, Keyes WD, Corbett JJ, Gentry LR (1986) High resolution computed tomography of the basilar artery. 1. Normal size and position. AJNR 7: 55-60

12. Smoker WRK, Corbett JJ, Genry LR, Keyes WD, Price MJ, et al. (1986) High resolution computed tomography of the basilar artery. 2. Vertebrobasilar dolichoectasia: Clinical pathologic correlation and review. AJNR 7: 61-72.

13. Ince B, Petty GW, Brown RD Jr, Chu CP, Sicks JD, et al. (1998) Dolichoectasia of the intracranial arteries in patients with first ischemic stroke: a population-based study. Neurology 50: 1694-1698.

14. Passero S, Filosomi G (1998) Posterior circulation infarcts in patients with vertebrobasilar dolichoectasia. Stroke 29: 653-659.

15. Casas Parera I, Abruzzi M, Lehkuniec E, Schuster G, Muchnik S (1995) Dolichoectatic intracranial arteries. Advances in images and therapeutics. Medicina (B Aires) 55: 59-68.

16. Levine RL, Turski PA, Grist TM (1995) Basilar artery dolichoectasia. Review of the literature and six patients studied with magnetic resonance angiography. J Neuroimaging 5: 164-170.

17. Rautenberg W, Aulich A, Röther J, Wentz KU, Hennerici M (1992) Stroke and dolichoectatic intracranial arteries. Neurol Res 14: 201-203.

18. Mizutani T, Aruga T (1992) "Dolichoectatic" intracranial vertebrobasilar dissecting aneurysm. Neurosurgery 31: 765-773.

19. Hegedüs K (1985) Ectasia of the basilar artery with special reference to possible pathogenesis. Surg Neurol 24: 463-469.

20. Sahlbeck R, Busse O, Reinbold WD (1993) MRI findings megadolichoectatic basilar artery. Cerebrovasc Dis 3: 309-312.

21. Coull BM, Williams LS, Goldstein LB, Meschia JF, Heitzman D, et al. (2001) Anticoagulants and antiplatelet agents in acute ischemic stroke. Report of the Joint Stroke Guideline Development Committee of the American Academy of Neurology and the American Stroke Association. Neurology 59: 13-23.

22. Nakamura Y, Hirayama T, Ikeda K (2012) Clinicoradiologic features of vertebrobasilar dolichoectasia in stroke patients. J Stroke Cerebrovasc Dis 21: 5-10.

23. Wolters FJ, Rinkel GJ, Vergouwen MD (2013) Clinical course and treatment of vertebrobasilar dolichoectasia: a systematic review of the literature. Neurol Res 35: 131-137.

24. Passero SG, Rossi S (2008) Natural history of vertebrobasilar dolichoectasia. Neurology 70: 66-72.