Dolichoectasia - an easily identifiable and potentially treatable stroke mechanism

The Durban Cerebrovascular Data Bank (DCDB) experience

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Abstract

Intracranial artery dolichoectasia is recognised as an underdiagnosed yet potentially treatable stroke mechanism. A prospective analysis of patients in the Durban Cerebrovascular Data Bank (n=762) was undertaken over a 4 year period and 32 patients identified as meeting established criteria. No significant difference was found between those patients presenting with stroke as opposed to transient ischaemic attacks. There was a trend to a preponderance in males and most patients had hypertension and presented with posterior circulation ischaemia or infarction. All patients were identified by first tier investigation with conventional brain scanning (MRI or CT) but contemporary imaging modalities such as MRA and transcranial Doppler sonography aided in the diagnosis. Six patients were treated with anticoagulation after failing antiaggregant therapy with aspirin with no recurrent events over a 15.6 mean month follow up period.

Background

Most drug interventions in acute stroke have been negative.[1,2] Those recently published, that are beneficial, have shown a disappointing small benefit ratio [3-5] implying subgroups in the stroke population may have a better or worse response. Sroke in itself is considered too generic for a single treatment to be effective and the focus appears to be emerging that we will need to identify mechanisms of stroke to tailor treatment more effectively, clinically and to save cost.

Elongation and tortuosity (dolichoectasia) of the basal intracranial vessels is known to cause cerebral ischaemia and infarction, compressive cranial neuropathies, hydrocephalus and a variety of brainstem symptoms.[6,7] Megadolichoectatic basilar artery syndromes have been the most extensively studied by autopsy, angiography, CT and MRI. No distinct clinical syndrome is recognised, probably leading to under-diagnosis.[6] The reported incidence is 0.06-5.8% 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]

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The prospective Durban Cerebrovascular Data Bank specifically included this as a predefined entity and the results to date are presented.

Methods

Recruitment

All patients with stroke or transient ischaemia between October 1992 and October 1996 admitted to a Durban metropolitan acute stroke unit were recruited for the study. The definition of stroke was that of the WHO definition of stroke[10] but in addition those with appropriate brain scan (CT, MRI or SPECT) changes consistent with stroke were entered into a digitised registry. A transient ischaemic 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.

Investigations

A three tier investigative protocol was used, incorporating a basic minimum workup, tests often used and tests seldom used. The latter two tiers were used as appropriate - tailored to each individual patient's conundrum of clinical details. The minimum workup included basic stroke relevant blood tests - complete blood count, platelets, serum electrolytes, urea, creatinine, lipogram, erythrocyte sedimentation rate, serum glucose, International Normalised Ratio (INR), partial thromboplastin time (PTT), brain scan (CT or MRI), chest radiograph and electrocardiogram. Additional workup when appropriate, the second tier, included transcranial Doppler, duplex Doppler sonography, MR angiography, SPECT scanning, in-depth neuropsychological assessment, prothrombotic tests, cerebral angiography, cerebrospinal fluid analysis, Holter monitoring and trans oesophageal cardiac echo. A category of seldom required tests, the third tier, included examination for rare, often inherited disorders (including homocystinuria, sickle cell disease, haemoglobinopathies, mitochondrial cytopathies, other genetic and metabolic causes of stroke) and brain biopsy to diagnose some of the vasculitides is also catered for.

Neurological scales and classifications

To enable comparison with other data banks and stroke trials, the stroke patients were further categorised into several standardised scales incorporated into the registry protocol. These are a 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 disability scale; the Barthel Index (BI), a handicap scale; the Rankin Disability Scale (R); and an expanded aetiopathogenetic (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. All patients were assessed clinically and a final diagnosis made with all available investigative data by the same cerebrovascular neurologist.

For a diagnosis to be made within the framework of the extended TOAST classification, the diagnosis needed to be one of exclusion in which all clinically indicated tests, according to the hierarchical protocol, were negative save for the factor in question. It is acknowledged that some would be definite diagnoses, some probable and some possible by this method.

Radiological dolichoectasia criteria

Ectasia=>4.5mm diam

Basilar artery lies lateral to the margin of the clivus in the cerebellopontine angle or above the level of the suprasellar cistern. [11,12]

Cognitive testing

This was deemed to be important so as not to miss the true extent of neurological deficit as this is not reflected adequately in the current neurological scales. A HCFD screening examination is applied to all alert patients in the DCDB in the first two weeks of presentation. Neuropsychological testing is performed in those alert patients with mild deficits on bedside testing or where the screening examination suggests but does not decisively delineate a syndrome. A formal battery of neuropsychological tests was administered to 70 of the 762 patients of the DCDB by these criteria by the same neuropsychologist within one month of the stroke onset.

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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

The dolichoectasia radiographic diagnoses were sought in stroke (n=762) and TIA patients (n=312) and were not significantly different in terms of frequencies or mean age. Gender differences attained marginal significance (Table I). Hypertension was by far the most common vascular risk factor (Table II) and the most common syndrome presentation was a posterior circulation presentation (Table III). In addition, however, isolated symptoms such as facial neuralgias, dysesthesias, parethesias, vertigo, facial paresis (Bell's palsy), ataxia, and diplopia were noted (Table III). Anatomical brain scan imaging revealed posterior circulation infarcts in 69% of the dolichoectasia stroke subgroup with multiple infarcts also seen anteriorly in 31% of the stroke subgroup. Ventriculomegaly was noted in 4 patients and was thought to be an aetiopathogenetic factor in 3 of the 4 patients who presented with a frontal lobe syndrome.

Table I: Demographics

	Stroke	TIA	P value
Number	762	312	
Radiological evidence of dolichoectasia (%)	27 (3.5)	5 (1.6)	0.108 (NS)
Gender (male/female)	22/5	2/3	0.093*
Age range stroke group (mean age)	43-81(66)	45-73(62)	0.191(NS)

* Marginal significance (Fisher's Exact Test)

Table II: Associated medical and neurological conditions in the stroke cohort

Hypertension	24
Hyperlipidaemia	10
Smoking	8
Alcohol excess	5
Ischaemic heart disease	4
Diabetes	3

Table III: Clinical presentations

i) Syndromes	
Posterior circulation	16
Anterior circulation	6
Frontal lobe syndrome	3
Lateral medullary syndrome	1
ii) Isolated symptom (1 or 2 of the following)	
Facial neuralgias, dysesthesias or parethesias	5
Vertigo	4
Bell's palsy	3
Imbalance/ataxia	3
Diplopia/polyopia	3
Exertional headache	3
Tinnitus	2
Hemifacial spasms	2
Pulsating neck mass with bruit	1

With respect to the aetiopathogenetic diagnoses according to the TOAST classification, all received the label of "Other" but concomitant pathology was diagnosed in 9 patients. These included 4 cardiac, 2 with significant carotid stenosis, 1 with small subdural haematoma, 1 with facial herpes Zoster vasculitis and 1 with sleep apnoea syndrome with a respiratory disturbance index of 17 diagnosed by polysomnography.

The radiographic investigations listed in Table IV reveal that all patients' dolichoectasia were diagnosed by parenchymal brain imaging. Those that required angiography, both invasive and non-invasive, had these for reasons of comorbidity and for verification of the diagnosis. TCD revealed a typical low velocity, high pulsatility signal in the majority (72%) of patients in whom this investigation was done.

Table IV: Radiological investigations

i) Brain parenchymal imaging and angiography (MRA, catheter angiography, spiral CT)		
Arterial territories	**n**	**%**
Basilar artery	32	(100)
Vertebral artery	2	(6)
Anterior circulation - carotid	1	(3)
Anterior circulation - middle cerebral arteries	1	(3)
Aortic arch with "Shaggy aorta syndrome"	1	(3)
ii) Brain parenchymal imaging abnormalities in the stroke cohort (CT and MRI)		
Posterior circulation infarcts	27	(100)
Multiple	18/26	(69)
Ventriculomegaly	4/31	(13)
iii) Sonography - Transcranial Doppler		
Low velocity and increased pulsatility	18/25	(72%)

In the stroke cohort, patients generally presented with minimal deficit as evidenced by the Canadian Neurological Scale mean value of 10.7 (maximum score is 11.5, minimum 0). Table V reveals the preponderance of posterior circulation infarction as defined by the standarised OCSP scale.

Table V: Clinical neurological scale (OCSP)

	n	(%)
POC	19	(70)
PAC	5	(19)
LAC	2	(7)
TAC	1	(4)
	27	(100)

POC - posterior circulation
PAC - partial anterior circulation
LAC - lacunar
TAC - total anterior circulation

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Treatment

All patients except one (who was thought to have dissection of the basilar artery and possible subarachnoid haemorrhage) received aspirin in the first instance. In 6 patients who had recurrent symptoms while on aspirin (aspirin failures), including recurrent strokes in 4, warfarin was instituted with an INR range of 2.0-3.0. Over a mean period of 15.6 (range 3-36) months no further symptoms were reported in these 6 patients.

The figures represent typical examples of vertebrobasilar dolichoectasia as imaged by contrast enhanced brain CT scanning, MRI brain scanning and MRA. Figures 1 and 2 show two different appearances of the dilated and laterally displaced basilar artery on contrast enhanced CT scanning. Figure 3 shows a very large (megadolichoectatic basilar artery) in coronal T2 weighted MRI image and Figure 4 an example of basilar dolichoectasia as seen on MRA.

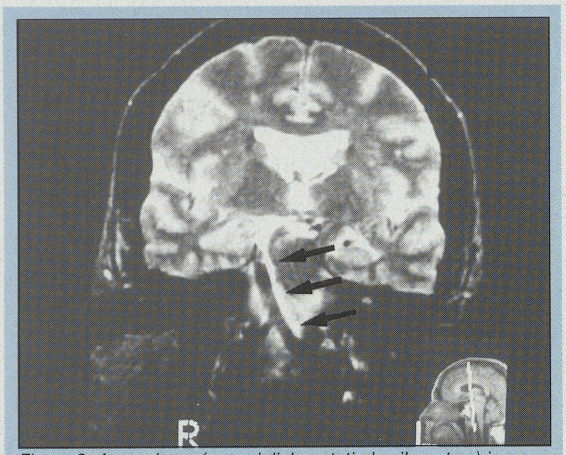

Figure 3: A very large (megadolichoectatic basilar artery) in coronal T2 weighted MRI image.

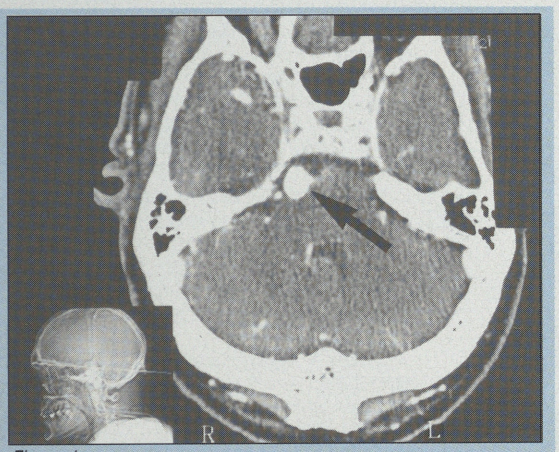

Figure 1

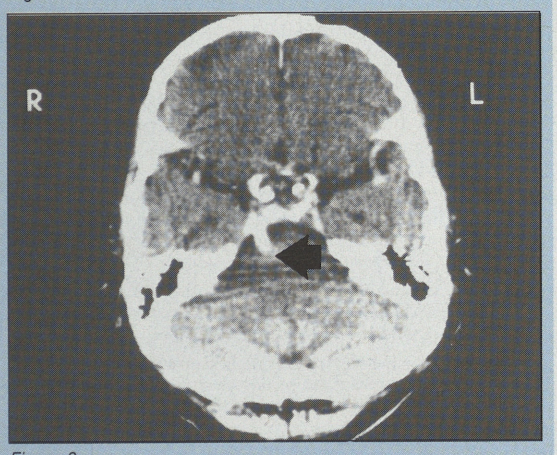

Figure 2

Figures 1 and 2: Two different appearances of the dilated and laterally displaced basilar artery on contrast enhanced CT scanning.

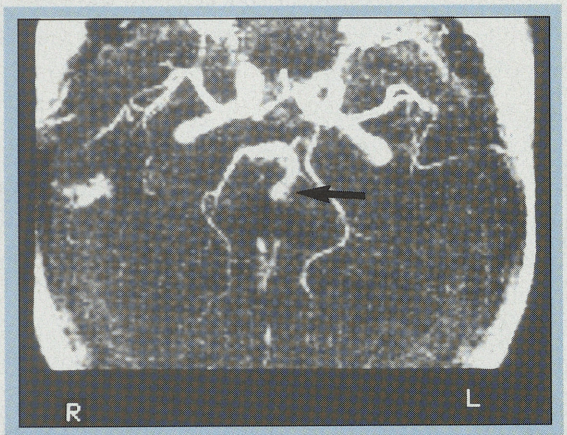

Figure 4: An example of basilar dolichoectasia as seen on MRA.

Discussion

This study represents one of the largest series and one of few prospectively evaluated consecutive case series within a large data bank series of dolichoectasia of the cerebral arteries. This has allowed delineation of the frequencies of different stroke syndromes associated with this disorder as well as follow up i.e. posterior circulation stroke and/or isolated symptoms such as facial paresis (Bell's palsy), facial neuralgia and hemifacial spasm. The diagnosis can easily be made in most cases within the first tier (CT brain or MRI brain scanning) of the investigative protocol, negating the necessity of resorting to invasive studies. This is an important clinical point as the majority of these patients present with posterior circulation ischaemia or stroke, a syndrome in which invasive angiography is associated with a significant morbidity and mortality.

In this series all patients were identified by CT or MRI brain scanning. MRA was done in 6 patients, catheter angiography in 3 and spiral CT in 1. Angiography in these 10 patients was used to better delineate the ectatic arteries and confirm the diagnosis, the latter often necessitated by the presence of comorbidity. Transcranial Doppler sonography has a specific wave form associated with this syndrome and in agreement with Rautenberg *et al* [6], in this study it was found to be a useful adjunctive test in cases where there may be some doubt as to the presence of dolichoectasia.

In agreement with the other larger series on this topic[13-16], the three main modes of clinical presentation - ischaemic, cranial nerve compression and mass effect - were noted, albeit mostly ischaemic (85%). In the ischaemic

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group the vast majority presented with posterior circulation strokes (63%). Patients with posterior circulation ischaemia 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 Class III evidence (Appendix) of benefit from warfarin or aspirin. As most patients in this series were relatively minimally disabled (CNS mean score of 10.7), the opportunity to avoid further strokes by identification of the correct stroke mechanism becomes all the more important. This does not detract from the rare possibility of dissection of the basilar artery with poor outcome as was seen in one patient. With respect to the postulated biological mechanism as proposed by Hegedues, Sahlbeck *et al* and Schwartz *et al* [6, 17,18], 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 (transcranial Doppler evidence).[6] Ring shaped layering of thrombus formation occurs with a smaller patent lumen and the thrombus may enter the 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. 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 disease.

In conclusion, dolichoectasia as a stroke mechanism can be diagnosed non-invasively with established brain parenchymal scanning and with greater accuracy with newer imaging modalities such as MRA and TCD. It should be suspected in patients presenting with posterior circulation ischaemia or stroke syndrome, particularly if hypertensive and associated with one or more of the symptoms in Table III. The diagnosis is important as it usually necessitates additional specific therapy such as anticoagulation with warfarin and, in some, antiaggregant therapy with aspirin, dipyridamole or ticlopidine.

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Appendix

Posterior circulation (one or more of the following)

Dizziness, vertigo, nausea, vomiting, drop attacks, diplopia, tinnitus, bilateral weakness or numbness, hiccoughing, imbalance, ataxia, blurring of vision.

Anterior circulation (one or more of the following)

Unilateral weakness and/or numbness, aphasia, apraxia, anosognosia, aprosodia, neglect syndrome, visuospatial impairment.

Levels of evidence from clinical trials (adapted from the American Academy of Neurology)

Level I. Evidence provided by means of one or more well designed randomized controlled clinical trials. Low false positive (alpha or specificity) and low false negative (beta or sensitivity) errors.

Level II: Evidence provided by one or more well designed observational studies with concurrent controls such as case control and cohort studies. Also data from randomized trials with high false positive (alpha) and a high false negative (beta) errors.

Level III: Evidence provided by expert opinion, case series, case reports and studies with historical controls.

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