Carotid-Bulb Atypical Fibromuscular Dysplasia in Young Afro-Caribbean Patients With Stroke

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Background and Purpose—An atypical form of fibromuscular dysplasia located in the internal carotid-bulb (CaFMD) is thought to be uncommon and is poorly described as a cause of ischemic stroke in the young. This study aimed to obtain a better description of CaFMD in Afro-Caribbean population, who could be particularly affected by it.

Methods—This study included consecutive patients <55 years consulting at Fort-de-France University Hospital Stroke Center (Martinique, FWI) found to have CaFMD as the only cause after a comprehensive work-up. CaFMD was diagnosed when computed tomographic angiography showed a bulbar spur without calcification.

Results—Twenty-five patients with stroke and CaFMD were identified. Computed tomographic angiography showed 2 CaFMD patterns: a thin (n=15) or thick (n=10) spur. Three patients initial computed tomographic angiography images showed a mural thrombus overlying the CaFMD. CaFMD was surgically removed from 7 of 25 and 20 of 25 patients who received antiplatelet therapy; after mean follow-up of 25.3±19.5 months, their respective recurrence rates were 0% and 30%.

Conclusions—CaFMD could be a common condition in young Afro-Caribbeans with carotid-territory ischemic stroke. Recurrences were frequent under antiplatelet treatment, while surgical CaFMD removal seemed more effective.

Key Words: blacks ■ fibromuscular dysplasia ■ stroke ■ young adult

Fibromuscular dysplasia (FMD) is a rare ischemic stroke-associated arterial disease commonly described in middle-aged white women. It’s typical appearance is that of the distal internal carotid as a string of beads. Another type of FMD, called septae, diaphragm, or atypical FMD has been reported anecdotally, mainly in blacks or in Asians. Atypical FMD is focal, located in the carotid-bulb (CaFMD) or, more rarely, the vertebral artery, predominantly involves the intima, and its angiographic image resembles a spur, usually on the posterolateral side of a megabulb. Curiously, all but one report on CaFMD are not recent, which might explain our suboptimal knowledge about this cause of stroke affecting the young and potentially recurrent.

Because Martinique, a French West Indies island, is inhabited mostly by Afro-Caribbeans, we expected to find CaFMD responsible for ischemic strokes in young Martinicans. Therefore, we systematically sought CaFMD in young patients with stroke. Herein, we describe the findings of the first 5 years of this study.

Methods
The study, conducted in the Fort-de-France University Hospital Stroke Center, Martinique, lasted 5 years (January 2008 to February 2013). Inclusion criteria were age ≤55 years, defining young; nonlacunar carotid-territory infarction downstream from CaFMD; CaFMD as described above on computed tomographic angiography (CTA) images; no other stroke cause after comprehensive work-up, including brain MRI within 48 hours, transthoracic and transesophageal echocardiographies, 24-hour ECG Holter, routine biological tests, carotid and vertebral duplex ultrasound (DUS) and extracranial artery CTA; and no evidence of calcification or patent atherosclerosis of extra-intracranial arteries. This 5-year study had 2 phases: during part 1 (January 2008 to October 2011), CTA was done only when DUS showed a mural thrombus overlying the CaFMD. CaFMD was surgically removed from 7 of 25 and 20 of 25 patients who received antiplatelet therapy; after mean follow-up of 25.3±19.5 months, their respective recurrence rates were 0% and 30%.

Conclusions—CaFMD could be a common condition in young Afro-Caribbeans with carotid-territory ischemic stroke. Recurrences were frequent under antiplatelet treatment, while surgical CaFMD removal seemed more effective.

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Results
During 5 years, 25 patients with CaFMD were included in this study, 10 during part 1 and 15 during part 2. These patients baseline characteristics were as follows: mean age, 45.7±6.5 years; 9 men and 16 women; mean admission National Institutes of Health Stroke Scale score, 6.3±6.7; 68% without vascular risk factors; mean 3-month modified Rankin Scale score at 3 months, contacted by phone every 6 months and updated in December 2013.

Discussion
CaFMD could be a common cause of ischemic stroke in the young. It is a disease mainly affecting young Afro-Caribbeans living in Martinique, French West Indies. This disease is poorly described and its recurrence appears frequent. CaFMD is a true cause of ischemic stroke and surgery is necessary to prevent further attacks.
Rankin Scale score 1.36±1.2, with 5 patients functionally dependent (modified Rankin Scale, ≥3); and mean follow-up 25.3±19.5 months. Among patients receiving only antiplatelets, 6 of 20 (30%) experienced another ischemic event in the same carotid-territory: 3 major strokes (National Institutes of Health Stroke Scale, >10), 2 minor strokes (National Institutes of Health Stroke Scale, <4) and 1 transient ischemic attack. Median time to recurrence was 12 months, with the earliest occurring at 1 month and all others after ≥6 months: 4 recurrences during study part 1 and 2 during part 2, with respective mean times to recurrence of 18 and 3.5 months. According to Kaplan–Meier survival analysis, the 1-, 2-, and 3-year recurrence rates in medically treated patients were 20% (95% confidence interval, 2.6–37.4), 27.3% (95% confidence interval, 6.3–48.3), and 36.4% (95% IC, 11.7–61.1).

During study part 2, 2 part-1 patients with recurrent strokes and 5 new-stroke patients underwent successful CaFMD surgical excision. No recurrences occurred after surgery during the median postoperative follow-up of 14 months.

Among the 21 of 25 patients with DUS, 18 of 21 had mostly inconspicuous bulbar outgrowths. The 25 patients’ CTA longitudinal views showed 2 CaFMD patterns: a thin spur (15 patients, including 4 histologically proven) or a thick spur (10 patients, including 3 histologically proven; Figure 1). For 3 patients, the spur was visualized only on a second CTA obtained after 3 months of oral anticoagulation, whereas the initial CTA feature had been consistent with a mural thrombus superimposed on the spur (Figure 2). For all 25 patients, atypical FMD was located on the posterolateral side of an internal carotid megabulb. Finally, 1 patient underwent conventional angiography, which visualized transient contrast-medium stagnation within a CaFMD.

The 7 surgical patients’ specimens exhibited the same pathological changes. The arterial wall was disorganized, comprised a loose matrix with edematous tissue and sparse spindle cells, especially in the outgrowth, resulting in intimal hyperplasia. The media was only minimally involved, with discreet depletion of elastic fibers replaced by fibrous tissue. No inflammatory infiltrate, calcifications, or thrombus was observed (Figure 3). The final diagnosis was intimal CaFMD.

**Discussion**

Herein, we described the largest case series of 25 young Afro-Caribbean patients with stroke and CaFMD, collected >5 years. CaFMD was apparently a common cause of potentially devastating, ischemic strokes in young Martinicans; with 30% recurrences under antiplatelet therapy. Two major questions are discussed. How robust are the arguments for the causal role of CaFMD in cerebrovascular events? How should this anomaly, which can be subtle, be detected?

We hypothesize that blood stagnation leads to thrombus formation within CaFMD, followed by artery-to-artery embolism.
Indeed, conventional angiography showed transient blood stagnation in 1 patient. Notably, intra-CaFMD thrombi were found during surgery or autopsy.\(^2\) Although no thrombus was ever found in our 7 surgical patients, the 3 others’ CTAs showed evolutive images suggestive of an overlying thrombus trapped in the CaFMD and disappearing under oral anticoagulation. Finally, that explanation is supported by the absence of recurrences in operated patients, unlike those treated medically.

CaFMD may produce only subtle nonspecific changes on DUS. Although DUS has the advantage of being widely available, no specific changes were seen, mainly a mild bulbar outgrowth possibly misdiagnosed as fibrotic plaque. Moreover, CaFMD can easily be missed on DUS. CTA anomalies may also be subtle or confused with plaque. However, some images evoked CaFMD: a thin\(^2,6,7\) or thick\(^8\) spur, located on the posterolateral side of the bulb, megabulb appearance\(^2\) and no carotid calcification. Moreover, the absence of vascular risk factors in 68% of our young patients is not suggestive of atherosclerosis.

Our study has several limitations. CaFMD was histologically proven for only 7 of 25 patients. However, the other 18 patients’ CTA images were indistinguishable from histologically proven CaFMD. The 25-month mean follow-up is probably too short to detect all recurrences, thereby possibly underestimating recurrent events. Obviously, additional studies, including more histologically proven CaFMD and longer follow-up, are required. In Martinique, we undertook this systematic search for CaFMD in young patients with stroke as a starting point.

In conclusion, CaFMD could be a common cause of carotid-territory ischemic stroke in young Afro-Caribbeans and surgical removal could be a therapeutic option\(^3\) to limit recurrent strokes.

Disclosures

None.

References

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