Angiographic Spectrum of Cervical and Intracranial Fibromuscular Dysplasia

ANNE G. OSBORN, M.D. AND ROBERT E. ANDERSON, M.D.

SUMMARY Cephalocervical or intracranial fibromuscular dysplasia (FMD) can be identified by its characteristic angiographic appearance. Most of these lesions occur adjacent to the C3-2 interspace, characteristically sparing the origins and proximal segments of the major extracranial vessels. Approximately 65% of our patients had bilateral involvement of the cervical internal carotid arteries. Thirty percent were associated with symptoms of either subarachnoid hemorrhage or focal cerebral ischemia.

FIBROMUSCULAR DYSPLASIA (FMD) is a non-atheromatous angiopathy of unknown etiology. Originally thought to involve only the renal arteries, FMD has been identified in a large number of small and medium-sized arteries and — most recently — in the renal and mesenteric veins. Cephalocervical arterial fibromuscular dysplasia is relatively uncommon, usually affecting only the extracranial internal carotid and vertebral arteries. Intracranial FMD is rare, with only sporadic cases reported in the literature. In many of these reported cases FMD was limited to the intrapetrosal internal carotid artery or involved only the carotid siphon. Hence, true intradural intracranial FMD is distinctly uncommon.

We present a series of 25 patients illustrating the broad spectrum of angiographic findings in cephalocervical fibromuscular dysplasia. Included in the series are four cases of true intracranial FMD. Serious clinical sequelae are often associated with this angiopathy.

Patients

Twenty of the 25 patients were females. Their ages ranged from four to 71 years, with an average age of 45.6 years. All but one patient presented with cerebrovascular symptoms indicating significant clinical disease (table 1). Ten of the 25 patients had transient ischemic attacks and six had definite cerebral infarctions. Nine patients had had documented episodes of subarachnoid hemorrhage. All angiograms were selective studies and were performed via the transfemoral approach.

Angiographic Findings

The angiographic findings are summarized in table 1. Seventeen of the 25 patients had isolated cervical FMD affecting one or both internal carotid arteries, while an additional patient had both cervical and intracranial disease. Two patients had diffuse FMD affecting both vertebral arteries and the left internal carotid artery, while four additional patients had FMD affecting all four vessels. The involvement was bilateral in approximately 65% of all cases where both internal carotid arteries were examined. Thirty percent were associated with intracranial aneurysm.

Cervical fibromuscular dysplasia

With one exception all cervical lesions were in the midportion of the internal carotid or vertebral artery adjacent to the first and second cervical vertebrae. The common carotid bifurcation and proximal internal carotid artery were spared in all these patients.

An angiographic pattern of multiple arterial dilatations separated by irregularly spaced concentric stenoses was found in eighteen (fig. 1A, B). An additional patient demonstrated this characteristic pattern in one internal carotid artery while smooth tubular stenosis, involving a long segment, was found in the contralateral internal carotid artery (fig. 2). The angiographic diagnosis of tubular FMD was documented at surgery in this artery.

One patient had typical FMD in one cervical internal...
<table>
<thead>
<tr>
<th>Patient #</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical presentation</th>
<th>Angiographic findings</th>
<th>Pathology</th>
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<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>F</td>
<td>Left homonymous hemianopsia</td>
<td>“String of beads”, right supraclinoid internal carotid artery and right middle cerebral artery</td>
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<td>2</td>
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<td>F</td>
<td>CVA</td>
<td>Unilateral “string of beads”, cervical internal carotid artery</td>
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<td>Right homonymous hemianopsia</td>
<td>“String of beads,” left posterior cerebral artery with occluded distal branch</td>
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<tr>
<td>4</td>
<td>43</td>
<td>M</td>
<td>Subarachnoid hemorrhage</td>
<td>Anterior communicating artery aneurysm. Bilateral cervical ICA “String of beads”</td>
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<tr>
<td>5</td>
<td>68</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>Anterior communicating artery aneurysm. Bilateral cervical ICA “string of beads”</td>
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<tr>
<td>6</td>
<td>50</td>
<td>F</td>
<td>Subarachnoid hemorrhage</td>
<td>Anterior communicating artery aneurysm. Bilateral cervical ICA “string of beads”; no aneurysm found. Unilateral renal FMD</td>
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<td>7</td>
<td>47</td>
<td>F</td>
<td>Left hemiparesis</td>
<td>Unilateral long segment smooth stenosis cervical ICA. Contralateral “string of beads”</td>
<td>Intimal fibroplasia</td>
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<td>8</td>
<td>71</td>
<td>F</td>
<td>Scintillating scotomata</td>
<td>“String of beads”; right cervical ICA. Bifurcation normal. Left carotid not studied</td>
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<td>9</td>
<td>56</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>“String of beads” left cervical ICA. Atypical FMD involving contralateral ICA opposite CI-2</td>
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<td>55</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>Bilateral ICA “string of beads”</td>
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<td>11</td>
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<td>Left hemiparesis, hypertension</td>
<td>“String of beads”, right middle cerebral artery. Typical FMD involving both renal and superior mesenteric arteries</td>
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<td>12</td>
<td>45</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>Fibrous septum at origin right ICA with intraluminal thrombus</td>
<td>Fibromuscular hyperplasia</td>
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<tr>
<td>13</td>
<td>50</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>“String of beads”, both cervical ICA’s. Severe, bilateral renal FMD “String of beads”, both cervical ICA’s. Renal, mesenteric arteries normal</td>
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<td>14</td>
<td>63</td>
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<td>Bilateral cerebral infarcts</td>
<td>Bilateral cervical ICA “string of beads”. Posterior communicating artery aneurysm. Bilateral renal FMD</td>
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<td>15</td>
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<td>Subarachnoid hemorrhage</td>
<td>Bilateral cervical ICA “string of beads”. renal, mesenteric arteries normal</td>
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<td>16</td>
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<td>Tinnitus, dizziness</td>
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<td>17</td>
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<td>Bilateral cervical ICA “string of beads”</td>
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<td>18</td>
<td>45</td>
<td>F</td>
<td>Subarachnoid hemorrhage</td>
<td>Unilateral ICA tubular FMD. Posterior communicating artery aneurysm</td>
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<td>19</td>
<td>52</td>
<td>F</td>
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<td>Bilateral cervical ICA “string of beads”. Right posterior communicating artery aneurysm. Renal, mesenteric arteries normal</td>
<td></td>
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<tr>
<td>20</td>
<td>58</td>
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<td>CVA, hypertension</td>
<td>Bilateral cervical ICA, bilateral vertebral “string of beads”. Unilateral renal FMD</td>
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<tr>
<td>21</td>
<td>30</td>
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<td>Left hemiplegia</td>
<td>Left internal carotid tubular FMD. Right carotid and vertebrobasilar system were normal. Renal arteries were not examined</td>
<td></td>
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<tr>
<td>22</td>
<td>41</td>
<td>M</td>
<td>Multiple transient ischemic attacks</td>
<td>Bilateral internal carotid atypical FMD. Right cavernous ICA aneurysm. Vertebrobasilar, renal arteries normal</td>
<td>Abnormally thickened media, internal carotid artery, with cervical aneurysm resected</td>
</tr>
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Dysplasia is now recognized as one of the more common non-atherosclerotic causes of carotid artery stenosis. The pathological features of this angiopathy have been extensively reviewed. Three distinct histological types of FMD have been identified: intimal fibroplasia, medial fibroplasia or fibromuscular hyperplasia, and subadventitial hyperplasia.

Discussion

First identified angiographically in 1964, fibromuscular dysplasia is now recognized as one of the more common non-atherosclerotic causes of carotid artery stenosis. The pathological features of this angiopathy have been extensively reviewed. Three distinct histological types of FMD have been identified: intimal fibroplasia, medial fibroplasia or fibromuscular hyperplasia, and subadventitial hyperplasia.

A review of the literature plus analysis of our own series demonstrated three characteristic angiographic patterns associated with cephalocervical FMD (fig. 8).

By far the most common finding — considered pathognomonic of FMD by many investigators — is the so-called "string of beads" appearance (type 1, fig. 8). This pattern was seen in approximately 80% of our patients (c.f. table 1) and the roentgenographic appearance is created by multiple irregularly spaced concentric constrictions with normal or dilated intervening segments in the involved vessel. Medial fibroplasia is the most common histological type of FMD associated with this angiographic finding. The angiographic differential diagnosis includes stationary arterial waves or circular spastic contractions (fig. 9) of the extracranial carotid and vertebral arteries. In these latter entities the constrictions are more regular, evenly spaced, and occur without the dilatation of intervening segments so typical of FMD.

A second, much less common, roentgenographic pattern is unifocal or multifocal tubular stenosis (type 3, fig. 8). This angiographic finding was present in three of our patients as well as approximately seven percent of those reported in the literature (fig. 8). These smooth, concentric tubular lesions are less specific than the "string of beads" appearance and can be associated with any histological type of FMD. The angiographic differential diagnosis includes Takayasu’s arteritis, arterial hypoplasia, diminished vessel caliber secondary to decreased distal blood flow, and vascular spasm from the catheterization itself. Takayasu’s and other arteritides involving the aortic arch and its major vessels usually affect the origins and proximal segments of the aortic branches. Arterial hypoplasia, diminished vessel caliber secondary to decreased distal blood flow, and vascular spasm can usually be identified by their associated angiographic abnormalities. Atherosclerotic lesions usually involve the proximal 1–2 cm of the internal carotid arteries or the origin of the arch vessels themselves. FMD characteristically spares the origins and proximal segments of these vessels.

A third angiographic type of FMD has been termed "atypical fibromuscular dysplasia" by Houser et al.
Figure 1. Common carotid angiogram, early arterial phase, in a middle-aged female with fibromuscular dysplasia. A: AP view. B: Lateral view. The multiple irregular, concentric stenoses of the internal carotid artery (arrows) form the typical "string of beads" appearance associated with fibromuscular dysplasia. The location opposite Cl-2 is characteristic of FMD. Note that the carotid bifurcation and proximal internal carotid artery are normal.
Common carotid angiogram, early arterial phase, lateral view, in a 47-year-old female. A long segment of smooth, concentric tubular stenosis is present (arrows). The lesion spares the carotid bifurcation and extends superiorly to the level of the petrous carotid canal. Fibromuscular dysplasia was documented at surgery. Usually only one wall of the affected segment is involved and shows a diverticulum-like smooth or corrugated outpouching. As with our patient #22, the diverticulae may enlarge progressively and become true saccular aneurysms of the affected vessel. The angiographic findings in atypical FMD are non-specific and may be indistinguishable from atherosclerosis or post-traumatic aneurysm of the internal carotid artery. Again, atherosclerosis usually involves the proximal internal carotid artery, while the lesions of FMD are typically located adjacent to the Cl-2 level.

As with our patients #7 and #9, the typical “string of beads” appearance may be identified in one internal carotid artery while either tubular or atypical FMD is present in the contralateral vessel. FMD of the intracerebral vessels is rare. While none of our cases was biopsy-proven, one was associated with typical lesions in the extracranial internal carotid arteries, one had typical FMD of the renal and superior mesenteric arteries and the other two demonstrated classical angiographic findings of FMD. While granulomatous angiitis and related entities may resemble the “string of beads” appearance considered characteristic for FMD, the clinical presentation of these vasculitides is quite different. Granulomatous angiitis ordinarily terminates fatally in one to twelve months and characteristically spares the extracranial vessels.

The clinical significance of FMD is becoming increasingly apparent. While early authors regarded cephalocervical FMD as primarily an incidental angiographic finding, evidence that this lesion can be associated with significant clinical disease is accumulating. Boudin, Guillard and Romion have correctly pointed out that the precise nature of this relationship is unclear. The first reported cases of cephalocervical FMD were identified in patients undergoing cerebral angiography for such lesions as intracranial neoplasm, subarachnoid hemorrhage, or trauma. In our series, all but one patient had symptoms indicative either of subarachnoid hemorrhage or focal cerebral ischemia. In several of our patients with cervical FMD, distal intracranial branch occlusion was documented at angiography. In two additional instances, surgical excision or dilatation of the affected segment was associated with cessation of the symptoms.

Review of the literature indicates that almost two-thirds of reported patients also had definite cerebrovascular symptomatology. Nonetheless, caution should be exercised in postulating a definite causal relationship between cerebrovascular symptoms and the presence of FMD. The exact incidence of asymptomatic cephalocervical FMD is unknown, although Stanley et al. found ten
FIGURE 3. Common carotid angiogram, early arterial phase in a 56 year old female. A: AP view. B: Lateral view. A corrugated diverticulum-like outpouching is present and probably represents atypical FMD. The "string of beads" pattern of FMD was found in the contralateral internal carotid artery.
cases of "extra-renal fibrodysplastic lesions" out of 152 patients with FMD.

The number of renal lesions associated with cephalocervical FMD may be higher than previously suspected. Stanley et al. found concomitant renal lesions in five of 17 patients with cephalocervical FMD. Ten of our patients had abdominal angiography at the time of the cerebral study; renal lesions typical of FMD were found in six patients (fig. 10). Four of these six patients had long-standing hypertension.

Little is known about the natural history of fibromuscular dysplasia. Long-term follow-up of renal FMD has disclosed definite evidence of progression in some cases. Two of our patients had had a cerebral angiogram at another institution three years prior to our study. Comparison with previous examinations revealed slight but

FIGURE 4. Right common carotid angiogram, early arterial phase, lateral view. A web-like septum (large arrow) is identified at the origin of the internal carotid artery. An intraluminal thrombus (small arrows) is also present. Fibromuscular dysplasia was documented pathologically. (Case kindly furnished by Drs. G. Joseph Poole and Dixon M. Moody, Bowman Gray School of Medicine).

FIGURE 5. Right common carotid angiogram, early arterial phase, AP view. The "string of beads" appearance of FMD is seen involving the right supraclinoid internal carotid and middle cerebral arteries (arrows).

FIGURE 6. Left vertebral angiogram, early arterial phase, lateral view. Multiple irregular, discrete stenoses of the left posterior cerebral arteries are present (arrows). Obstruction of a distal branch of this artery was seen on later films.
FIGURE 7.  A: Right common carotid angiogram, mid-arterial phase, AP view in a 30 year old female. CSF was normal at the time of angiography. B: Oblique view. Multiple concentric stenoses of both posterior cerebral arteries (large arrows) as well as the anterior inferior cerebellar arteries (small arrows) are identified. The basilar artery shows some fusiform narrowing. Lesions typical for FMD were identified in both cervical internal carotid arteries.
definite interval increase in the degree of stenosis associated with FMD. Only three other patients with cervical FMD have been reported with follow-up angiograms; these were obtained three to nine months after the initial study. These short-term follow-up examinations disclosed no progression in two patients but development of a new lesion in the contralateral internal carotid artery was demonstrated in the third.

References


FIGURE 8. Anatomic sketch of the three major characteristic angiographic patterns seen in cervical fibromuscular dysplasia. The typical "string of beads" appearance is by far the most common pattern identified. Note that all three types spare the carotid bifurcation and characteristically occur opposite the CI-2 level. Only two documented cases of FMD have been reported involving the origin of the internal carotid artery.

FIGURE 9. Left common carotid angiogram, mid-arterial phase, lateral view in a patient with 90% stenosis of the carotid siphon. Note the regularity and smoothness of the arterial deformity (arrows). This represents circular spastic contractions or standing waves secondary to the injection and is distinguished from FMD by its smoothly corrugated outline.

FIGURE 10. Right renal angiogram, mid-arterial phase, AP view. Same patient as figure 1. Classical findings of FMD are present in the mid-portion of the right renal artery (arrows). Note that the origin and proximal segment of this artery are not involved by the lesion.
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A G Osborn and R E Anderson

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