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 C1-2 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.

Our patients had documented episodes of subarachnoid hemorrhage. All angiograms 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

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TABLE 1  Clinical and Angiographic Findings in Twenty Patients with Cephalocervical Fibromuscular Dysplasia

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical presentation</th>
<th>Angiographic findings</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>F</td>
<td>Left homonymous hemianopsia</td>
<td>&quot;String of beads&quot;, right supraclinoid internal carotid artery and right middle cerebral artery</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>F</td>
<td>CVA</td>
<td>Unilateral &quot;string of beads&quot;, cervical internal carotid artery</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>M</td>
<td>Right homonymous hemianopsia</td>
<td>&quot;String of beads,&quot; left posterior cerebral artery with occluded distal branch</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>43</td>
<td>M</td>
<td>Subarachnoid hemorrhage</td>
<td>Anterior communicating artery aneurysm. Bilateral cervical ICA &quot;String of beads&quot;</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>68</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>Anterior communicating artery aneurysm. Bilateral cervical ICA &quot;string of beads&quot;</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>F</td>
<td>Subarachnoid hemorrhage</td>
<td>Anterior communicating artery aneurysm. Bilateral cervical ICA &quot;string of beads&quot;; no aneurysm found. Unilateral renal FMD.</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>47</td>
<td>F</td>
<td>Left hemiparesis</td>
<td>Unilateral long segment smooth stenosis cervical ICA. Contralateral &quot;string of beads&quot;</td>
<td>Intimal fibroplasia</td>
</tr>
<tr>
<td>8</td>
<td>71</td>
<td>F</td>
<td>Scintillating scotomata</td>
<td>&quot;String of beads&quot;, right cervical ICA. Bifurcation normal. Left carotid not studied</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>56</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>&quot;String of beads&quot; left cervical ICA. Atypical FMD involving contralateral ICA opposite Cl-2</td>
<td>—</td>
</tr>
<tr>
<td>10</td>
<td>55</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>Bilateral ICA &quot;string of beads&quot;</td>
<td>—</td>
</tr>
<tr>
<td>11</td>
<td>12</td>
<td>F</td>
<td>Left hemiparesis, hypertension</td>
<td>&quot;String of beads&quot;, right middle cerebral artery. Typical FMD involving both renal and superior mesenteric arteries</td>
<td>—</td>
</tr>
<tr>
<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>
</tr>
<tr>
<td>13</td>
<td>50</td>
<td>F</td>
<td>Multiple transient ischemic attacks and hypertension</td>
<td>&quot;String of beads&quot;, both cervical ICA's. Severe, bilateral renal FMD &quot;String of beads&quot;, both cervical ICA's. Renal, mesenteric arteries normal</td>
<td>—</td>
</tr>
<tr>
<td>14</td>
<td>63</td>
<td>F</td>
<td>Bilateral cerebral infarcts</td>
<td>Bilateral cervical ICA &quot;string of beads&quot;. Posterior communicating artery aneurysm. Bilateral renal FMD</td>
<td>—</td>
</tr>
<tr>
<td>15</td>
<td>48</td>
<td>F</td>
<td>Subarachnoid hemorrhage</td>
<td>Bilateral cervical ICA &quot;string of beads&quot;</td>
<td>—</td>
</tr>
<tr>
<td>16</td>
<td>55</td>
<td>F</td>
<td>Tinnitus, dizziness</td>
<td>Unilateral cervical ICA and and bilateral vertebral &quot;string of beads&quot;. Renal, mesenteric arteries normal</td>
<td>—</td>
</tr>
<tr>
<td>17</td>
<td>45</td>
<td>F</td>
<td>Multiple transient ischemic attacks</td>
<td>Bilateral cervical ICA &quot;string of beads&quot;</td>
<td>—</td>
</tr>
<tr>
<td>18</td>
<td>45</td>
<td>F</td>
<td>Subarachnoid hemorrhage</td>
<td>Unilateral ICA tubular FMD. Posterior communicating artery aneurysm</td>
<td>—</td>
</tr>
<tr>
<td>19</td>
<td>52</td>
<td>F</td>
<td>Subarachnoid hemorrhage</td>
<td>Bilateral cervical ICA &quot;string of beads&quot;. Right posterior communicating artery aneurysm. Renal, mesenteric arteries normal</td>
<td>—</td>
</tr>
<tr>
<td>20</td>
<td>58</td>
<td>F</td>
<td>CVA, hypertension</td>
<td>Bilateral cervical ICA, bilateral vertebral &quot;string of beads&quot;. Unilateral renal FMD</td>
<td>—</td>
</tr>
<tr>
<td>21</td>
<td>30</td>
<td>F</td>
<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>
</tr>
<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. Vertebobasilar, renal arteries normal</td>
<td>—</td>
</tr>
<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. Vertebobasilar, renal arteries normal</td>
<td>Abnormally thickened media, internal carotid artery, with cervical aneurysm resected</td>
</tr>
</tbody>
</table>
carotid artery as well as an unusual lesion in the contra-
lateral carotid artery opposite the body of C2 (fig. 3A, B).
Only the anterior wall of this artery was involved, showing a
corruated diverticulum with non-circumferential narrow-
ing. This finding has been termed "atypical FMD" by
Houser et al.17, 18 A second patient demonstrated this pattern
in both the cervical internal carotid arteries. In this
instance the lesions progressed over several years from
minor atypical FMD to definite cervical saccular
aneurysms. The presence of atypical FMD with aneurysm of
the cervical internal carotid artery was documented at sur-
gery.

One patient had an isolated lesion at the origin of the in-
ternal carotid artery. A smooth, well-defined web or septa-
tion was identified at angiography (fig. 4). The lesion was
histologically proven fibromuscular dysplasia. This
appearance is highly unusual for FMD; only two other
documented cases have demonstrated this angiographic pattern.18, 19

Four of the 25 patients had characteristic findings of
FMD involving the intracranial vessels. Two cases (fig. 5)
had the typical "string of beads" appearance involving the
supraclinoid internal carotid and right middle cerebral
arteries. One of these cases also had lesions typical of FMD
involving the renal and superior mesenteric arteries. One
patient had isolated involvement of the left posterior
cerebral artery (fig. 6) while the fourth patient had typical
lesions in both mid-cervical internal carotid arteries (fig. 7A)
as well as diffuse involvement of the vertebrobasilar system.
In this patient, characteristic lesions were found even in the
anterior inferior cerebellar arteries (fig. 7B).

Discussion

First identified angiographically in 1964,14 fibromuscular
dysplasia is now recognized as one of the more common
non-atherosclerotic causes of carotid artery stenosis.20 The
pathological features of this angiopathy have been exten-
sively reviewed.2, 21 Three distinct histological types of FMD
have been identified: intimal fibroplasia, medial fibroplasia
or fibromuscular hyperplasia, and subadventitial hyper-
plasia.

A review of the literature18, 20, 22-30 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 radiographic appearance is created by multi-
ple 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 en-
tities 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 or
sclerosing 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.15, 18
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 CI-2 is characteristic of FMD. Note that the carotid bifurcation and proximal internal carotid artery are normal.
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 CI-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.18

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.9 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,8 evidence that this lesion can be associated with significant clinical disease is accumulating.16, 19, 41, 42 Boudin, Guillard and Romion have correctly pointed out that the precise nature of this relationship is unclear.49 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.6,18, 30, 38-39, 41, 43 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.1 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.
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.

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 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.
ANGIOGRAPHIC SPECTRUM OF FMD/Osborn, Anderson

CERVICAL FIBROMUSCULAR DYSPLASIA

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 C1-2 level. Only two documented cases of FMD have been reported involving the origin of the internal carotid artery.

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.

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.

References


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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