Variable Angiographic Findings in Patients With Stroke and Neurosyphilis

Gianluca Landi, MD, Flavio Villani, MD, and Nicoletta Anzalone, MD

We describe four patients with cerebral infarction and active neurosyphilis who had variable angiographic findings. Patients 1 and 2 had evidence of arteritis and an atheromatous ulcerated stenosis of the extracranial carotid artery, respectively. The third and fourth patients had symptoms of lacunar infarction, but cerebral angiography was normal in patient 3, whereas patient 4 had evidence of concomitant atheromatous and arteritic lesions. Neither age nor presence of cerebrovascular risk factors was of aid in predicting angiographic features. The concomitance of cerebral infarction and active neurosyphilis does not imply a cause-and-effect relation, since atherosclerotic lesions may coexist with arteritis or may even represent the only angiographic feature. Our findings underscore the importance of angiography to confirm the diagnosis in cases of suspected syphilitic arteritis. (Stroke 1990;21:333–338)

Althought the introduction of antibiotics has decreased the overall prevalence of neurosyphilis (NS), the relative frequencies of vascular and atypical forms of NS have increased. However, only a few authors have reported angiographic findings in vascular NS, and since most of these reports have been limited to the study of the intracranial vessels, they may not have demonstrated atherosclerotic lesions, which are more frequently extracranial. We therefore reviewed the angiographic findings in four patients who had symptoms of cerebral infarction (Table 1) and concomitant clear-cut evidence of NS.

Case Reports

Case 1
A 62-year-old right-handed man was hospitalized because of the sudden onset of a left hemiparesis. He was a smoker and had a history of arterial hypertension that was well-controlled with atenolol; he denied previous venereal diseases. Neurologic examination on admission revealed a hyperreflexic left hemiparesis and a left homonymous hemianopsia. General physical examination, routine blood tests, electrocardiogram (ECG), and chest radiogram were normal. Computed tomography (CT scan) revealed a right temporocerebellar hypodense lesion.

Serologic and cerebrospinal fluid (CSF) findings demonstrated NS (Table 2). Four-vessel cerebral angiography demonstrated no abnormalities of the aortic arch or of the extracranial and intracranial carotid arteries; the vertebral and basilar arteries were also normal, but there was a tight and irregular segmental narrowing of both posterior cerebral arteries, consistent with arteritis (Figure 1).

The patient received a 10-day course of intravenous penicillin G (20×10⁶ units/day), which was repeated after 3 months and again after 7 months. Twelve months after the first hospital admission, syphilis serology remained positive but CSF examination disclosed an almost-normal cell count with normal protein concentrations (Table 2). During the entire follow-up period of 58 months the patient has been treated with 500 mg aspirin/day and has remained asymptomatic.

Case 2
A 62-year-old right-handed man was hospitalized because of the sudden onset of a left hemiparesis. He was a smoker and reported previous hypercholesterolemia. Before admission he was in good health, and he denied previous venereal diseases.

Neurologic examination on admission revealed a left-sided hyperreflexic hemiparesis. The general physical examination, routine blood tests, ECG, and chest radiogram were normal. Blood pressure was 140/80 mm Hg. Serologic and CSF findings demonstrated NS (Table 2). Brain CT scan revealed a right temporoparietal hypodense lesion. Cerebral angiography showed an ulcerated lesion at the origin of the right internal carotid artery, which was attributed to arteritis (Figure 2).

The patient was given two successive 10-day courses of intravenous penicillin G (20×10⁶ units/day), and he was started on long-term aspirin, 500 mg/day. Ten months later, syphilis tests on serum and CSF were still positive, but CSF cell count and protein concentration were almost normal (Table 2). One year later, while still on aspirin, the patient experienced an...
### TABLE 1. Clinical Features and Results of Computed Tomography and Angiography in Four Men With Neurosyphilis and Cerebral Infarction

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Cerebrovascular risk factors</th>
<th>Computed tomography</th>
<th>Findings on Angiography</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62</td>
<td>Smoking, hypertension</td>
<td>R temporo-occipital infarct</td>
<td>Normal</td>
<td>Tight irregular narrowing of both posterior cerebral arteries</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>Smoking, previous hypercholesterolemia</td>
<td>R temporoparietal infarct</td>
<td>Ulcerated stenosis at origin of R internal carotid artery</td>
<td>Mild irregularity of R carotid artery siphon</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
<td>Smoking</td>
<td>L capsular lacunar infarct</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>Smoking, hypertension</td>
<td>R temporoparietal infarct; lacunar infarcts in R basal ganglia</td>
<td>Plaque on innominate artery; ulcerated plaque at origin of R internal carotid artery</td>
<td>Occlusion of R middle cerebral artery stem; arteritic lesions of R anterior cerebral artery</td>
</tr>
</tbody>
</table>

**Findings on Angiography**
- **Extracranial:**
  - Normal
  - Ulcerated stenosis at origin of R internal carotid artery
  - Plaque on innominate artery; ulcerated plaque at origin of R internal carotid artery
- **Intracranial:**
  - Normal
  - Mild irregularity of R carotid artery siphon
  - Occlusion of R middle cerebral artery stem; arteritic lesions of R anterior cerebral artery

**Follow-up**
- 58 months; asymptomatic on 500 mg aspirin/day
- 26 months; myocardial infarction after 22 months on 500 mg aspirin/day
- 49 months; asymptomatic on 500 mg aspirin/day
- 15 months; asymptomatic on 500 mg aspirin/day

R, right; L, left.

Acute myocardial infarction, followed by unstable angina. Aspirin was replaced by acenocoumarol; 4 months later the patient was asymptomatic.

**Case 3**

A 35-year-old right-handed man was hospitalized because of the sudden onset of a right hemiparesis. He was a smoker; before admission the patient was in good health, and he also denied previous venereal diseases. Blood pressure was normal (140/80 mm Hg).

On admission, neurologic examination disclosed a right pure motor hemiparesis; speech, visual fields, and sensation were normal. General physical examination, routine blood tests, and ECG as well as M-mode and two-dimensional echocardiograms were normal.

**Figure 1.** Case 1. Cerebral angiogram demonstrates irregular segmental narrowings of both posterior cerebral arteries (arrows).
normal. CSF examination revealed an increased number of cells and increased concentrations of proteins and IgG, and syphilis tests on CSF and serum were positive (Table 2). Brain CT scan showed a lacunar infarct in the posterior limb of the left internal capsule. Four-vessel cerebral angiography revealed normal extracranial and intracranial vessels.

The patient was treated with a 10-day course of intravenous penicillin G (20×10⁶ units/day) and with long-term aspirin (500 mg/day). The patient has been followed for 49 months. He refused further serologic and CSF examination and has remained asymptomatic.

Case 4

A 58-year-old right-handed man was hospitalized because of a left-sided hemiparesis. He was a smoker and had untreated arterial hypertension. Six years prior to admission he had been hospitalized for a reversible episode of left hemiparesis. On that occasion, positive syphilis serology had been found, and he had received several courses of penicillin therapy.

On admission, neurologic examination revealed a left faciobrachiofacial hemiparesis. Blood pressure was 180/110 mm Hg, and nifedipine therapy was started together with 500 mg aspirin/day. General physical examination, routine blood tests, and chest radiogram were normal. ECG revealed several ventricular ectopic beats. M-mode and two-dimensional echocardiograms demonstrated a left ventricular hypertrophy. CSF examination revealed a normal number of cells but an increased concentration of proteins. Syphilis tests on serum and CSF showed an active luetic infection (Table 2). Brain CT scan revealed several lacunar infarcts in the right basal ganglia and two larger hypodense lesions in the right occipital and frontoparietal lobes.

Four-vessel cerebral angiography demonstrated a number of abnormalities (Figure 3). Extracranial views demonstrated a large lesion on the lateral wall of the innominate artery and a possibly ulcerated moderate stenosis at the right internal carotid artery origin, consistent with atheroma; intracranial views revealed occlusion of the right middle cerebral artery stem and multiple irregular segmental narrowings along the horizontal portion of the anterior cerebral artery, which were compatible with arteritis.

The patient received a 10-day course of intravenous penicillin G (20×10⁶ units/day), which was repeated after 8 months. Fifteen months after angiography, while still on aspirin, the patient remained asymptomatic. However, syphilis serology and CSF examination demonstrated persistence of the luetic infection (Table 2).

Discussion

Our four patients had clear-cut evidence of NS as they all had positive serum and CSF VDRL, fluorescent treponemal antibody absorption, and microhemagglutination assays for Treponema pallidum. Moreover, they all had hyperproteinorrachia and, with the exception of patient 4 who had been previously treated with penicillin, CSF pleocytosis with no other apparent cause.

Although, as in most angiographic series, our patients were selected on the basis of their younger age and their good recovery from neurologic deficits, their arteriographic findings deserve attention in light of the paucity of available studies on this subject. Indeed, most reports describe single patients with arteritic lesions of the intracranial vessels.8 Among six patients with NS described by Aupy et al,8 four had angiographic evidence of occlusion of the middle or posterior cerebral arteries. Concomitance of extracranial and intracranial abnormalities has been reported in only one case, in whom the diagnosis of NS was considered probable.9
FIGURE 3. Case 4. Cerebral angiograms demonstrating (top left) large plaque on lateral wall of innominate artery (arrows) and (bottom left) atheromatous plaque, possibly ulcerated, at origin of right internal carotid artery (large arrow); irregular narrowing of anterior cerebral artery is also apparent (small arrow). Top right: Multiple irregular narrowings along horizontal portion of right anterior cerebral artery (small arrows) and occlusion of middle cerebral artery stem (large arrow).
TABLE 2. Results of Cerebrospinal Fluid Examinations and Serology in Four Men With Neurosyphilis and Cerebral Infarction

<table>
<thead>
<tr>
<th>Case</th>
<th>Cerebrospinal fluid examination</th>
<th>Syphilis tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cells/μl</td>
<td>Total proteins (mg/dl)</td>
</tr>
<tr>
<td>1</td>
<td>On admission</td>
<td>45.6</td>
</tr>
<tr>
<td></td>
<td>After three courses of intravenous penicillin</td>
<td>5.3</td>
</tr>
<tr>
<td>2</td>
<td>On admission</td>
<td>138.4</td>
</tr>
<tr>
<td></td>
<td>After two courses of intravenous penicillin</td>
<td>16.3</td>
</tr>
<tr>
<td>3</td>
<td>On admission</td>
<td>23.6</td>
</tr>
<tr>
<td></td>
<td>After one course of intravenous penicillin</td>
<td>ND</td>
</tr>
<tr>
<td>4</td>
<td>On admission</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>After two courses of intravenous penicillin</td>
<td>0.9</td>
</tr>
</tbody>
</table>

ND, not done; OCB, oligoclonal bands; VDRL, Veneral Disease Research Laboratory test; TPHA, Treponema pallidum microhemagglutination assay; FTA-Abs, fluorescent treponemal antibody absorption assay.

Our four patients had variable angiographic findings. Patient 1 had irregular segmental narrowing of both posterior cerebral arteries. Although atherosclerosis may give rise to such lesions, isolated bilateral symmetrical posterior cerebral artery atherostenosis is exceedingly rare since only one case was identified in a 7-year angiographic review at a large hospital; moreover, these authors noted that patients with atherostenosis of the posterior cerebral artery commonly present with transient ischemic attacks rather than stroke. Therefore, although atherosclerosis could not be definitely ruled out in our patient, his final—albeit presumptive—diagnosis was arteritis. On the contrary, patient 2 had a stenosis of the symptomatic internal carotid artery at its origin, which was ascribed to atheroma in view of its location and ulcerated appearance, in the absence of concomitant aortitis. Patient 3 presented with a pure motor hemiparesis due to a capsular infarct and had a normal angiogram, as is commonly seen in lacunar strokes. Patient 4 had a stenosis of the innominate artery (an uncommon location for syphilitic arteritis) and an ulcerated lesion of the symptomatic carotid artery bifurcation that was attributed to atheroma. However, since there were concomitant segmental narrowings of the anterior cerebral artery consistent with arteritis, it remains unsettled whether his middle cerebral artery occlusion was due to atherosclerosis (possibly through an embolic mechanism) or to arteritis.

These findings demonstrate that the occurrence of cerebral infarction in the setting of NS does not imply a cause-and-effect relation since atherosclerotic lesions may coexist (case 4) or may even represent the only angiographic abnormality (case 2). It is noteworthy that neither age nor the presence of cerebrovascular risk factors could help in predicting the angiographic features; our four patients were all smokers, and hypertension, the most important risk factor for cerebral atherosclerosis, was present in both cases with evidence of arteritis.

Two of the three patients who had CSF examination after penicillin treatment showed decreases in the cell count and protein concentration (Table 2), which is considered to be the most reliable measure of therapeutic success. On the contrary, patient 4 (the only one who on admission had a history of treated cutaneous infection) showed a persistently raised protein content on control CSF examination. Besides high-dose penicillin courses, all of our patients were treated with long-term aspirin, both to prevent thromboembolism from atherosclerotic lesions and to inhibit platelet activation, which may result from proliferation of endothelial cells in Nissl's endarteritis. None of our patients experienced stroke recurrence during an average follow-up of 37 months, although myocardial infarction occurred in a patient with carotid atherosclerosis. However, the small number of our cases and their heterogeneous angiographic findings do not allow us to draw therapeutic or prognostic conclusions. Further data on the prognosis of neurovascular syphilis should be collected in patients who have undergone angiography, which represents the only method to obtain a pathogenetic diagnosis in cases of cerebral ischemia and coexistent NS.

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