Mesencephalic and Associated Posterior Circulation Infarcts

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Background and Purpose—The purposes of this study were to evaluate and review the risk factors and clinical features of patients with posterior circulation stroke involving mesencephalon and neighboring structures and to describe the clinical syndromes according to the mesencephalic arterial territory involved.

Methods—We studied all patients with acute posterior circulation stroke involving mesencephalon who were admitted consecutively to our stroke unit over a 6-year period. We selected these patients (3%) from 1296 patients with posterior circulation infarct. Neurological and radiological investigations, including MRI and angiography, were performed in all cases. We classified patients into 4 groups on the basis of MRI findings: (1) isolated mesencephalic infarcts (9 patients); (2) distal territory infarcts (19 patients), including mesencephalon, thalamus, medial temporal and occipital lobes, and cerebellum; (3) middle territory infarcts (12 patients), including the pons and anterior inferior cerebellar artery territory; and (4) proximal territory infarcts (1 patient), including the medulla and posterior inferior cerebellar artery territory.

Results—Middle mesencephalon involvement was the most common in all groups, and the anteromedial territory was frequently affected, depending on the direct perforators of basilar artery. In patients with isolated mesencephalic infarct, the clinical picture was dominated by nuclear or fascicular third-nerve palsy and contralateral motor deficits. The distal territory involvement was the most common and associated with consciousness disturbances, gait ataxia, ocular motor disturbances, and visual field deficits. The neurological picture of middle territory infarcts was dominated by consciousness disturbances with dysarthria, horizontal ocular motor disorders, and hemiparesis. Proximal territory involvement was rare and associated with acute unsteadiness, vertigo, dysphagia, dysphonia, tetra-ataxia, and motor weakness. The most common cause of stroke was large-artery disease in 16 patients (39%), cardioembolism in 8 (20%), and small-artery disease with lacunar mesencephalic infarct in 10 (24%). Bilateral mesencephalic infarcts were not uncommon (27%), mainly in patients with multiple and extended infarcts in the posterior circulation, and were associated with poor outcome compared with unilateral infarct.

Conclusions—Our study highlights the topographic and clinical heterogeneity of the acute posterior circulation infarcts involving mesencephalon. The variety of the underlying potential causes of stroke requires detailed investigations of the extra and intracranial arteries and the heart. (Stroke. 2002;33:2224-2231.)

Key Words: atherosclerosis ■ magnetic resonance imaging ■ mesencephalon ■ stroke, ischemic

The first report on mesencephalic infarct was emphasized in 1853 by Marotte. Shortly thereafter, Weber described a patient with unilateral third-nerve palsy associated with a crossed hemiplegia resulting from a hematoma affecting the paramedian and lateral midbrain. The report of Claude and Loyez describing a combination of third-nerve palsy and contralateral cerebellar findings (Claude’s syndrome) and another report on the combination of the third-nerve palsy with contralateral involuntary abnormal movements (Benedikt’s syndrome) expanded the knowledge of midbrain symptomatology. Although isolated, mesencephalic infarcts are rare because the arterial blood supply to mesencephalon is complex compared with medulla oblongata and pons and there are overlaps between arterial territories of infratentorial structures. Despite its small anatomical structure, it receives branches from the posterior cerebral artery (PCA), basilar artery, and superior cerebellar artery (SCA), depending on the level of mesencephalon. Mesencephalic infarct more often was accompanied by ischemia of neighboring structures than it occurred in isolation. In recent years, some series have reported mesencephalic infarcts with or without involvement of neighboring vascular territories.

We studied the clinical pictures, topographic patterns, and concomitant diseases in a series of patients with mesencephalic infarct proved by MRI and attempted to clarify the clinical and etiological differences between isolated mesencephalic infarcts and associated extended or multiple infarcts in the posterior circulation.
Materials and Methods

We studied 41 consecutive patients with acute infarct involving mesencephalon proven by MRI who were admitted to our stroke unit over 6 years (1995 to 2001). Patients were included in the series if there was evidence of infarction within the mesencephalon alone or with concomitant multiple infarcts in the vertebrobasilar territory on MRI using standard axial sequences. All patients were assessed by at least 2 senior neurologists (E.K., G.B.). All patients were assessed with a standard protocol of investigations, including complete blood cell count and urinalysis, transcranial Doppler, duplex sonography of the carotid and vertebral arteries, and 12-lead ECG; in selected cases, transthoracic or transesophageal echocardiography and catheter angiography were also performed. Cerebral MRI and MR angiography were performed with a Siemens Magnetom 1.5-T imager, and readings were done by a neuroradiologist blinded to the findings on the neurological evaluations. T1-weighted (repetition time [TR], 450 to 600 ms; echo time [TE], 12 to 20 ms), T2-weighted (TR, 2000 to 5500 ms; TE, 80 to 120 ms), proton density–weighted (TR, 2000 to 5500 ms; TE, 10 to 40 ms), diffusion-weighted (B = 1000 s/mm²) MR examinations (in 12 patients), and MR angiography (3-dimensional time-of-flight technique sensitive to arterial flow) were performed within the first week of stroke. The anatomic midbrain boundaries were assessed by use of anatomic diagrams of the midbrain at 3 levels (upper, middle, and lower) in respect to the MRI findings. The vascular territories of mesencephalon were defined according to the map of brainstem arterial territories published elsewhere16: (1) The anteromedial mesencephalic artery territory receives paramedian branches from the basilar artery at the lower part of mesencephalon, and the upper median part is supplied mainly through direct branches from the distal basilar artery; (2) the anterolateral mesencephalic territory arises from the P2 segment of PCA; (3) the lateral mesencephalic territory (short circumferential) is supplied by branches from the P1 segment at the level of middle mesencephalon, and posterior choroidal arteries supply the lateral part of mesencephalon at the level of upper midbrain; and (4) the dorsal mesencephalic territory receives branches from the P1 segment at the level of mesencephalon, and the SCA supplies the caudal two thirds of the mesencephalon. The templates displaying the arterial territories of the upper, middle, and lower mesencephalon are shown in Figure 1. The extent of posterior circulation infarction was assessed according to the criteria of the New England Medical Center17 as follows: The proximal territory includes the medulla and cerebellum and is supplied by the posterior inferior cerebellar artery (PICA); the middle territory includes the pons and the anterior inferior cerebellum and is supplied by the caudal two thirds of the basilar artery; and the distal territory or tip of the basilar artery territory includes the midbrain, thalamus, superior cerebellum, and temporoparietal cortex and is fed by the rostral basilar artery.

We recorded vascular risk factors such as hypertension, diabetes mellitus, regular smoking, hypercholesterolemia, venous hematocrit (>50) at admission, and history of migraine and heart disease (including old myocardial infarct, left ventricular aneurysm, hypokinesia or akinesia, chronic nonvalvular atrial fibrillation, and mitral stenosis). Presumed midbrain stroke causes was categorized into 5 subgroups: (1) large-artery disease in patients with vertebral or basilar artery stenosis of >50% or obstruction on 3-dimensional images; (2) small-artery disease in patients with longstanding hypertension or diabetes mellitus and a small (<15 mm) infarct sparing the surface of the mesencephalon on MRI in the absence of other causes; (3) potential cardiac sources of embolism, including mainly nonvalvular atrial fibrillation, left ventricular dyskinetic segment, intracardiac thrombus or tumor, mitral stenosis, and other less common sources; and (4) other origins, including dissection, dolichoectatic vertebral/basilar artery, and undetermined. We considered 4 classic lacunar syndromes: pure motor stroke, pure sensorial stroke, ataxic hemiparesis, and dysarthria–clumsy hand syndrome. Functional outcome was assessed at discharge and 3 months after stroke onset, and follow-up was considered as independent, dependent, or death.
Statistical data on risk factors and stroke mechanisms were analyzed by use of descriptive statistics.

**Results**

There were 41 patients (25 men [mean±SD age, 64±14 years]; 16 women [age, 63±13 years]) with acute stroke involving mesencephalon. Patients with mesencephalic involvement represent 0.9% (41 of 4800) of our registry and 3% of the patients with posterior circulation infarct (1296 patients). Seven patients (17%) had transient ischemic attacks with motor or visual loss symptoms 1 week to 1 month before stroke onset.

**Vascular Risk Factors and Cause of Infarct**

The main risk factors was hypertension in 26 patients (63%), followed by diabetes mellitus in 13 (32%), smoking in 12 (29%), hyperlipidemia in 5 (12%), previous myocardial infarction history in 3 (7%), and arteriosclerotic ischemic heart disease in 12 (29%). One patient (patient 30) with mesencephalic infarct had Behçet vasculitis, and 2 young patients (patients 37 and 39) had spontaneous vertebral artery dissection. The most common cause of stroke was large-artery disease in 16 patients (39%), a potential cardiac source of embolism (atrial fibrillation and myocardial infarction with mural thrombus) in 8 (20%) (2 of them had atherosclerotic stenosis of >50% in basilar artery), and small-artery disease with lacunar mesencephalic infarct in 10 (24%). In 4 patients, the presumed stroke cause remained undetermined (the Table).

**Topography of Infarcts**

According to MRI findings, 4 categories of patients were identified. First, isolated midbrain infarcts (9 patients) were usually small and limited to the upper and middle lower part of the mesencephalon without other rostral or caudal involvement. Bilateral mesencephalic involvement was found only in 1 patient (Figure 2). Second, distal territory syndrome with mesencephalic infarct (19 patients) occurred with associated lesions in the thalamus (16 patients), PCA (12 patients), or SCA (5 patients) territories. Posterior choroidal artery territory involvement was present in 1 patient (patient 17). Thalamic lesions were contralateral to mesencephalic infarct in 4 patients, and 2 patients had coexisting infarcts in the posterior temporal lobe. Five patients had bilateral mesencephalic lesion: 4 with bilateral lesions in the anteromedial territory and 1 with lesions in the anteromedial and antero-
lateral territories. In 15 patients, mesencephalic lesions involved the upper and middle mesencephalon, whereas only 4 patients had isolated upper mesencephalic infarct. Third, middle territory syndrome was considered in patients with mesencephalic infarct (12 patients) associated with pontine (10 patients with unilateral, 2 with bilateral lesions) and anterior inferior cerebellar artery (AICA) territory lesions (3 patients had only AICA territory lesions [patients 29, 31, and 39] and 2 had AICA and PICA territory lesions [patients 32 and 40]). Two patients had an additional unilateral thalamic infarct (patients 34 and 36), and 2 others had bilateral thalamic infarcts (patients 29 and 37). Fourth, proximal territory syndrome was found in 1 patient who had a unilateral medullar infarct–associated bilateral anteromedial infarct in the mesencephalon and PICA territories.

Clinical Findings

Isolated Midbrain Infarcts

At stroke onset, none of the patients had consciousness disturbances, and 6 patients (patients 3 through 8) presented such nonspecific symptoms as dizziness, unsteadiness, and gait ataxia. Upper mesencephalon was involved in 3 patients (patients 1, 6, and 8), and 1 of the patients with dorsal lesion had vertical gaze impairment and gait ataxia (patient 1). Of 9

<table>
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<tr>
<td>1</td>
<td>PCSE</td>
<td>Diplopia, vertical gaze palsy, limb/limb ataxia, CNP (III, lateral)</td>
<td>Independent</td>
</tr>
<tr>
<td>2</td>
<td>SAD</td>
<td>Diplopia, M, CNP (III, lateral), [Weber’s syndrome]</td>
<td>Independent</td>
</tr>
<tr>
<td>3</td>
<td>SAD</td>
<td>Dizziness, limb/limb ataxia, CNP (II, lateral)</td>
<td>Independent</td>
</tr>
<tr>
<td>4</td>
<td>SAD</td>
<td>Unsteadiness, CNP (III, lateral), M, CNP</td>
<td>Independent</td>
</tr>
<tr>
<td>5</td>
<td>LAD</td>
<td>Dizziness, dysarthria, tetra-atatic hemiparesis</td>
<td>Dependent</td>
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<tr>
<td>6</td>
<td>SAD</td>
<td>Dizziness, gait ataxia, hyperesthetic atactic hemiparesis</td>
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<tr>
<td>7</td>
<td>SAD</td>
<td>Unsteadiness, vertigo, CNP (II, facialis), Dependent choroid movement, emotional torpor</td>
<td>Dependent</td>
</tr>
<tr>
<td>8</td>
<td>Unknown</td>
<td>Dysarthria, atactic hemiparesis</td>
<td>Independent</td>
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patients with anteromedial infarct, 6 had signs of involvement of the third nerve or nucleus. Two (patients 2 and 4) had clinical evidence of nuclear involvement of the third nerve (bilateral ptosis, bilateral superior rectus superior weakness, and unilateral adduction/upward/downward palsy), and 4 patients (patients 1, 3, 5, and 8) with anterolateral infarct presented a fascicular type of third-nerve palsy (unilateral adduction/upward/downward palsy with mydriasis and ptosis). Five patients had motor deficits: patients 2 and 4 had Weber syndrome, patients 6 and 9 had ataxic hemiparesis, and patient 7 with infarct involving lateral lower and upper mesencephalon showed hypesthetic ataxic hemiparesis on the contralateral side of the lesion. One patient (patient 8) with anteromedial infarct presented Benedikt’s syndrome (Figure 3).

**Distal Territory Syndrome**

At stroke onset, 8 patients (patients 15 through 17, 19, 21, and 24 through 26) had disturbances of consciousness, and 6 patients (patients 10, 13, 14, 27, and 28) presented somnolence with disorientation to time and place. Two (patients 10 and 16) developed peduncular hallucinosis during hospitalization. Thirteen patients had unilateral motor weakness on the contralateral upper and lower limbs, 5 patients presented tetraparesis, and 1 had decerebration rigidity (patient 26). Nine patients had third-nerve palsy: 4 (patients 13, 14, 16, and 18) had clinical evidence of nuclear involvement, and 5 (patients 12, 15, 24, 26, and 28) had peripheral type of third-nerve palsy. Five patients (patients 10, 11, 20, 22, and 28) with posterior parieto-occipital lesion had transcortical sensorial aphasia (reduced comprehension, alexia, anomia but with normal repetition); in these patients, the posterior circulation was supplied by the posterior communicating artery. Five patients (patients 15, 17, 19, 21, and 26) with bilateral lesions had clinical evidence of mesencephalic locked-in syndrome, and 6 patients (patients 10, 11, 16, 20, 27, and 28) had top of the basilar syndrome. One patient (patient 12) with anterior thalamic infarct presented decreased verbal fluency with Claude’s syndrome; 1 patient (patient 23) had sensorimotor stroke with dysarthria (Figure 4).

**Middle Territory Syndrome**

Initially disturbed consciousness was present in 4 patients with headache (patients 31, 33, 39, and 40), and 2 other
patients had stupor or somnolence (patients 29 and 32). Two weeks after stroke onset, 4 patients (patients 32, 33, 39, and 40) had tetraparesis with limited horizontal ocular movements and partial vertical palsy. Two patients (patients 32 and 33) with bilateral involvement of the brainstem had peripheral type of third-nerve palsy associated with tetraparesis; in 2 others (patients 36, and 47), it was associated with contralateral hemiparesis to lesion. Patient 29 presented Horner’s syndrome, ipsilateral ataxia, fourth-nerve palsy, skew deviation, contralateral hemihypesthesia, and mild faciobrachial palsy, suggesting involvement of the SCA territory, and 2 patients (patients 30 and 38) had pure motor hemiparesis involving predominantly the face and upper limb (Figure 5).

Dysarthria and cheiro-podo-oral hypesthesia was present in 1 patient (patient 35) with infarct compatible with involvement of medial lemniscus at the upper pons and middle mesencephalon.

At stroke onset, internuclear ophthalmoplegia was present in 1 patient (patient 32), but after 1 week, after a recurrent stroke, he developed one-and-a-half syndrome associated with upgaze palsy. Two patients had ipsilateral horizontal gaze palsy (patients 31 and 34) with sensorimotor stroke and dysarthria (Figure 5).

**Proximal Territory Syndrome**

In this group, there was 1 patient who had acute unsteadiness and vertigo at stroke onset, as well as dysphagia, dysphonia, tetra-ataxia, left-sided weakness, and dysmetria involving predominantly the face and upper limb (Figure 6).

**Outcome**

The median follow-up was 8±3 months after stroke onset. There were 6 deaths (15%) during hospitalization; 4 patients (patients 10, 15, 16, and 28) had multiple and bilateral infarcts in the distal territory, and 2 (patients 32 and 33) had middle territory infarcts. At 3 months after stroke onset, most patients with extended and multiple infarcts in the distal territory and middle territory were dependent (68% and 58%, respectively).

**Discussion**

In our series, mesencephalic infarct occurred in 1% of all ischemic strokes, and isolated mesencephalic ischemic stroke was found in 0.7% of patients with posterior circulation infarcts. In previous series, the frequency of isolated mesencephalic ischemic lesion varied between 0.7% and 8% of...
Our series showed that mesencephalic infarct is 5-fold as likely to be accompanied by multiple posterior circulation infarcts as to occur in isolation. This result justifies the data of New England Medical Center, which reported that isolated mesencephalic infarct was 10-fold less frequent than those with multiple neighboring lesions.14

Most infarcts could easily be matched to the known anatomic arterial territories. As reported before,12–14 most infarcts were unilateral, and the middle mesencephalon was affected more frequently than the other locations. Bilateral involvement was present in only 1/10 of patients with isolated mesencephalic infarct, although it was present in one third of the patients with multilevel involvement, suggesting probable embolic mechanisms in patients having multilevel or extended infarcts. In our series, the paramedian territory was the most frequently involved territory in all groups, which was followed by the mesencephalic PCA and SCA territory involvement. Posterior choroidal artery territory involvement was rare, which can be explained by the blood supply variability in the upper mesencephalon.18–20

Initial consciousness disturbances were present in 59% of patients with multilevel or extended infarcts, and this fact can explain why most patients with multiple infarcts in the posterior circulation presented with a lack of complex ocular motor deficits, sensory deficits, and visual field deficits. Unilateral distal territory and middle territory infarcts usually led to somnolence, whereas bilateral infarcts were associated with coma at stroke onset.6 Specific oculomotor signs, mainly third-nerve palsy, may help to identify and localize the mesencephalic infarct, whereas in the presence of multiple and extended infarcts in the posterior circulation, MRI can give valuable information about the lesion side. Paramedian infarcts are often associated with nuclear syndrome of the third nerve,21–25 whereas more lateral infarcts led to the fascicular lesions of the third nerve, either in isolation or with contralateral hemiparesis or hemiataxia.3,4,9,26–31 Fascicular third-nerve involvement resulting from a mesencephalic lesion may not be easily differentiated from a peripheral lesion, also because of the common lack of associated central neurological dysfunction(s).11 We found that classic Weber’s syndrome was present in 2 patients with isolated mesencephalic infarct, whereas other patients with multiple infarcts having third-nerve involvement and hemiparesis in the posterior circulation had additional clinical symptoms of thalamic infarct and PCA or SCA territory involvement. In addition to oculomotor disorders, we observed upgaze or downgaze palsy,32–35 horizontal and vertical one-and-a-half syndrome,8 internuclear ophthalmoplegia,36–38 skew deviation,19 and ocular bobbing,13 but we did not note isolated extrinsic third-nerve palsy, which can mimic diabetic third-nerve palsy.40,41 Vertical gaze impairment is a specific localizing neurological symptom suggesting a lesion in the dorsal upper midbrain. We noted only 1 patient with SCA syndrome, although in previous series,32–44 SCA territory infarct with ipsilateral fourth-nerve palsy, Horner syndrome, and contralateral ataxia were rarely reported, which can be explained by the rich supply of PCA to the lateral-dorsal region of the rostral mesencephalon. Patients with lower mesencephalic infarct may have tetra-ataxia resulting from involvement decussation of the superior cerebellar peduncles11 and hand-foot-mouth hypesthesia resulting from involvement of the medial lemniscus and ventral ascending tract of the trigeminal nerve.45 We observed 2 patients with nonspecific pictures of pure motor hemiparesis resulting from mesencephalic peduncular lesion as reported before,9,46

Large-artery disease and cardioembolism were more common in patients with distal territory syndrome than in those with middle territory syndrome or isolated mesencephalic infarct, suggesting an embolic stroke mechanism in patients with multiple infarcts in the distal part of upper brainstem. We found that in patients with isolated mesencephalic infarct, small-artery disease is the leading cause of stroke as in the previous series.11,14 In these patients, small-artery disease could be associated with vertebrobasilar artery atherosclerotic stenosis, which can cause ischemia by either perfusion failure of the perforating mesencephalic arteries or microembolism to perforant intrinsic arteries.

In conclusion, the plurality of the clinical spectrum of posterior circulation stroke involving mesencephalon requires special clinical investigation to delineate precisely the topography of lesions and causes of mesencephalic infarcts. Our study highlights the diversity of the underlying stroke causes between isolated mesencephalic and associated multiple or extended posterior circulation infarcts.

References


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