Brain Stem Infarction Syndromes

4

Jong S. Kim

Medullary Infarction

The medulla is mainly supplied by a number of penetrating arteries arising from the intracranial vertebral arteries (Vas). The dorsal tegmental area is also supplied by branches arising from the medial posterior inferior cerebellar artery (PICA) and posterior spinal artery. The most rostral part can be supplied by branches from the basilar artery (BA) or anterior inferior cerebellar artery (AICA). The caudal part of the anterior medulla is supplied by penetrating arteries arising from the anterior spinal artery (ASA).

Lateral Medullary Infarction

Since the first description of Wallenberg's syndrome more than 100 years ago [1], clinical [2–5] and pathological [6] findings of lateral medullary infarction (LMI) have been reported. Recent studies using MRI [7–11] have rapidly expanded our understanding of LMI syndromes. One study reported that LMI represents 1.9% of all admitted acute stroke [2]. It is likely that institutes frequently using MRI may find more cases than previously reported.

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Clinical Manifestations

Symptoms/signs of LMI are summarized in Table 4.1. The onset may be sudden, but in more than half of the patients, symptoms/signs develop progressively or stutteringly. While headache, vertigo, nausea/vomiting, or gait instability are usually the early symptoms/signs, hiccup tends to occur later [10]. Some of the symptoms/signs may appear days or even weeks after the onset. The progressive onset is usually associated with enlargement of the ischemic area detected by follow-up MRI, associated with persistent or progressive thrombosis. Thus, progressive addition of symptoms seems to be equivalent to the early neurological deterioration in patients with internal capsular infarction.

Dizziness, Vertigo, and Ataxia

A dizzy sensation and gait instability are the most common symptoms occurring in more than 90% of patients. Whirling vertigo, a symptom attributed to involvement of vestibular nuclei and their connections, occurs in approximately 60% [10]. Vertigo is an early sign that usually improves within days or weeks, although dizziness and gait instability last longer. Vertigo is usually accompanied by nystagmus and vomiting. Gait instability and dizziness can be attributed to either the dysfunctional vestibular or cerebellar system. In the acute stage, approximately 60% of patients are unable to stand or walk. Gait ataxia is usually more common and severe than limb incoordination [10, 12]. Lateropulsion (forced to sway when

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Table 4.1 Neurologic symptoms and signs published in the largest series (In, Kim, Pure lateral medullary infarction: clinical-radiological correlation of 130 acute, consecutive patients. Brain 2003;126:1864–72)

Items	N = 130
Sensory symptoms/signs	125 (96)
Ipsilateral trigeminal	34 (26)
Contralateral trigeminal	32 (25)
Bilateral trigeminal	18 (14)
Isolated limb/body	27 (21)
Isolated trigeminal	13 (10)
Gait ataxia	120 (92)
Severe gait ataxia[a]	79 (61)
Dizziness	119 (92)
Horner sign	114 (88)
Hoarseness	82 (63)
Dysphagia	84 (65)
Severe dysphagia[b]	52 (40)
Dysarthria	28 (22)
Vertigo	74 (57)
Nystagmus	73 (56)
Limb ataxia	72 (55)
Nausea/vomiting	67 (52)
Headache	67 (52)
Neck pain	9 (7)
Skew deviation of eyes	53 (41)
Diplopia	41 (32)
Hiccup	33 (25)
Facial palsy	27 (21)
Forced gaze deviation	8 (6)

Data are expressed as number (%)
[a]Unable to stand or walk alone
[b]Requires nasogastric feed for feeding

patients stand or sit) seems to be attributed to lesions affecting the vestibular nuclei and vestibulospinal projections [13], while limb and gait ataxia are related to damage to the inferior cerebellar peduncle, spinocerebellar fibers, or the cerebellum itself [12, 14]. Occasionally, patients fall to any direction [14]. Limb ataxia may be described as "weakness" or "clumsiness" by the patient.

Nystagmus and Ocular Motor Abnormality

Involvement of the vestibular nuclei and their connections lead to nystagmus. The nystagmus is mostly horizontal or horizontal-rotational to the side opposite to the lesions [5, 6]. Although forced conjugate eyeball deviation to the lesion side (ocular lateropulsion) [15] is uncommon, milder degree of eyeball deviation is frequently observed when patients are ordered to close and then open the eyes, when correctional eyeball movements occur. Skew deviation, with the ipsilateral eye going down, and ocular tilt reaction occur [13]. Patients describe the symptoms as blurred vision, diplopia, oscillopsia, or tilting of visual images [5, 13]. Detailed mechanisms are described in Chap. 7.

Nausea/Vomiting

Nausea/vomiting is usually an initial and transient symptom closely associated with vertigo [10] and is probably caused by involvement of vestibular nuclei and their connections. It may also be caused by involvement of a putative vomiting center near the nucleus ambiguus [5, 12].

Horner Sign

Elements of the Horner sign are frequent (about 90%), caused by involvement of the descending sympathetic fibers in the lateral reticular substance. A constricted pupil with ipsilateral palpebral fissure narrowing is more frequently observed than facial anhidrosis.

Dysphagia, Dysarthria, and Hoarseness

Involvement of the nucleus ambiguus results in paralysis of the ipsilateral palate, pharynx, and larynx producing dysphagia, dysarthria, and hoarseness. Dysarthria may also be attributed to the concomitant involvement of the cerebellum. Dysphagia is present in approximately 2/3 of LMI patients, among whom about 60% require a nasogastric tube for feeding [10, 12]. Swallowing difficulty usually improves within days or months, but rare patients require persistent assistance in feeding. Dysphagia in LMI is more often associated with problems in the range of, than the timing of, hyolaryngeal excursion [16]. Hoarseness is equally common, while dysarthria is less common, occurring in about 1/4 of patients with pure LMI patients [10]. Some patients may show paralysis of the ipsilateral vocal cord.

Hiccup

Approximately 1/4 of patients develop hiccup [10, 12], often days after stroke onset. Hiccup

usually goes away within a few days but can persist for weeks or even months when it becomes an annoying symptom. Involvement of the dorsal motor nucleus of the vagus, solitary tract, and neurons related to expiration and inspiration in the reticular formation near the nucleus ambiguus may be responsible for hiccup [5, 10].

Sensory Symptoms/Signs

Sensory symptoms/signs are one of the most common manifestations of LMI. In the largest series, sensory function was intact in only 4% of patients [10]. Sensory symptoms/signs occur more frequently in the contralateral body/limbs (in approximately 85%) than in the face (58–68%), [7, 9] and the sensory defect in the face usually clears more quickly than that on the body/limbs. Although a selective loss of spinothalamic sensation is a rule, vibration sensation is occasionally involved as well in the hypalgic body/limbs, [9] due probably to the fact that some of the vibratory sensations are carried through the lateral column [17].

Crossed (ipsilateral trigeminal-contralateral limb/body) sensory changes have been considered a classical sensory pattern in LMI. However, sensory manifestations are much more diverse in the acute stage [9]. In the largest series [10], the patterns included ipsilateral trigeminal-contralateral limb/body in 26%, contralateral trigeminal-contralateral limb/body in 25%, bilateral trigeminal-contralateral limb/body in 14%, limb/body involvement without trigeminal involvement in 21%, and trigeminal involvement without limb/body involvement in 10%. Although the arm and leg are usually equally involved, in approximately 30% of the patients, there is a discrepancy; some have more severe sensory deficits in the arm while others have more severe deficits in the leg [9]. The latter occasion is more common, and some may have a sensory level on the trunk mimicking a spinal cord syndrome [18].

These diverse sensory manifestations are related to the varied patterns of involvement of the spinothalamic tract, descending trigeminal tract, and ascending secondary trigeminal fibers (Fig. 4.1). Notably, approximately 7% of LMI patients have ipsilateral tingling sensation often associated with lemniscal sensory deficits, more

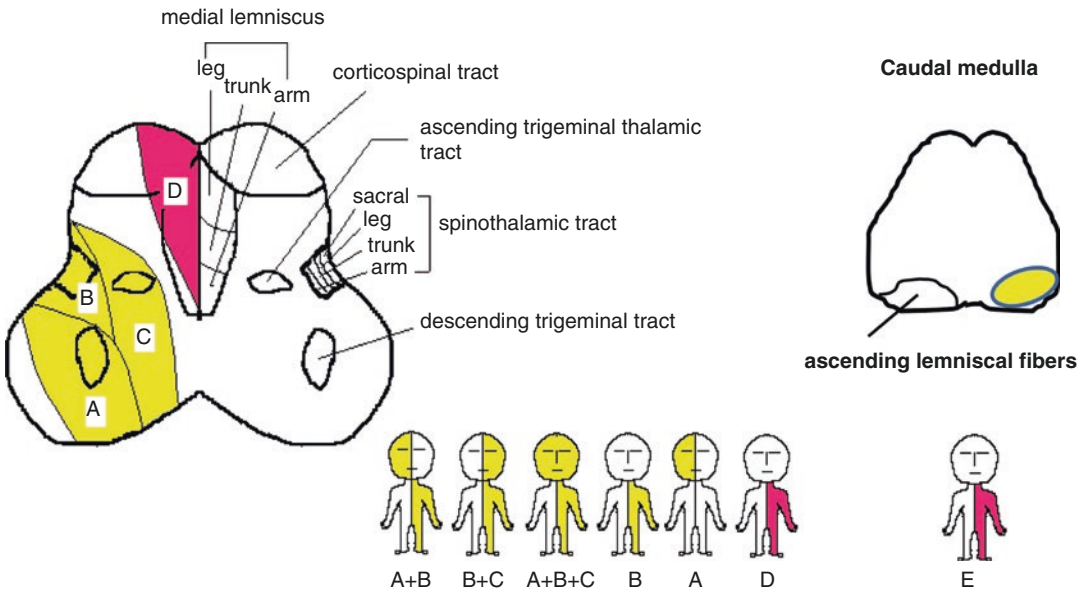


Fig. 4.1 Anatomic structures of the medulla and various patterns of sensory dysfunction caused by medullary infarction (see text for details). Yellow, spinothalamic sensory deficits; red, lemniscal sensory deficits; A + B, ipsilateral trigeminal-contralateral body/limb; B + C, contralateral trigeminal-contralateral body/limb; A + B + C, bilateral trigeminal-contralateral body/limb; B, contralateral body/limb; A, ipsilateral trigeminal; D, contralateral body/limb (lemniscal sensation); E, ipsilateral body/limb (lemniscal sensation). (Modified from Kim et al., Neurology 1997; Brain 2003)

marked in the arm than in the leg. Due to the leminscal sensory impairment, these patients often have feeling of "clumsiness" or "weakness" in the ipsilateral extremities. This sensory pattern is related to involvement of the lowermost medulla and explained by involvement of lemniscal sensory fibers at the upper-most part of the fasciculus cuneatus/gracilis or crossing fibers to the medial lemniscus [19] (Figs. 4.1E and 4.2).

In the descending trigeminal tract, the V3-representing area is located most dorsally and V1 most anteriorly, but in the ascending secondary trigeminal tracts, V3 is located most medially and V1 most laterally. Therefore, trigeminal sensory involvement is often inhomogeneous, more so on the contralateral side than the ipsilateral side. On both sides, the inhomogeneity is either divisional or segmental (onion-skin) pattern [4, 5, 9]. Bilateral perioral paresthesia, often observed in patients with large infarcts extending medially [9], may be caused by the simultaneous involvement of the descending and ascending V3 pathways near its decussation [20, 21].

Patients occasionally complain of facial pain. The pain usually appears at onset, heralding other symptoms and signs [5]. It is described as sharp, stinging, stabbing, or burning, tingling, and numb. The eyeball and the surrounding area are the most commonly affected, but the entire face, including the lips and inside the mouth, may be involved. Although facial pain usually improves, it may last permanently in some patients. Involvement of the sensory nucleus of the descending tract of the fifth cranial nerve may explain the facial pain.

Headache

Headache occurs in about half of the patients [10, 12]. It usually begins at onset or a few days before other symptoms/signs and subsides within several days. It most often occurs in the ipsilateral occipital or upper nuchal area followed by the frontal region and is usually described as dull, aching, or

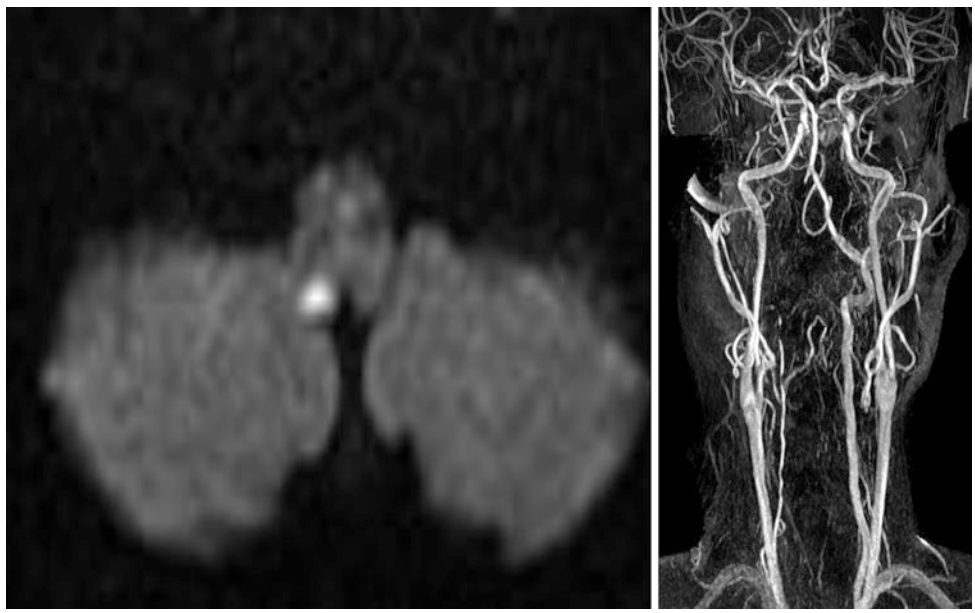


Fig. 4.2 A 69-year-old hypertensive man developed gait instability and numb sensation in the right hand, most markedly in the first-third finger tips. Neurological examination showed slightly decreased position and vibration sensation in the right fingers and impaired tandem gait. Diffusion-weighted MRI (left image) showed dorsally located infarct in the medullary-spinal cord junction. MRA (right image) showed right distal vertebral artery (VA) atherosclerotic occlusion. The ipsilateral sensory symptoms are probably due to involvement of the most rostral part of the ipsilateral lemniscal fibers (nucleus cuneatus) before decussation. The infarct was probably caused by occlusion of perforators (or posterior spinal artery) associated with VA atherosclerotic disease

throbbing. Considering that headache occurs before other symptoms and is not related to any symptoms/signs of LMI, [10] headache seems to be caused by an intracranial VA pathology, possibly related to dilated collateral vessels after VA stenosis/occlusion, [12] rather than the medullary lesion itself. Involvement of the descending spinal tract of the fifth cranial nerve and its nucleus may also be responsible for frontal headache. Prominent and persistent nuchal-occipital pain may be a manifestation of VA dissection.

Facial Palsy

Facial palsy, usually mild and upper neuron type, is present in 1/5 to 1/4 of patients [10]. It is presumably caused by involvement of aberrant corticobulbar fibers that loop caudally before traveling rostrally toward the facial nucleus [22]. In patients with upper-most medullary (or pontomedullary junction) lesion, there occurs relatively severe peripheral-type facial palsy due to direct involvement of facial nerve fascicles [23].

Respiratory Difficulty and Other Autonomic Signs

The medullary reticular formation contains neurons related to the control of respiration, and patients may show respiratory arrest or decreased respiratory drive, especially during sleep (Ondine's curse) [24]. Severe respiratory abnormalities calling for medical attention are uncommon unless patients have bilateral or extensive lesions [12]. In pure LMI, aspiration pneumonia associated with dysphagia is the most common reason for respiratory care, in which case, it is often difficult to assess how much respiratory control abnormality contributes to the patients' condition. Other autonomic disturbances such as tachycardia, bradycardia, sweating, orthostatic hypotension, gastric motility dysfunction, and urinary retention are sporadically observed.

Ipsilateral Hemiparesis

Ipsilateral hemiparesis may be associated with other typical symptoms of LMI [25].

The pathogenic mechanism of this so-called Opalski syndrome remains debatable. Recent imaging techniques such as diffusion-weighted MRI (DWI) and diffusion tensor imaging (DTI) showed that infarcts occurring at the lower-most medullary area or the medulla–spinal cord junction involve the ipsilateral corticospinal tract after the pyramidal decussation [26, 27]. This observation corroborates with Opalski's original patients who showed hyperreflexia and Babinski signs.

In addition, patients with ipsilateral ataxia or lemniscal sensory dysfunction (see above) may complain of "clumsiness" or "weakness" in their limbs [19]. In view of transient motor deficits and absent reflex abnormalities in the majority of these patients, most of the patients with ipsilateral "weakness" may have a pseudoparesis unrelated to pyramidal damage [19]. Thus, true Opalski syndrome is a rare entity.

Clinical–Topographical Correlation

The symptoms/signs of LMI differ according to the topography of lesions [5]. Kim et al. [10, 11] analyzed the MRI-identified lesions in a three-dimensional manner and made clinical–topographical correlation (Fig. 4.3).

Generally, rostral lesions tend to involve ventral (Fig. 4.3A), deep areas, while caudal lesions involve lateral-superficial region [10, 11] (Fig. 4.3C). This is probably related to the anatomical course of the VA; the intracranial VAs are located adjacent to the lateral surface at a caudal medulla level, which ascend ventrorostrally to fuse into the BA at the pontomedullary junction. The rostral-ventral lesions tend to produce ipsilateral trigeminal sensory symptoms (Fig. 4.1B+C), whereas caudal-lateral-superficial lesions tend to produce sensory symptoms limited to the extremities (occasionally with a gradient worse in the leg) sparing the face (Fig. 4.1B). A large, wide lesion is associated with a bilateral trigeminal sensory pattern (Fig. 4.1A+B+C), [10] which is quite uncommon in patients with caudal lesions.

The more important rostrocaudal difference is dysphagia, which is distinctly more prevalent and severe in patients with rostral than in caudal lesions [10, 11]. This may be explained by the following: (1) caudal medullary lesions are usually thin (Fig. 4.3C) and do not extend deeply as to involve the nucleus ambiguus and (2) the lower part of the nucleus ambiguus is not directly

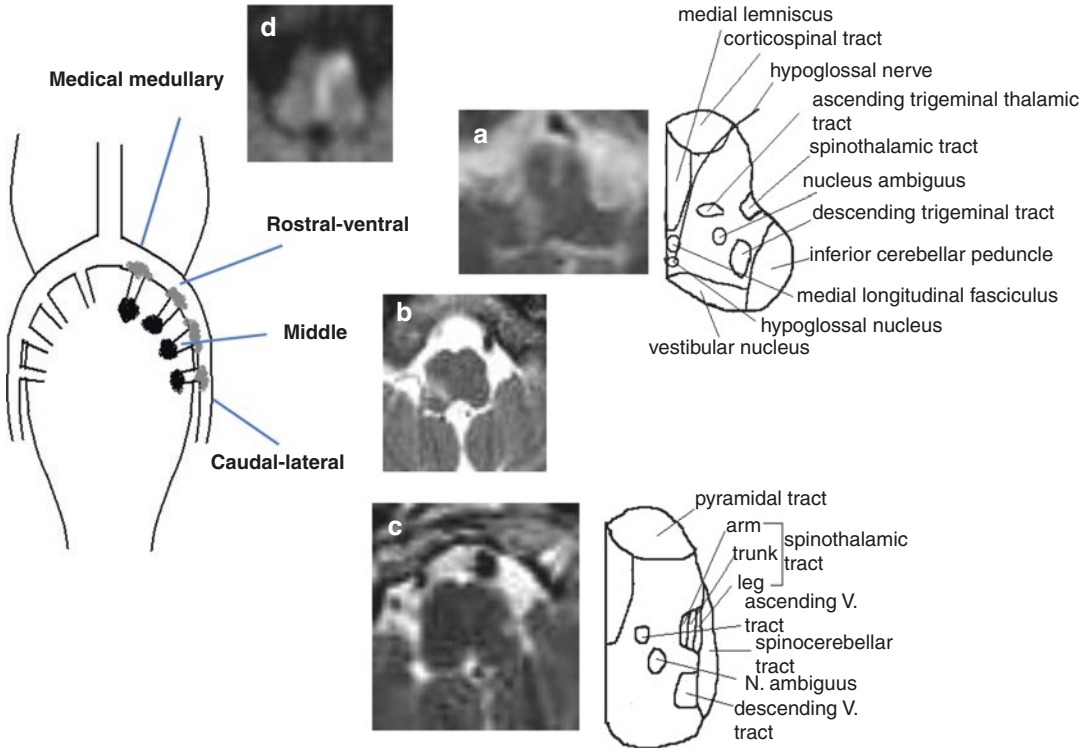


Fig. 4.3 Schematic drawing of stroke mechanism of various types of medullary infarction. Rostral type (**A**), middle type (**B**), and caudal-lateral type (**C**) lesions are categorized as "lateral medullary infarction" and determined according to the rostrocaudal location of the responsible perforating arteries. Medial medullary infarction (MMI) (**D**) seems to be produced by the most rostral vertebral artery disease. Patient A had severe dysphagia due to involvement of upper part of the nucleus ambiguus and contralateral trigeminal type sensory symptoms, whereas patient C had severe gait ataxia and sensory symptoms limited in the lower extremities. Patient B had ipsilateral trigeminal symptoms. Patient D had symptoms of MMI such as contralateral hemiparesis and hemihypesthesia (lemniscal sensation)

related to pharyngeal muscle motility [28]. Facial palsy is also more common in rostral lesions [10]. In patients with most rostral lesions, often at the pontomedullary junction, dysphagia is slight or absent because the nucleus ambiguus is spared at this level [29]. These patients often show severe, ipsilateral, peripheral-type facial palsy.

The caudal lesions are closely associated with severe lateropulsion and gait ataxia, probably due to frequent involvement of the laterodorsally located spinocerebellar tract and vestibular nuclei (Fig. 4.3C). Dissection and headache are also more common, while dysphagia is absent or minimal in this group. The middle medulla shows intermediate characteristics and classical ipsilateral trigeminal-contralateral body/limb pattern sensory deficits (Figs. 4.1B+C, 4.3B).

Stroke Mechanisms

Although Wallenberg initially considered PICA disease as a cause of LMI [1], Fisher et al. [6] found sole involvement of the PICA in only two of their 17 cases of LMI and 14 patients showed VA steno-occlusion. Thus, the most common cause of LMI is occlusion of penetrating branches associated with intracranial VA steno-occlusive disease [6] (Fig. 4.4). In a large series that investigated 123 LMI patients [10], ipsilateral VA steno-occlusive disease was present in 83 (67%) (33 intracranial VA disease, 34 whole VA disease, and 5 extracranial VA disease) and PICA disease in 12 (10%) patients. Atherothrombosis is a dominant pathology, while dissection of the VA or PICA is the cause of steno-occlusive lesions in approximately 14–33% of cases [7, 8, 10] (for

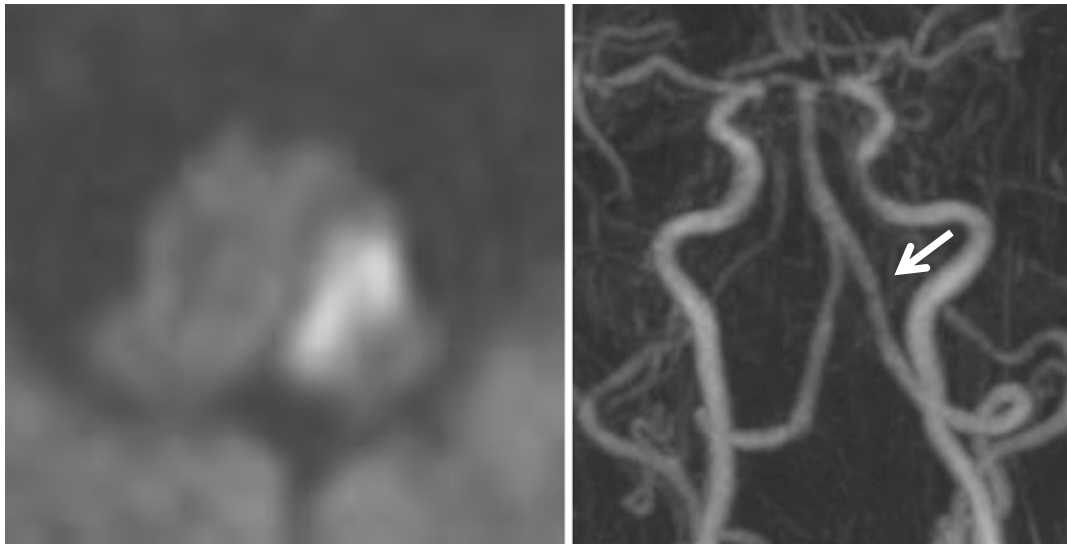


Fig. 4.4 Diffusion-weighted MRI showed an infarction in the left rostral medulla. MRA showed focal, atherosclerotic narrowing (arrow) that probably occluded a perforator

dissection, see Chap. 14). In patients with normal angiographic findings, perforating artery disease seems to be the mechanism of infarction. Embolic occlusion of the PICA or distal VA from diseased heart or proximal artery atherosclerosis may also produce LMI [30, 31], but concomitant infarcts in other parts (mostly, cerebellum) of the brain are usually present in these patients.

Prognosis

The prognosis of pure LMI is benign, mainly due to the absence of significant motor dysfunction. The hospital mortality ranges from 0.8% to 11.6% [2–4, 10]. Patients with large, rostral lesions tend to have severe dysphagia and aspiration pneumonia, requiring ICU care. Sudden respiratory (Ondine's curse) or other autonomic failures may produce respiratory-cardiac arrest, and physicians may have to keep this possibility in mind. Nevertheless, recent studies have shown very low hospital mortality, which is probably related to improved care for respiration, infection, and dysphagia [10]. Old age, having dysphagia [32], and rostral LMI lesions [33] were found to be factors related with unfavorable prognosis.

Despite the relatively benign outcome, the majority of survivors have at least one remaining sequelae. The most important one is sensory symptoms/signs, followed by dizziness and dysphagia [34]. Usually, the persistent and disturbing sequela correlates with the most severe initial symptom. Approximately 1/4 of the patients develop uncomfortable painful paresthesia (central post-stroke pain, CPSP) [35], which are described as numb, burning, or cold [34]. The symptoms usually occur in the body parts where the initial sensory perception deficit was most severe.

Patients with severe and extensive VA diseases more often develop recurrent cerebral infarction or coronary disease than those without [2]. The presence of posterior fossa hypoperfusion may predict poor prognosis [36]. In patients with concomitant infarcts in other areas, the prognosis is influenced by the location and extent of the extramedullary lesions. In patients with large PICA territory cerebellar infarction, massive edema and consequent herniation may yield a poor prognosis. However, a recent study showed that although the short-term outcome is poorer in LMI patients with extramedullar lesions, long-term residual symptoms such as dizziness, dysphagia, and sensory symptoms are more prevalent in pure LMI patients [33]. This is probably because in the former patients, PICA occlusion is the main pathogenesis and LMI lesions are usu-

ally limited to a small, dorsal part of the medulla, an area supplied by the PICA. On the contrary, the lesions associated with distal VA disease in pure LMI patients tend to be larger.

Medial Medullary Infarction

Medial medullary infarction (MMI) was initially described by Spiller in 1908 [37]. Dejerine later proposed a triad of symptoms: contralateral hemiplegia sparing the face, contralateral loss of deep sensation, and ipsilateral hypoglossal paralysis [38]. Pathological findings were first reported by Davison in 1937, who described thrombotic occlusion of the anterior spinal artery (ASA) and the adjacent intracranial VA [39].

With the advent of MRI, the premortem diagnosis of MMI can now be easily made. Kim et al. [40] compared their own series of 17 patients diagnosed by MRI, with 26 previously reported patients. They found that in the former group, bilateral lesions, quadriparesis, lingual paresis, and respiratory difficulty were much rarer, and the prognosis was much better. Subsequent studies using MRI showed that patients usually present with relatively benign, unilateral sensorimotor stroke [40–45]. Clinical symptoms/signs of MMI are summarized in (Table 4.2).

Table 4.2 Neurologic symptoms and signs published in the largest series (In Kim JS, Han Y, Medial medullary infarction: clinical, imaging, and outcome study in 86 consecutive patients, 2009;40: 3221–5)

Symptoms and signs (n = 86)	
Motor dysfunction	78 (91)
	Hemiparesis 68, quadriparesis 8, monoparesis 2
Facial paresis	21 (24)
Sensory dysfunction	59 (73)
	Paresthesia 55
	Impairment of objective sensory perception
	Vibration 48
	Position 41
	Touch 32
	Pinprick 17
	Cold 22
Lim ataxia	36 (42)
Dysarthria	54 (63)
Dysphagia	25 (29)
Ipsilateral hypoglossal palsy	3 (3)
Contralateral tongue deviation	9 (10)
Vertigo/dizziness	51 (59)
Nausea/vomiting	14 (16)
Nystagmus	38 (44)
Diplopia	7 (8)
Headache	9 (10)

Number in parenthesis indicates percentage

Clinical Manifestations

Limb Weakness

Contralateral hemiparesis sparing the face is the most characteristic sign of MMI occurring in approximately 90% [46]. Quadriparesis occurs in less than 10% of the patients [45]. Although rare, hemiparesis may occur on the ipsilateral side due to the lower-most lesion involving the crossed pyramidal tract [40]. The degree of motor dysfunction is variable; in one study [45], it was severe (Medical Research Council scale ≤3) in 37%, 2/3 of whom had a gradual progression of weakness during several days after onset.

Facial Palsy

Although sparing of the face is one of the characteristics of MMI, mild and transient facial paresis occurs in 1/4 to 1/2 [12, 44, 45], probably related to involvement of yet-uncrossed corticobulbar fibers directed to the contralateral cranial nuclei at the level of the upper medulla [22].

Dysarthria and Dysphagia

Dysarthria and dysphagia were reported to occur in 63% and 29%, respectively [45]. These symptoms are much more severe in patients with bilateral MMI. In unilateral cases, a nasogastric tube is required in less than 10%. A study using videofluoroscopic swallowing tests showed that dysphagia in MMI is associated with delayed timing rather than a reduced range of hyolaryngeal excursion [16] and may be attributed to damage to the corticobulbar tract or adjacent pattern generator regulating the nucleus ambiguous.

Ipsilateral Hypoglossal Nerve Palsy

Ipsilateral hypoglossal nerve palsy, if it presents, is an important localizing sign [38]. Its prevalence is reported extremely variably, from 3% to 82% [11, 40–45]. Recent MRI-based studies found a lower prevalence of ipsilateral hypoglossal palsy than earlier studies; a large series showed that definite ipsilateral hypoglossal paresis occurred in only 3% of patients while clumsy tongue movements with occasional contralateral tongue deviation were more common [45]. Because MMI lesions most often involve the rostral medulla, the hypoglossal nerve nucleus and fasciculus, located in the lower medulla, are frequently spared.

Sensory Dysfunction

Sensory dysfunction is the second most important symptom/sign of MMI. Unlike LMI patients, MMI patients typically complain of tingling sensation from the onset. The involved area is usually hemibody/limbs below the ear or neck (Fig. 4.1D). However, sensory symptoms may extend to the face, probably due to additional involvement of the secondary ascending trigeminal sensory tract. The facial sensory symptoms are usually mild, incomplete, and transient. Occasionally, the sensory abnormality is restricted to a certain body part, such as the lower leg [47]. Dermatomal distribution sensory abnormalities are also reported [48]. Although lemniscal sensory deficits are characteristic, mild and transient impairment of pain/temperature perception is occasionally present due possibly to involvement of the spinoreticulothalamic system that regulates the spinothalamic sensory system [41, 42, 44, 45].

Ataxia

Limb incoordination is occasionally noted [42] and is usually attributed to involvement of pontocerebellar fibers and/or associated proprioceptive sensory dysfunction. Gait instability or body lateropulsion may be related to involvement of the vestibulocerebellar tract, inferior olivary nucleus, or more laterally located spinocerebellar tract [42].

Vertigo/Dizziness, Nystagmus, and Ocular Motor Disturbances

These symptoms/signs are closely related to involvement of the dorsal medulla, [44, 49] where the vestibular nuclei, medial longitudinal fasciculus (MLF), and the nucleus prepositus hypoglossi (NPH) are located. In contrast to LMI, nystagmus is mostly ipsilesional, and ocular lateropulsion is to the contralateral side (contrapulsion) [50]. Upbeat nystagmus is observed in 1/10 to 1/5 of patients, [44, 45, 49] which may be explained by involvement of the VOR pathways from both anterior semicircular canals [51]. Unilateral lesion may also produce upbeat nystagmus [45] (see Chap. 7 for detailed mechanisms).

Emotional Disturbances

Previous reports have described patients presenting with pathological crying and laughing, depression, and psychotic behaviors [52, 53]. A recent study showed that emotional incontinence in MMI patients is as common as in those with pontine base infarction [54].

Clinical–Topographical Correlation

The majority of MMI lesions involve the rostral part of the medulla, and lesions limited to the caudal medulla are rare [45]. Ventro-dorsally, ventral lesions are closely related to motor dysfunction, middle lesions to sensory symptoms, and dorsal lesions are associated with vertigo, ataxia, and ocular motor dysfunction (Fig. 4.5). The symptom correlation according to ventrodorsal distribution is similar to that of pontine base infarction (see below, pontine infarction). Unlike pontine infarction, the face is mostly spared because the lesions are below the level of the facial nerve nucleus/fascicles. Sensory abnormalities are mostly lemniscal because lemniscal and spinothalamic tracts are separated in the medulla (Fig. 4.1D). In a large series, the lesion patterns include ventral in 20%, ventral+middle in 33%, and ventral+middle+dorsal in 41% [45].

Bilateral MMI

Bilateral MMI is uncommon. In one study, bilateral lesions occurred in 14%. Because the lesion

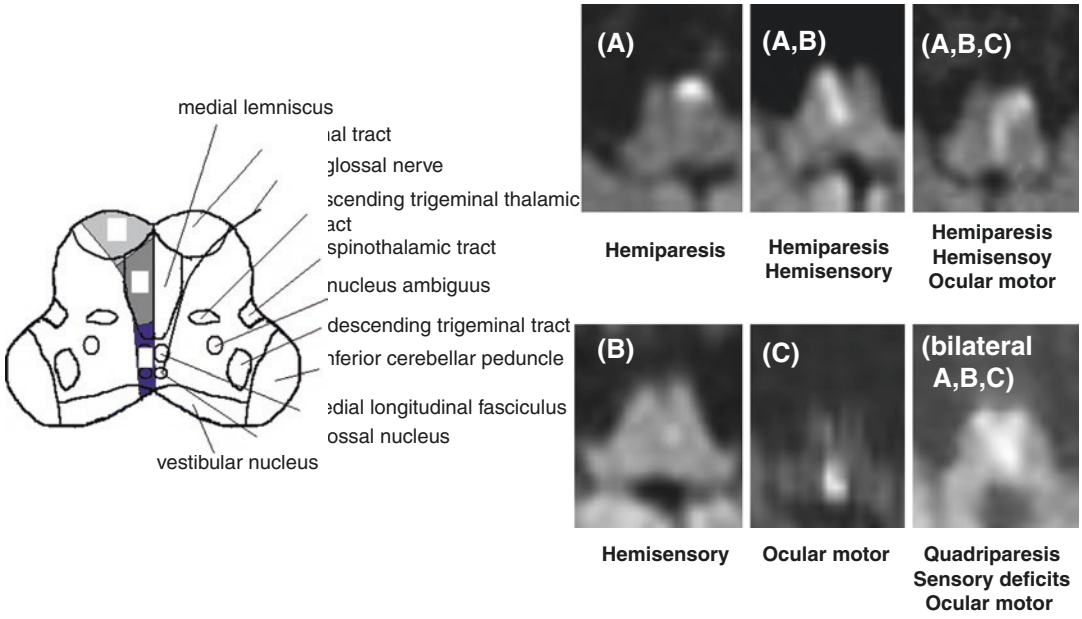


Fig. 4.5 Illustrative patients and schematic drawings of patterns of medial medullary infarction. Patterns of involvement of A (pure motor stroke), A + B (sensorimotor stroke), or A + B + C (sensorimotor stroke + ocular dysfunction) are common, while others are uncommon. Selective involvement of B and C produces pure hemisensory stroke and pure ocular motor dysfunction, respectively. Bilateral involvement of A + B + C accounts for less than 10% of medial medullary infarction and leads to quadriparesis, bilateral sensory loss, and ocular motor dysfunction

on the one side is occasionally small and asymptomatic, quadriparesis was observed in 9% [45]. In patients with quadriparesis, MRI lesions are usually symmetrical and heart shaped (Fig. 4.5, bilateral A,B,C). Patients have severe bulbar palsy and sensory symptoms, mimicking pontine locked-in syndrome (see below, pontine infarction). Unless the dorsal pons is concomitantly involved, gaze is generally preserved.

Stroke Mechanism

Although ASA occlusion has traditionally been emphasized, [37–39] recent studies showed that MMI is more often caused by intracranial VA or VA–BA junction atherothrombotic diseases that obliterate perforating branches [55] (Figs. 4.3 and 4.6 upper panel). In one series, relevant intracranial VA atherosclerotic disease was present in 62% of patients while perforator occlusion without VA disease (small artery disease) occurred in 28% of patients [45]. Infarcts associated with intracranial VA atherothrombotic disease tend to extend deeper (Fig. 4.6 upper panel) than those with small vessel disease (Fig. 4.6, lower panel), perhaps associated with either multiple perforator occlusion or more extensive hypoperfusion in the medulla. VA dissection may cause MMI but is less common than in LMI.

ASA occlusion, although uncommon, may produce caudal MMI infarction. Rarely, embolic occlusion of ASA branches by talc [56], fibrocartilaginous material, [57] or syphilitic arteritis [58, 59] can cause MMI. Embolism from the diseased heart or proximal VA disease is an uncommon cause of pure MMI. Bilateral MMI may be caused by occlusion of one ASA supplying both parts of the medulla. However, a large study [45] showed that bilateral MMIs are generally located rostrally in the territory of the distal intracranial VA or proximal BA. It seems that bilateral MMIs are usually caused by intracranial VA–BA atherothrombotic disease that obliterates multiple perforators bilaterally.

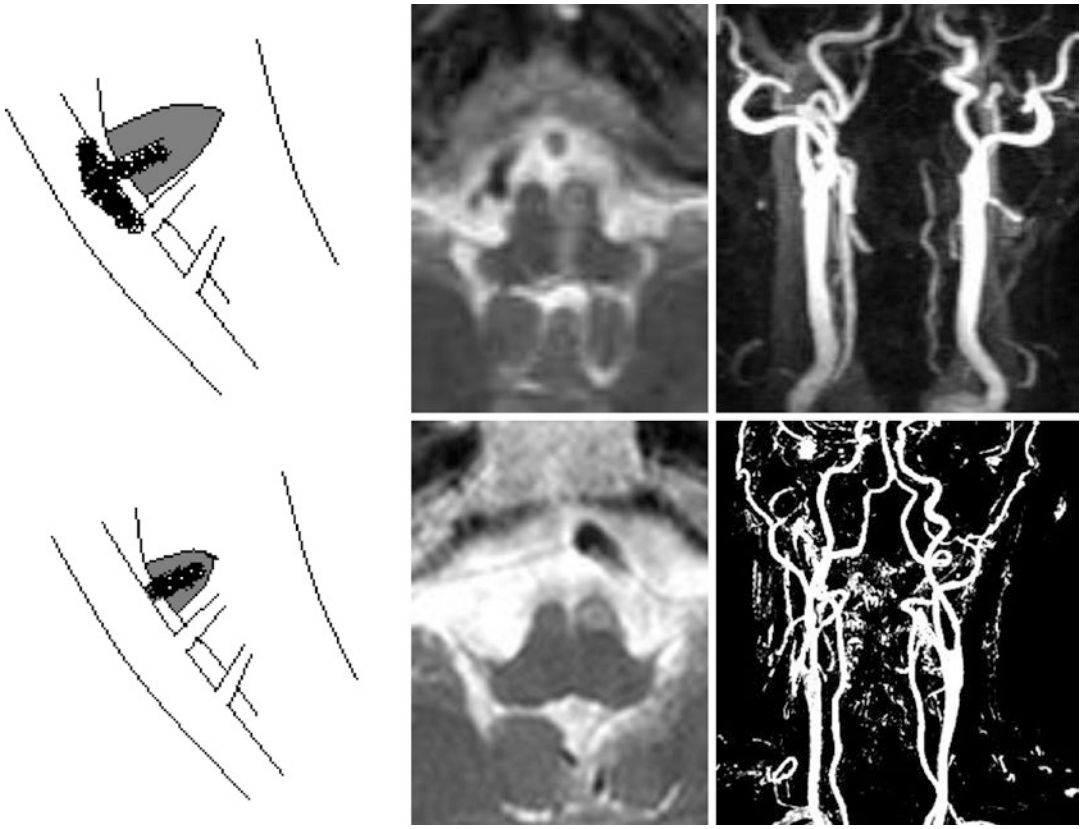


Fig. 4.6 Examples of a patient with large, dorsally extended medial medullary infarction (MMI) that is associated with distal vertebral artery disease (upper panel) and a patient with small, ventral MMI that is associated with small artery disease (lower panel)

Prognosis

Unlike LMI, aspiration pneumonia is uncommon in MMI except for those with bilateral lesions. The prognosis of MMI is better than that reported in the pre-MRI era; in a series of 86 patients, only 3 died during admission [45]. Due to the presence of significant motor dysfunction, functional outcome is generally worse in MMI than in LMI [34]. Severe initial motor dysfunction is a main predictor for poor functional outcome [45]. In the chronic stage, sensory dysfunction is equally prevalent and troublesome, which consists of both joint pain associated with motor dysfunction/spasticity and CPSP. In one study, CPSP defined by visual analog scale ≥4 was present in 36% [45]. The CPSP is most frequently expressed as numb followed by aching, and unlike LMI patients, "burning" sensation is rarely described [34]. Dizziness is reported in approximately 1/3 of the patients [45].

Combined LMI and MMI

LMI and MMI may occur simultaneously or consequently. This hemimedullary syndrome was first described in 1894 by Reinhold [60] and by Babinski and Nageotte [61] 8 years later. Hemimedullary infarction is usually associated with concomitant infarcts in the posterior circulation, and its occurrence in isolation is rare. Clinical symptoms/signs are essentially the combination of LMI and MMI. The usual etiologies are intracranial VA atherosclerosis or dissection that extends to block both lateral and medial medullary perforating branches.

Table 4.3 Clinical manifestations of pontine infarction

Author	Macdonell et al.	Kase et al.	Tohgi et al.
Country	Australia	USA	Japan
Published year	1987	1993	1993
Diagnosis	CT based	CT/MRI based	CT/MRI based
Number of patients	30	66	293
Symptoms			
Dizziness/vertigo	80	50 (vertigo)	70
Nausea/vomiting	63	52	56
Gait difficulty (or truncal ataxia)	77	71	40
Headache	40	53	32
Dysarthria	60		20
Signs			
Limb ataxia	70	61	59
Truncal ataxia	67	62	45
Nystagmus	53	64	38
Decreased consciousness	36		34
Ocular movement disorder	27		
Hemi(mono) paresis	7		20
Facial palsy	13		8

Pontine Infarcts

Pontine infarction may occur in isolation or in association with other posterior circulation infarction. Hospital registry studies showed that patients with isolated pontine infarcts account for 2.6–3% of ischemic stroke and 12–15% of patients with posterior circulation infarcts [62–64]. One study from Asia showed a higher prevalence: 7.6 % of cerebral infarcts and 28% of vertebrobasilar artery territory infarcts [65] (Table 4.3).

Clinical Features

Motor Dysfunction (Including Dysarthria and Ataxia)

The pontine base contains fibers regulating motor function, including descending corticospinal, corticopontocerebellar, and corticobulbar tracts (Fig. 4.7A). Accordingly, pontine base infarction easily produces motor system dysfunction. Although limb weakness is the most common symptom, the clinical features depend upon the degree of involvement of each fiber tract. Fisher and his colleagues described pure motor stroke [55], ataxic hemiparesis [66], and dysarthria-clumsy hand syndromes [67] as "lacunar" syndromes. However, other combinations are observed such as dysarthria-hemiataxia or dysarthria-facial paresis [68]. The categorization is not strict as patients with ataxic hemiparesis may evolve into pure motor stroke as the limb weakness progresses over time, or vice versa. Patients with ataxic hemiparesis may have additional ataxia on the side ipsilateral to the lesion [68–70] due probably to involvement of the crossing corticopontocerebellar tracts [70].

Severe hemiparesis is usually associated with large lesions affecting the ventral surface of the caudal or middle pons whereas similar sized lesions tend to produce milder limb weakness but relatively prominent dysarthria (producing dysarthria-clumsy hand) when they are located in the rostral pons; here, pyramidal tract fibers are sparsely arranged and located relatively laterally and are therefore not extensively damaged by paramedian lesions [68].

Sensory Dysfunction

Small tegmental pontine infarcts or hemorrhages that selectively involve sensory tracts (medial lemniscus and spinothalamic tract) produce a pure or predominant hemisensory deficit without significant other neurological dysfunctions [71, 72] (Fig. 4.7C). Occasionally, patients have hemi-paresthesias without objectively detectable sensory deficits.

In the pontine medial lemniscal tract, the sensory projections from the arm, trunk, and leg are arranged from a medial to lateral direction. Therefore, a medially located lesion preferentially affects the face and arm, causing a cheiro-oral syndrome, whereas laterally located lesions produce leg-dominant sensory symptoms [71]. The most medially located lesions sometimes produce bilateral facial or perioral sensory symptoms due probably to involvement of trigeminothalamic fibers bilaterally [71]. Cheiro-oral-pedal

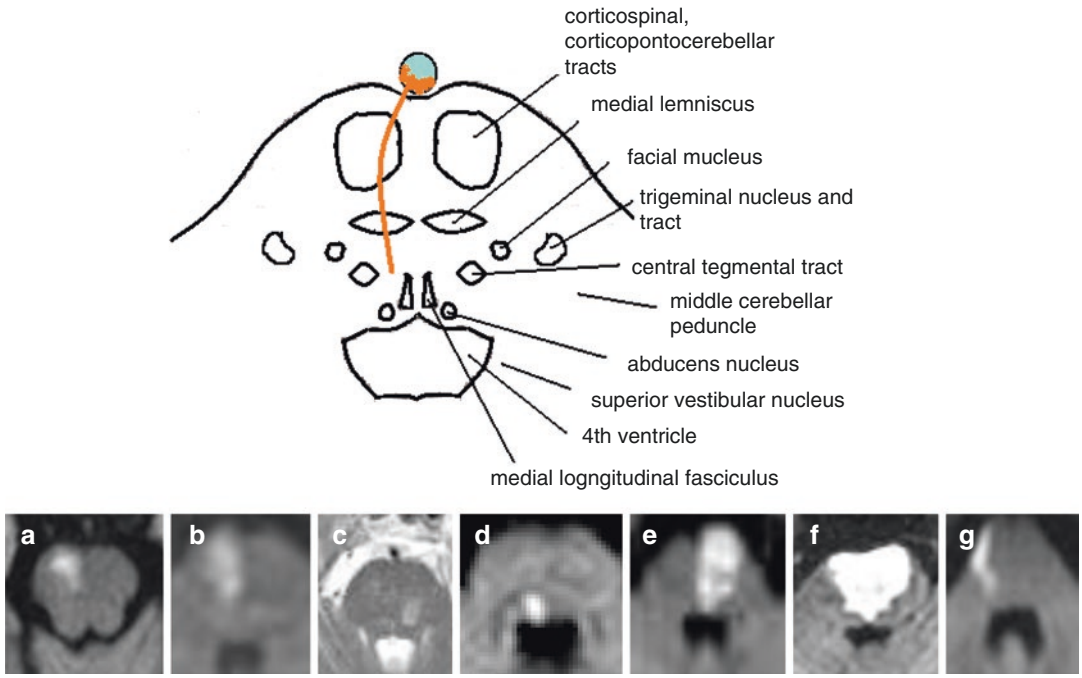


Fig. 4.7 Illustrative patients and schematic drawing showing patterns of infarcts in the pons that is associated with branch occlusion. See the text for details. Patients had left hemiparesis (**A**), left sensorimotor stroke (**B**), right pure sensory stroke (**C**), right internuclear ophthalmoplegia (**D**), left one-and-a-half syndrome and right sensorimotor stroke (**E**), quadriparesis, sensory loss, and horizontal gaze palsy (**F**), and left ataxia and sensory change (**G**)

[73] and oro-crural [74] sensory distribution patterns are also reported.

Trigeminal sensory deficits are often noticed in patients with infarcts affecting the lateral pons, usually accompanied by other symptoms of AICA territory infarction. Isolated trigeminal sensory symptoms without other neurological deficits may occur in patients with small strokes affecting the trigeminal fascicles or nucleus in the lateral pons [75]. Trigeminal sensory symptoms restricted to the intraoral area, and isolated involvement of taste sensation [76] were also reported.

Ocular Motor Dysfunction

Structures related to ocular motor function such as abducens nucleus and fascicles, paramedian pontine reticular formation (PPRF), and medial longitudinal fasciculus (MLF) are located in the paramedian, dorsal pontine tegmentum (Fig. 4.7D). Infarcts affecting this region cause various types of ocular motor dysfunctions. For a detailed description and mechanism, see Chap. 7.

6th Nerve Palsy

The abducens nucleus is located in the paramedian, dorsal, lower pons. Although rare, isolated 6th nerve palsy can result from a small pontine infarct that damages the abducens fascicles [77–79]. Because the abducens nucleus is surrounded by facial nerve fascicles, dorsal lesions involving the lower pons may produce both 6th and 7th nerve palsies in isolation (Fig. 4.8B), or more frequently, in association with contralateral hemiparesis (Millard–Gubler syndrome).

Internuclear Ophthalmoplegia

Internuclear ophthalmoplegia (INO) due to involvement of the MLF is much more common in patients with pontine infarction than 6th nerve palsy, probably because the MLF is a vertically long structure located in the paramedian area (Fig. 4.7D), easily involved by deep, paramedian pontine infarcts. In the largest series that included 30 patients with INO with minimal neurologic deficits, authors found that they account for

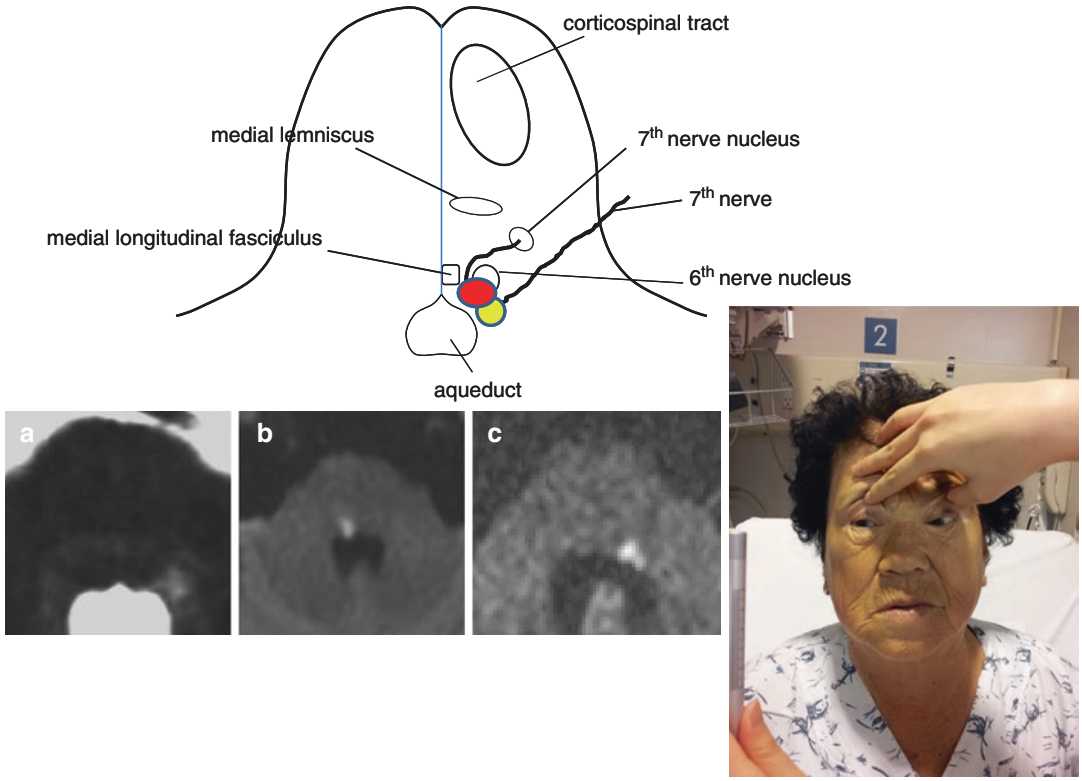


Fig. 4.8 Illustrative patients and schematic drawing of dorsal pontine structures. (**A**) An infarct that produced isolated left facial palsy indistinguishable from peripheral Bell's palsy, due to selective involvement of the genu portion of the seventh nerve (yellow circle). (**B**) An infarct producing right sixth and seventh nerve palsies due to involvement of the sixth nerve nuclei and the genu portion of the seventh nerve (red circle). (**C**) An infarct producing right internuclear ophthalmoplegia and facial palsy (71/2 syndrome) due to involvement of the medial longitudinal fasciculus and seventh nerve fascicle (not indicated in the diagram). Right image: Photography of patient B. She showed lateral gaze limitation of the right eye and decreased nasolabial fold in the right face. Consent was obtained from the patient for this presentation

0.47% of all ischemic stroke patients [80]. If the adjacent medial lemniscus or pontocerebellar fibers are involved, sensory symptoms, ataxia, and dysarthria are added. Lesions that extend laterally may result in additional facial paresis (71/2 syndrome) (Fig. 4.8C).

The symptoms of INO are characterized by (1) paralysis of adduction (or slowed adductive saccade when symptoms are mild) of the ipsilateral eye for all conjugate eye movements and (2) nystagmus in the contralateral eye when this eye is in abduction. Convergence is more often preserved than impaired. Occasionally, the contralateral eye is exotropic on neutral gaze, which is called "paralytic pontine exotropia." The exotropic gaze deviation is attributed to the unopposed tonic activity of the spared PPRF on the side opposite to a unilateral lesion. Although less common, some patients with bilateral INO show bilateral exotropia, a phenomenon referred to as "wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) [81]." The INO is frequently associated with contraversive ocular tilt reaction (OTR) (subjective visual vertical, ocular torsion, or skew deviation).

Conjugate Horizontal Gaze Palsy

Involvement of the paramedian pontine reticular formation (PPRF) near the 6th nerve nucleus leads to the absence of voluntary lateral gaze to the side of the lesion, including the quick phase of nystagmus. Patients' eyes remain at the mid-

line in attempted ipsilateral saccade, or when they begin in a position contralateral to the lesion, return to the midline slowly [82]. The vestibular ocular reflex (VOR) and ipsilateral smooth pursuit usually remain intact. Bilateral lesions involving the abducens nucleus and PPRF produce paralysis of all horizontal eye movements. Although vertical gaze is mediated at a more rostral level, patients with bilateral horizontal gaze palsies may show slow vertical gaze saccades. This is probably related to the fact that the omnipause neurons that modulate saccadic triggering are also involved in vertical saccades via sending signals to the riMLF [83].

One-and-a-Half Syndrome

One-and-a-half syndrome refers to "a paralysis of eye movements in which one eye lies centrally and fails completely to move horizontally while the other eye lies in an abducted position and cannot be adducted past the midline [84]." A unilateral pontine lesion involving both the PPRF and MLF produces an ipsilateral conjugate gaze palsy, and paralysis of adduction of the ipsilateral eye on conjugate gaze to the opposite side [85].

Ocular Bobbing and Other Related Signs

Fisher [86] introduced the term ocular bobbing: "The eyeballs intermittently dip briskly downward through an arc of a few millimeters and then return to the primary position in a kind of bobbing action." Ocular bobbing is an ominous sign, usually associated with extensive, bilateral pontine infarcts or hemorrhages [86, 87]. Quadriparesis and decreased consciousness are usually present. Bobbing is usually bilateral and symmetric but can be predominantly unilateral or asymmetric [84, 88]. Asymmetric bobbing is common in patients in whom there is an asymmetric paralysis of conjugate gaze. When bobbing is asymmetric, usually the eye ipsilateral to the side of limited gaze bobs when gaze is directed to that side [84, 86]. In patients with extensive pontine lesions, horizontal gaze is lost, but vertical gaze is preserved; the vertical vector of gaze may be accentuated so that the eyes "bob" down. In patients with bilateral pontine infarcts, ptosis of the upper eyelids is also frequent [89], usually attributed to involvement of descending sympathetic fibers in the lateral pontine tegmentum. The pupils become small (pinpoint pupil) [84], but pupillary response to light is usually preserved if examined by magnifying glass.

Involuntary Movements

Palatal Myoclonus

Palatal myoclonus is a rhythmic involuntary jerking movement of the soft palate and pharyngopalatine arch, often involving the diaphragm and laryngeal muscles as well [90].

Palatal myoclonus does not appear in the acute stage of stroke but develops several months later. Occasionally, rhythmic, jerky movements are also observed in the face, eyeballs, tongue, jaw, vocal cord, or extremities (mostly hands); they may or may not be synchronous with palatal movements. The movements of the palate vary in rate between 40 and 200 beats per minute. The movements may involve the eustachian tube and make a click that the patient can hear.

The posited anatomical lesion involves the "Guillain–Mollaret triangle," which includes the dentate nucleus of the cerebellum, the red nucleus in the midbrain, and the inferior olivary nucleus in the medulla and their interconnections [91]. The pathologic lesion most often seen in these patients is hypertrophic degeneration of the inferior olive. Enlarged neurons and diffuse gliosis are observed usually, though not always, bilaterally. In patients with pontine strokes, damage to the central tegmental tract and consequent hypertrophic degeneration of the inferior olive is considered to be a responsible mechanism. For unclear reason, the palatal myoclonus is more often observed in pontine hemorrhages than infarcts (Fig. 4.9).

Periodic Limb Movements and Restless Leg

Periodic limb movements [92] and restless leglike symptoms [93] may occur after unilateral pontine base infarction. The presumed mechanisms are disinhibited propriospinal/segmental spinal reflexes or dopaminergic fibers involvements due

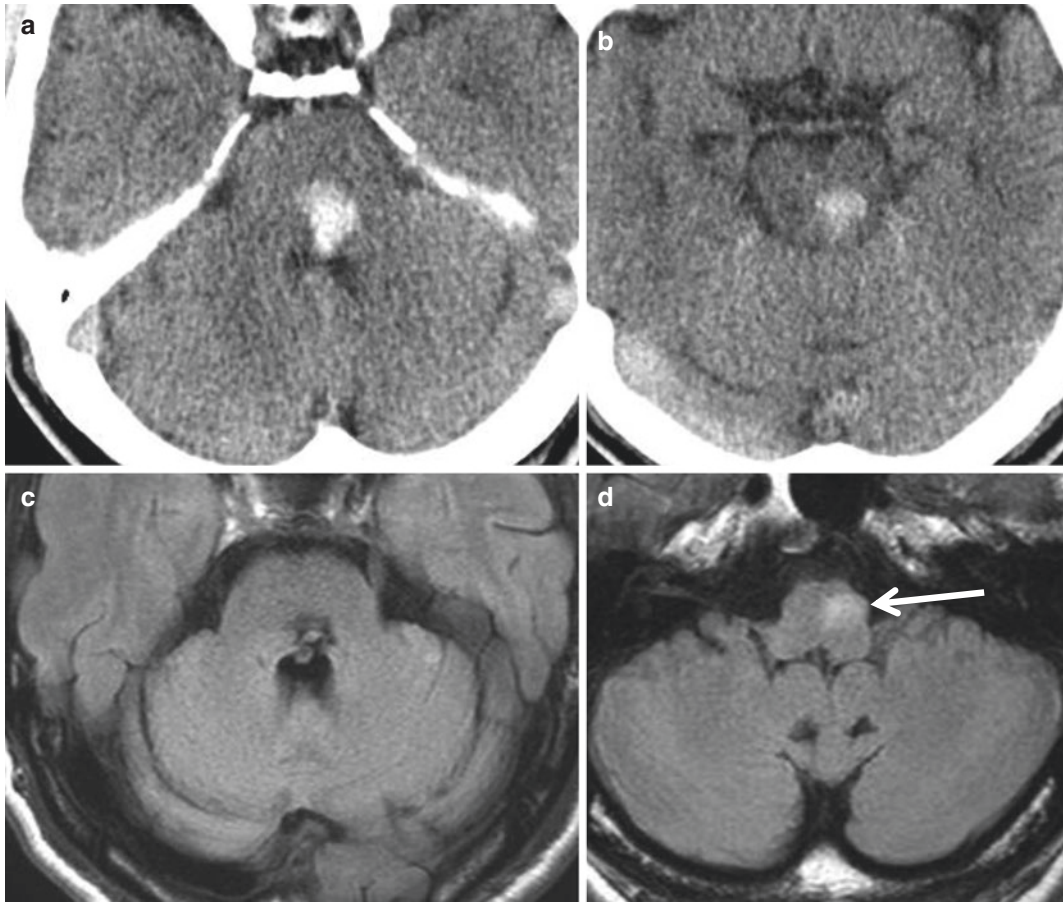


Fig. 4.9 A 68-year-old hypertensive man became drowsy. Neurological examination showed that he had bilateral horizontal gaze paresis, severe dysarthria, quadriparesis, bilateral ataxia, and sensory dysfunction. CT showed paramedian dorsal ponto-mesencephalic hemorrhage (**A**, **B**). He gradually improved but continued to have dizziness, diplopia, and gait ataxia. One year later, examination showed newly developed pendular nystagmus, palatal tremor, and auditory hallucination. MRI showed old, shrunken hemorrhages (**C**) and a high signal intensity in the swollen left medullary olive (arrow, **D**), consistent with inferior olivary hypertrophic degeneration

to lesions involving pontine reticular formation [92, 94].

Other Cranial Nerve Dysfunction

The 5th, 7th, and 8th nuclei or fascicles are involved when lesions are laterally situated. This issue will be discussed in the AICA syndrome (see Chap. 6). A very small infarct selectively damaging the genu portion of the 7th nerve may produce isolated 7th nerve palsy, indistinguishable from peripheral facial nerve palsy (Fig. 4.8A).

Auditory Symptoms

After entering into the cochlear nucleus, some auditory fibers ascend directly, while others traverse through the trapezoid body to the contralateral lateral lemniscus. Due to the bilateral, complex auditory pathways, hearing loss is rare in patients with pontine infarction unless the 8th nerve nucleus/fascicles are directly involved in AICA territory infarction.

However, extensive and destructive lesions involving the tegmental area may produce auditory symptoms. Bilateral total deafness has been rarely observed [95]. More often, tinnitus and auditory hallucination, usually associated with a certain degree of hearing impairment, are found in patients with pontine strokes [96–98] (Fig. 4.9). The auditory hallucinations are considered a central "release phenomenon" in the setting of

peripheral input deficiency. The hallucination often disappears as the hearing loss improves [98]. For unclear reason, hallucinations are often musical, i.e., songs, drum sound, etc. Contralateral hyperacousis has also been observed in a patient with unilateral pontine tegmental stroke [99], possibly attributed to hypersensitization phenomenon after damage on the sensory tract.

Consciousness Disturbances or Coma

Patients with bilateral, extensive pontine infarcts caused by sudden BA occlusion often present with decreased consciousness or even coma, probably related to involvement of brainstem reticular activating structures responsible for the regulation of alertness.

Abnormalities of Respiration

Abnormalities of respiration are also common, but their mechanism is difficult to determine, partly because of the extensiveness of the infarction and partly because of the usual presence of general medical problems (e.g., aspiration, fever, and hypoventilation) in these patients. Apneustic breathing with a hang-up of the inspiratory phase and grossly irregular breathing (ataxic respirations) occasionally occur in patients with BA occlusion and indicate an ominous prognosis [100].

Emotional Disturbances

Pathological laughing or crying occasionally occurs in patients with pontine infarction [65, 68, 69, 101]. Patients with bilateral pontine lesions have more frequent and severe symptoms. Recent studies [54, 102] focusing on this issue showed that excessive or inappropriate laughing/crying occurs in 33–50% of the patients with pontine base infarction (Fig. 4.10). Depression was less common, occurring in 16% [54]. Patients with tegmental lesions rarely showed emotional disturbances.

The emotional disturbances in patients with pontine base infarction may be attributed to involvement of profuse serotonergic fibers from the brainstem raphe nuclei projecting to the basal ganglia or the cerebellum [54, 103, 104]. Another closely related emotional symptom, excessive or inappropriate anger, is equally common in patients with pontine base infarction [102]. Mania [105] and psychotic behaviors [106, 107] are also observed but are distinctly uncommon.

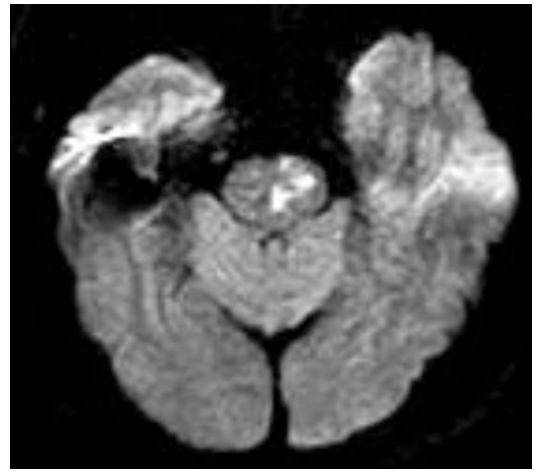


Fig. 4.10 A 58-year-old hypertensive man developed dysarthria and mild right hemiparesis due to left pontine base infarction. The symptoms gradually improved, but he complained of repeated episodes of excessive and inappropriate crying. This was the most distressing symptom of the patient. The symptom, emotional incontinence, improved greatly after escitalopram (10 mg/d) administration

Clinical–Topographical Correlation

In the era of MRI, unilateral pontine infarct is much more common than bilateral one, occupying approximately 90% of isolated pontine infarction [62, 63].

Unilateral Infarcts

In one study examining 49 patients with unilateral paramedian infarcts, 27 patients had basal infarcts, 15 basal-tegmental infarcts, and 7 had infarcts limited to the tegmental area [65].

Unilateral Paramedian Basal Infarcts

Paramedian infarction involving mainly the pontine base is the most common pattern occurring in 54–58% of isolated pontine infarction [62, 64, 65]. Motor dysfunction is the main symptom (Fig. 4.7A). Lesions extending dorsally to involve the tegmentum produce sensory symptoms as

well (Fig. 4.7B). According to a study that evaluated 37 patients with acute, unilateral infarcts that mainly involved the pontine base [68], the clinical presentations included pure motor hemiparesis in 17, sensorimotor stroke in 3, ataxic hemiparesis in 4, and dysarthria-clumsy hand syndrome in 6 patients. One patient had dysarthria-hemiataxia, two with quadrataxic hemiparesis, and four had dysarthria-facial paresis.

Acute or subacute neurologic progression occurs up to 1/4 of patients with pontine base infarction, along with subacute lesion volume increase [108]. It seems that infarcts in the lower pons are more often associated with progressive worsening and poorer functional outcome than those in the upper pons [65].

Unilateral Paramedian Tegmental Infarction

Unilateral tegmental infarction is the second most common pattern of pure pontine infarction, occurring in 12-31% of patients [62, 63, 65]. Unilateral tegmental infarcts frequently produce hemisensory syndromes [71] (Fig. 4.7C), while more dorsally located lesions produce ocular motor dysfunction, most often INO [80] (Fig. 4.7D). One-and-a-half syndrome and horizontal gaze palsy also occur [65]. Involvement of adjacent structures such as facial nerve/fascicules may produce INO plus peripheral-type facial palsy (Fig. 4.8C). Relatively large lesions result in both hemisensory syndromes and ocular motor dysfunction.

Combined Basal-Tegmental Infarction

Paramedian pontine base infarction may extend dorsally to involve the tegmental portion (Fig. 4.7E). The clinical features are essentially a combination of basal and tegmental syndromes.

Unilateral Circumferential Artery Territory (Ventrolateral) Infarcts

Ventrolateral territory infarcts were reported to occur in 17-25% of patients with isolated pontine infarction [62, 63]. However, it is often difficult to clearly differentiate the ventrolateral from the ventromedial group, and some studies did not separate them [64, 65]. Clinical features are similar to those of paramedian infarcts. However, hemiparesis is relatively mild, probably because pyramidal motor fibers located in the paramedian area are less severely involved (Fig. 4.7G). Accordingly, patients more often present with ataxic hemiparesis, dysarthria-clumsy hand syndrome, or predominant hemisensory symptoms.

Unilateral Dorsolateral Infarcts

The dorsolateral areas are supplied by AICA in the lower pons and SCA in the upper pons.

Infarction of this area is accompanied by concomitant cerebellar infarcts and rarely involved in isolation. Trigeminal sensorimotor dysfunction, 6th nerve palsy, 7th nerve palsy, auditory disturbances, and contralateral sensory dysfunction are usually observed. Contralateral hemiparesis is rare or mild when present.

Bilateral Infarcts

Bilateral infarcts are usually, though not always, associated with BA occlusion and result in grave neurological symptoms. As the bilateral lesions almost always involve the ventral part, involving the corticospinal tracts, quadriparesis is usual [106, 109, 110]. The quadriparesis may start from the beginning; more often, the initial motor dysfunction is lateralized to one side and then progresses [111]. Hemiparetic patients with BA occlusion often show some motor or reflex abnormalities on the nonparetic side such as clumsiness, ataxia, hyperreflexia, and extensor plantar reflex. Occasionally, there are abnormal movements such as shivering, twitching, shaking, or jerking of the relatively spared side, which may be precipitated by painful stimuli [112]. Unless a therapy (e.g., recanalization) is quickly performed, asymmetrical motor disturbances often progress to severe quadriplegia. The progression usually occurs within 24 h [113] but may be delayed up to several days (Fig. 4.7F).

Ataxia or incoordination is another common finding, observed in the limbs that are not severely paretic. The ataxia is invariably bilateral but is frequently asymmetric. Dysarthria and dysphagia due to bilateral bulbar muscle paresis are also common, associated with bilateral facial weakness, tongue weakness, and limited jaw move-

ments. Some patients become totally unable to speak, open their mouth, or protrude their tongue. The jaw, face, and pharyngeal reflexes may be hyperactive and even clonic. Secretions pool in the pharynx and are an important cause of aspiration pneumonia. Somatosensory abnormalities should also be common, but they are usually overshadowed by motor dysfunction and cannot be precisely assessed in patients with severe condition. Occasionally, patients complain of uncomfortable paresthesias or CPSP.

Because large bilateral pontine infarcts frequently involve the dorsal tegmental area, ocular motor dysfunction is also common, which include INO, horizontal gaze palsy, one-and-a-half syndrome, and sixth nerve palsies. Ocular bobbing, ptosis, and pinpoint pupils strongly suggest extensive, bilateral tegmental lesions (see above). Symptoms such as tinnitus, hearing loss, and auditory hallucination are related to involvement of the central auditory tracts or the eighth nerves/fascicles. Some may develop delayed-onset palatal myoclonus.

Altered consciousness is an important sign in patients with sudden BA occlusion and is related to bilateral medial tegmental pontine ischemia. Usually, the level of consciousness improves overtime even if other neurological deficits persist. Patients may show pathological crying and laughing spells that are triggered by minimal social-emotional stimuli. When all voluntary movements are lost, the deficit is referred to as the "locked-in" syndrome. Vertical eye movements are usually spared and are used for simple communications.

Stroke Mechanisms

Unilateral infarcts involving the ventral pons are caused either by large artery disease or penetrating artery disease. Studies primarily using MRA revealed that BA atherosclerotic stenosis was associated with 23% of pontine infarction [62] and 39–50% of pontine base infarction [63, 65, 108]. Therefore, branch occlusion associated with BA stenosis is an important stroke mechanism of pontine base infarction (Figs. 3.4A and 3.5 in Chap. 3). Even in patients without MRA-identified BA stenosis, small plaques that obstruct the orifice of perforating branches are occasionally seen if high-resolution vessel wall MRI is used [114] (lower panel of Fig. 3.5 in Chap. 3). Pontine infarcts limited to the tegmental area are mostly caused by penetrating artery disease (lipohyalinosis) (Fig. 3.4B in Chap. 3), unassociated with BA disease [62, 65, 71]. Although uncommon, however, the most dorsally located infarcts may be associated with significant, bilateral intracranial VA or BA steno-occlusive disease. Restoration of BA flow through collaterals (e.g., the posterior communicating artery) explains the sparing of the other parts of the pons [80].

In patients with bilateral pontine infarction, significant BA steno-occlusive disease is usually present [106]. Pathologically, the vast majority is atherothrombosis, and dissection is uncommon as compared to medullary infarction. Occasional patients with bilateral pontine infarcts have sequential infarcts caused by occlusion of BA branches on both sides. In these patients, a hemiparesis is followed days, weeks, or months later by another event that leads to paresis on the other side of the body. Embolism is a less common cause of isolated pontine infarction.

Prognosis

Unless accompanied by infarcts in other areas, the prognosis of unilateral pontine infarction is relatively favorable. Most patients survive the acute stage. Their functional deficits depend upon residual neurologic severity. Patients with initially severe hemiparesis, progressive worsening, bilateral ataxia, and lower pontine lesion have relatively unfavorable functional outcomes [62, 65, 68]. The prognosis of patients with tegmental lesions is even better. However, patients with severe sensory deficits may have difficulty in performing fine movements due to sensory deficits. More problematic is the development of CPSP, which usually remains persistent once it develops. When patients have INO as an isolated symptom, INO mostly improves [80]. However, in patients with more extensive ocular dysfunction associated with other major neurologic sequelae, residual ocular motor dysfunction frequently remains, and patients suffer from prolonged diplopia and

dizziness. The prognosis of bilateral pontine infarcts presenting with quadriparesis is ominous. Unless promptly and appropriately treated in the early stage, most patients die or remain bed-ridden with quadriparesis. There may be persistent sensory disturbances, diplopia, dizziness, or palatal myoclonus.

Midbrain Infarction

The midbrain is supplied by branches arising from the PCA, upper BA, SCA, and the anterior choroidal artery. It is often affected in patients with embolic stroke occurring in the posterior circulation, usually with the concomitant involvement of other structures such as the thalamus, cerebellum, and occipital lobe [115]. According to the New England Medical Center Registry, midbrain infarction is ten-fold more likely to be accompanied by ischemia of neighboring structures than it is to occur in isolation [116]. Isolated midbrain infarcts account for 0.2–2.3% of admitted ischemic strokes [117–119]. While one study showed that pure midbrain infarct occupied 0.7% of posterior circulation ischemic stroke [116], another reported that it represented 8% of posterior circulation infarcts [118].

Clinical Features

The third nerve palsy has been considered the most important clinical feature indicating midbrain stroke. However, with the advent of MRI, it has been recognized that nonlocalizing "lacunar" syndromes are actually more common. In the largest series that used MRI [117], clinical manifestations included gait ataxia (68%), dysarthria (55%), limb ataxia (50%), sensory symptoms (43%), third nerve palsy (35%), limb weakness (≤IV/V) (23%), and INO (13%).

Ocular Motor Dysfunction

Third Nerve Palsy

Third nerve palsy occurs in 33–50% [117, 118, 120] of patients with pure midbrain infarction due to involvement of either the third nerve fascicles or the nucleus. Lesions that affect the third nerve nucleus often cause bilateral ptosis and upgaze deficits; this is attributed to involvement of the caudal subnucleus supplying both levator palpebrae, and the crossing fibers from the contralateral subnucleus of the superior rectus, respectively, within the third nucleus complex [121].

The third nerve palsy is frequently incomplete, and certain ocular muscles may be selectively involved. For example, divisional oculomotor paresis was reported to be caused by midbrain lesions involving the fascicle suggesting the functional separation of superior (subserving levator palpebrae, superior rectus) and inferior (subserving inferior and medical rectus and inferior oblique) divisions within the brainstem in the fascicular portion of the nerve [122]. Patients with a tiny lesion within the third nucleus may even produce weakness of a single extraocular muscle such as the inferior rectus [79] or medial rectus [123]. A very small infarct was reported to produce isolated inferior rectus palsy due to selective involvement of the relevant fascicle [124].

Internuclear Ophthalmoplegia

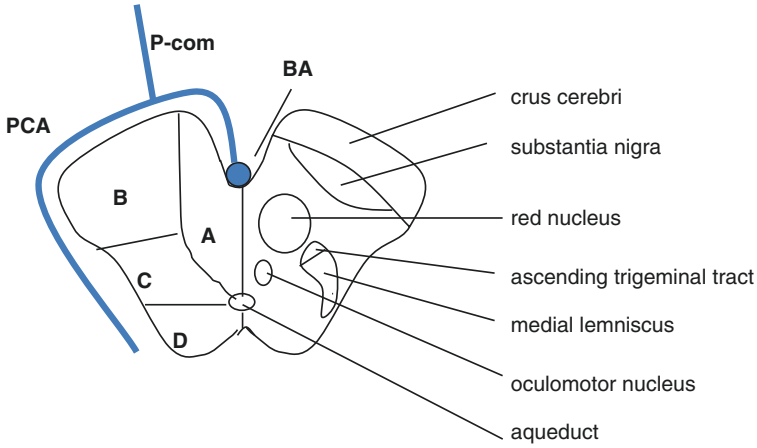
The lesions producing an INO are located in the paramedian, dorsal lower midbrain, involving the MLF. A detailed description of INO was included with the topic of pontine infarction. Patients frequently have ocular tilt reaction [125].

Vertical Gaze Disturbances

Involvement of the most rostral part of the midbrain produces vertical gaze paresis (see the section "Top of the Basilar Artery Syndrome").

Fourth Nerve Palsy

The trochlear nucleus lies in the lower midbrain caudal to the oculomotor nuclear complex. Unlike third nerve fascicles that travel in the paramedian area, the fourth nerve fascicles run dorsally around the aqueduct to decussate in the anterior medullary velum just caudal to the inferior colliculus. Because this dorsolateral part of the lower midbrain is mainly supplied by the SCA, fourth nerve palsy is almost always accompanied by concomitant SCA infarction [79, 126] (Fig. 4.11D). Because the lesions mostly dam-



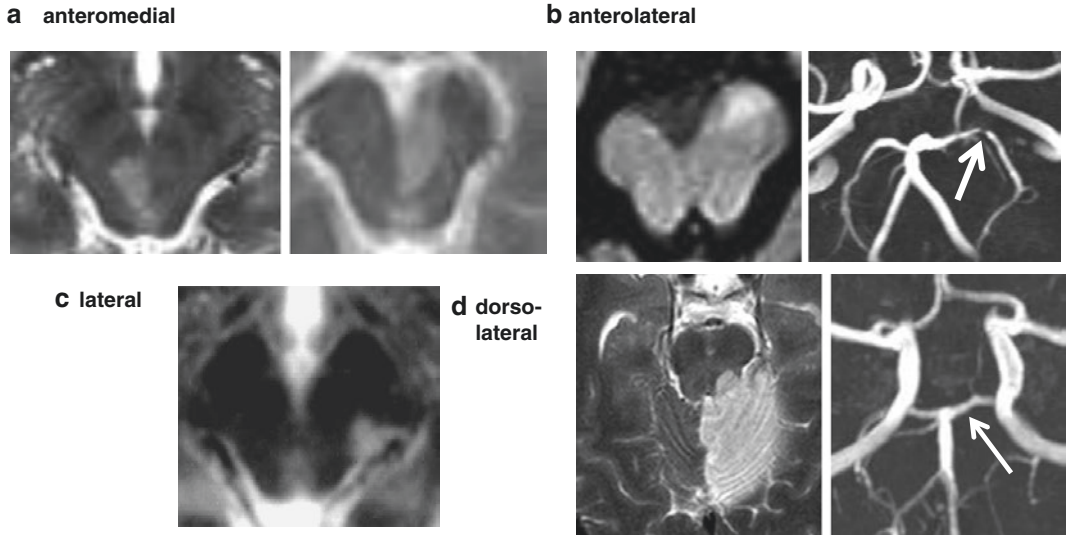


Fig. 4.11 Illustrative patients and schematic drawing of midbrain indicating important structures, supplying vessels and four topographic subgroups. (**A**) Anteromedial, (**B**) anterolateral, (**C**) lateral, and (**D**) dorsolateral (posterior). (**A**) Both patients had ipsilateral oculomotor disturbances and mild contralateral ataxia. (**B**) The patient had dysarthria and clumsy hand on the right side. MRA showed stenosis in the P2 portion of the left posterior cerebral artery (arrow). (**C**) The patient presented with pure sensory stroke. (**D**) The patient had concomitant cerebellar infarction. MRA showed occlusion of the superior cerebellar artery (arrow) due to cardiac embolism. He had left limb ataxia, decreased sensory perception on the right side, and right superior oblique palsy. (Modified from Kim JS, Kim J. Pure midbrain infarction: Clinical, radiologic, and pathophysiologic findings. Neurology 2005;64;1227–1232)

age the trochlear nucleus or the fascicle before decussation, superior oblique palsy usually develops in the eye contralateral to the midbrain stroke.

Hemiparesis and Other Motor Dysfunction

Although limb weakness is found in more than half of patients, a significant hemiparesis is present in only approximately 1/4 of patients when the pyramidal tract at the crus cerebri was heavily and densely involved [117] (Fig. 4.11). The uncommon occurrence of severe hemiparesis may at least in part be due to sparsely arranged pyramidal fibers in the crus cerebri as compared to the lower brainstem [68]. Dysarthria is invariably present, and hemiataxia may be observed in patients without severe hemiparesis.

Sensory Symptoms/Signs

Unlike the pons, where the sensory tracts are located in the paramedian area, the sensory tracts are located at the dorsolateral portion of the midbrain (Fig. 4.11). In one study, sensory disturbances were observed in 43% of pure midbrain infarction [117]. However, because infarcts preferentially involve the paramedian area, sensory symptoms are often minor and restricted to certain body parts. Cheiro-oral distribution is relatively common [117], probably because face and finger representation areas are located medially in the sensory tract, being vulnerable from paramedian infarction. Mesencephalic pure hemisensory syndrome is rare and is caused by small infarcts or hemorrhages affecting the dorsolateral area [71, 117] (Fig. 4.11C).

Ataxia

Ataxia is one of the most frequently observed symptoms/signs in midbrain infarction [117], probably related to the presence of abundant neuronal fibers connecting with the cerebellum in the midbrain: the descending corticopontocerebellar fibers at the crus cerebri and ascending cerebello-rubro-thalamic tracts in the paramedian area near the red nucleus (Fig. 4.11).

In the cerebral peduncle, descending cerebellar fibers areas are rarely involved in isolation, and concomitant involvement of the pyramidal tracts or corticobulbar tracts lead to syndromes such as ataxic hemiparesis or dysarthria with ataxia. Paramedian lesions affecting ascending cerebello-rubro-thalamic tracts at or near the red nucleus may produce ataxia without significant other motor dysfunction. Because paramedian lesions usually involve the oculomotor nucleus or fascicles, ipsilateral third nerve palsy is often combined with contralateral ataxia (Claude syndrome).

Patients with unilateral lower midbrain lesion may have bilateral ataxia usually worse on the contralateral side [117, 118]. This is attributed to bilateral involvement of crossing efferent dentato-rubral fibers at the lower midbrain level by lesions located in the paramedian area. Bilateral ataxia caused by a single lesion is a localizing sign for paramedian lower midbrain infarction. The outcome of such patients is unfavorable; they have marked dysarthria and long-lasting gait instability (Fig. 4.12).

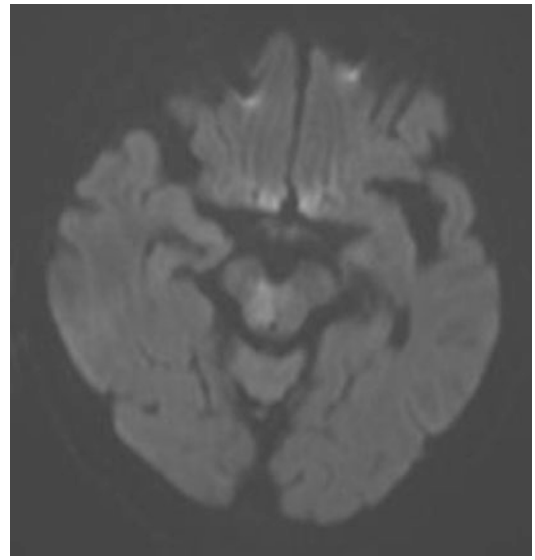


Fig. 4.12 An 81-year-old woman had dizziness, severe dysarthria, bilateral ataxia, and gait difficulty. Diffusion-weighted MRI showed left paramedian infarction in the midbrain. Despite rehabilitation therapy, the symptoms persist, and she was not able to walk alone after 5 years of follow-up

Involuntary Movements

Holmes Tremor

Patients with midbrain strokes occasionally develop a tremor, referred to as "rubral tremor" or "Holmes tremor." The characteristics of the tremor are as follows [127]:

(a) Intention and resting tremor, but some may show postural tremor as well.

The tremor may not be as regular as other tremors and occasionally shows jerky components.

(b) Tremor is of low frequency, mostly below 4.5 Hz.

(c) There is a variable delay (mostly 2 weeks to 2 years) between the onset of the lesion and the appearance of tremors.

The tremor is predominantly unilateral and mainly affects the hands and the proximal arm.

The responsible lesions are usually situated at the superior and external part of the red nucleus affecting the rubro-thalamic pathways. Lesions affecting the thalamus, the central tegmental tract in the pons, or deep nuclei of the cerebellum may cause similar movement disorders.

Dopaminergic PET imaging studies showed striatal dopaminergic dysfunction in these patients, probably due to the involvement of the nigrostriatal system [128, 129]. Some suggested that combined damage of the cerebellothalamic and nigrostriatal system may be required to generate Holmes tremor [130, 131]. Ipsilateral third nerve palsy accompanied by contralateral ataxia and tremor is referred to as Benedict syndrome.

Parkinsonism

Midbrain strokes may produce hemi-parkinsonism due to involvement of the substantia nigra [132–134]. The prevalence is very low, probably because parkinsonian symptoms are masked by other major deficits such as hemiparesis or ataxia. However, if carefully tested, subtle symptoms such as micrographia [135] or hypokinetic dysarthria and palilalia [136] are observed. Dopaminergic system dysfunction is documented by PET imaging in these patients.

Dystonia

Unilateral dystonia may be observed in patients with extensive ponto-mesencephalic tegmental lesions [137], usually associated with sensorimotor dysfunction and other involuntary movements such as rubral tremor or excessive twitching.

Asterixis

Paramedian midbrain infarcts may produce asterixis in the contralateral limbs [138], probably related to the involvement of the rubrospinal or cerebellar-rubral tracts that are involved in the regulation of postural/tonic control of extremities.

Neuropsychiatric and Emotional Disturbances

Symptoms such as emotional incontinence [54], agitation, and impulsive behavior [139] have been reported in patients with midbrain infarction. These features may be related to serotonergic or limbic dopaminergic system involvement.

Clinical–Topographical Correlation

According to MRI findings, the lesions are categorized as the following groups (Fig. 4.11).

Anteromedial (or Paramedian) Lesion

Approximately 50–60% of pure midbrain infarctions belong to this group [117, 120] (Fig. 4.11A). The lesions usually involve the third nerve fascicles or nucleus (at the upper midbrain), the MLF (at the lower midbrain), the red nucleus, and the medial part of the cerebral peduncle. The clinical features are characterized by ocular motor disturbances (third nerve palsy or INO), contralateral mild hemiparesis, and ataxia. Ataxia may be bilateral when the paramedian lesion is located in the lower midbrain (Fig. 4.12). Sensory deficits, when present, are usually mild and often present in restricted body parts such as the perioral or perioral-hand areas.

Anterolateral Lesion

Approximately 1/4 of patients belong to this group [117, 120] (Fig. 4.11B). Because the crus cerebri is primarily involved, patients' main symptom is hemiparesis. Although severe motor dysfunction in uncommon (see above), some patients may have progressively worsening hemiparesis. In patients who do not have severe hemiparesis, ataxic hemiparesis, dysarthria-clumsy hand syndrome, pure dysarthria, and dysarthria-ataxia may develop. If adjacent sensory tracts are involved, sensory deficits may be added.

Combined Lesions

Some patients have lesions in both anteromedial and anterolateral areas. Clinical features are the combination of the two: ocular motor disturbances, ataxia, and various motor syndromes.

Lateral Lesion

Although quite uncommon, lesions may be confined to the lateral part of the midbrain (Fig. 4.11C). The clinical features are characterized by hemisensory deficits caused by involvement of the laterally located sensory lemniscus. The clinical features are not distinguishable from a thalamic pure sensory stroke.

Dorsolateral Lesion

This area is supplied by the SCA, and infarcts occurring in this area are almost always accompanied by concomitant cerebellar infarction. Fourth nerve palsy, INO, ataxia, and contralateral sensory disturbances may be present (Fig. 4.11D).

Bilateral Lesions

Bilateral midbrain infarctions are almost always accompanied by extensive infarcts in the other parts of posterior circulation [117, 120]. Patients develop altered consciousness, quadriparesis, severe dysarthria, dysphagia, and, ultimately, a locked-in state. Patients may have bilateral oculomotor palsy [120], but ocular movements may remain intact if dorsal areas are spared [140, 141].

Stroke Mechanism

Approximately 2/3 of pure midbrain infarction is caused by large artery atherosclerotic disease. Anteromedial, anterolateral, and combined type lesions are usually caused by branch occlusion associated with PCA or rostral BA atherothrombosis [117] (Fig. 3.4A in Chap. 3, Fig. 4.11B). Small penetrating artery disease explains stroke in approximately 1/4 of the patients who have deep-seated lesions (Fig. 3.4B in Chap. 3). Cardiac embolism is rare in patients with isolated midbrain infarction [117, 120]. The stroke mechanism of the lateral group is uncertain, but artery-to-artery embolization from tightly stenosed BA was reported [117]. Dorsolateral infarcts are almost always caused by SCA occlusion, which is most often caused by cardiac embolism (Fig. 4.11D).

Prognosis

In patients with pure midbrain infarction, the lesions are mostly unilateral, and the prognosis is relatively good. Initial severe motor dysfunction may predict a worse prognosis. However, in one study, 36 out of 40 patients were functionally independent after 2 years of follow-up [117]. The functional outcome of patients with bilateral ataxia (Fig. 4.12) is unfavorable because they usually have persistent gait difficulty and dysarthria. As in patients with medullary or pontine infarction, underlying vascular diseases (BA or PCA) probably affect the future outcome of these patients. Patients with bilateral infarction have a grave prognosis; they often die due to aspiration pneumonia and frequently remain locked-in.

Top of the Basilar Artery Syndrome

Infarction of rostral brainstem and cerebral hemispheral regions fed by the distal BA causes a clinically recognizable syndrome characterized by visual, ocular motor, and behavioral abnormalities, often without significant motor dysfunction. Caplan [115] described this as "top of the basilar artery syndrome." Typically, there are bilateral, multiple infarcts in the paramedian midbrain, medial thalamus, medial temporal areas, and occipital lobes (Fig. 4.13). The clinical features vary greatly and depend on the topography of the damaged brain. Occasionally, bilateral SCA infarctions are the only manifestation of basilar tip occlusion when bilateral fetal type PCAs are present without anastomosis between the anterior and posterior circulations [142].

Clinical Features

Ocular Motor Dysfunction

See Chap. 7 for details.

Vertical Gaze Palsy

Vertical gaze pathways from the cerebral cortex converge on the periaqueductal region beneath the collicular plate, near the interstitial nucleus of Cajal and the posterior commissure. In this region, there is a cluster of neurons regulating vertical gaze, referred to as rostral interstitial

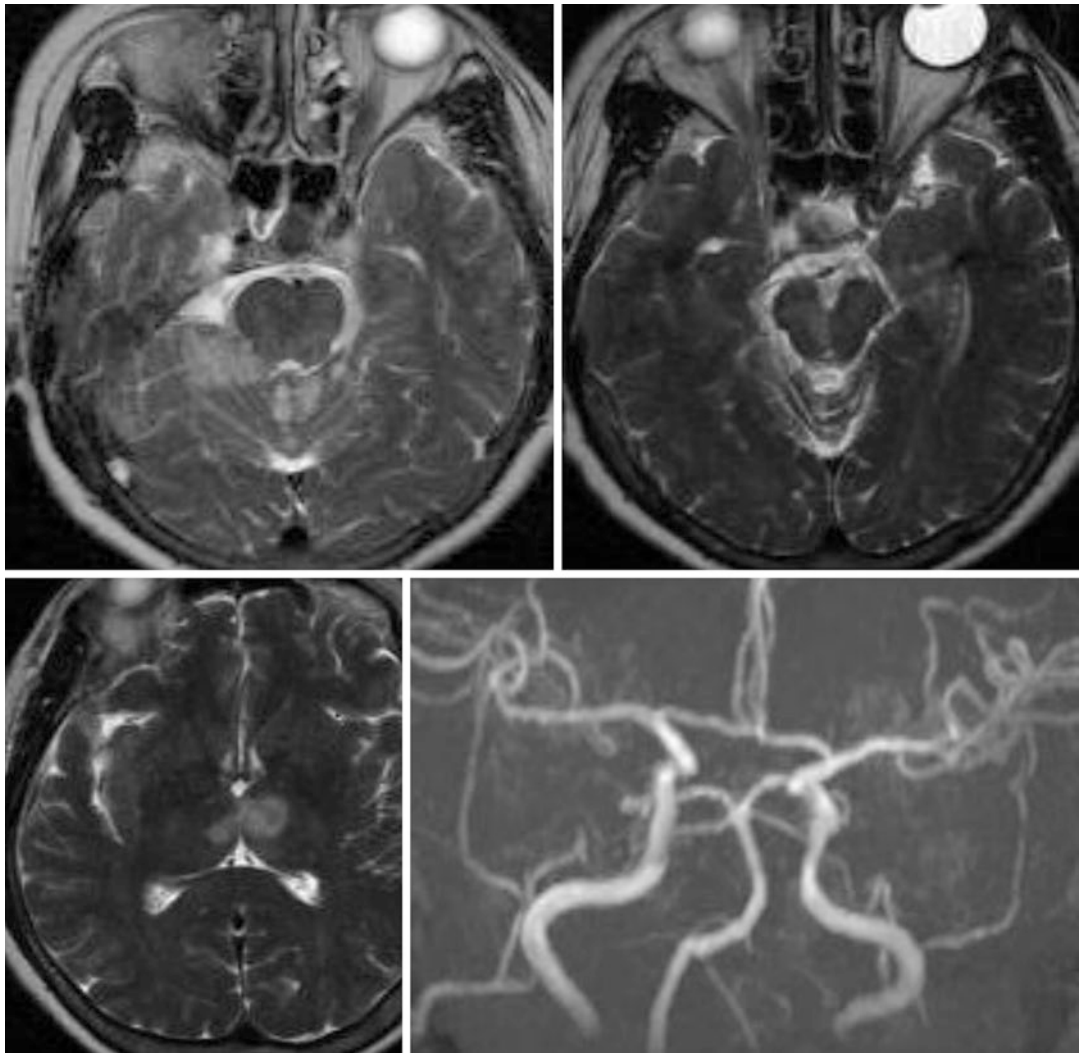


Fig. 4.13 A 75-year-old woman with atrial fibrillation became drowy and confused. Examination showed confused mentality, somnolence, anterograde memory impairment, vertical gaze failure, and gait ataxia. MRI showed multiple infarcts in the cerebellum, midbrain, and bilateral paramedian thalamus. MRA showed normal basilar artery, suggesting that occluded basilar tip was already recanalized

MLF (riMLF) [143, 144]. Extensive lesions occurring in the rostral midbrain result in both upgaze and downgaze failure. Vertical VOR is usually preserved. A unilateral lesion affecting the posterior commissure can cause upward saccadic failure due probably to the fact that fibers involved in upward saccades decussate through the posterior commissure, which connects the riMLF on both sides [145, 146]. Bilateral damage to the riMLF is usually required to produce down gaze paresis; therefore, isolated upgaze palsy is more common than down gaze paresis [147, 148]. If the connections from the riMLF to the third nuclei are selectively damaged just above the nucleus on one side, monocular upgaze palsy may occur [149–151]. A vertical one-and-a-half syndrome (upward gaze paresis with monocular downward gaze paresis or downward gaze paresis with monocular upward gaze paresis) is also observed [152, 153].

Convergence, Eyelid, and Pupillary Abnormalities

Ocular convergence is probably controlled in the medial midbrain tegmentum. Convergence vectors are frequently evident on an attempted upward gaze. Rhythmic convergence nystagmus may be elicited if patients are told to follow a downgoing opticokinetic target with their eyes. Convergence vectors may modify lateral gaze, and patients may show pseudo-sixth nerve palsy [115]. Lid abnormalities are also a sign of rostral brainstem infarction. Unilateral infarction of the third cranial nerve nucleus can lead to complete bilateral ptosis [89]. Retraction of the upper lid (Collier's sign) may be observed in patients with tectal lesions [154]. When ischemia affects the Edinger–Westphal nucleus, the pupils may be fixed and dilated, whereas if the lesion involves sympathetic fibers, the pupil size becomes smaller [155].

Somnolence and Loss of Attention

The medial mesencephalon and diencephalon contain the most rostral portions of the reticular activating system. Infarcts in these regions frequently produce excessive sleep and lack of attention. Because the reticular gray matter is adjacent to the third nerve nuclei, riMLF, and the posterior commissure, somnolence is frequently associated with relevant ocular motor disturbances.

Hallucinations

Patients with rostral brainstem infarction often have hallucinations (peduncular hallucinosis) [156]. The hallucinations tend to occur at twilight or during the night, and such patients usually have sleep disorders (nocturnal insomnia or daytime hypersomnolence) [115]. The hallucinations are usually vivid and mostly visual and contain multiple colors, objects, and scenes. Occasionally, auditory or tactile hallucinations are associated. Bilateral infarcts confined to the medial substantia nigra pars reticulata are reported to cause peduncular hallucinosis [157]. However, similar hallucinations are observed in patients with infarcts that involve the pons or the posterior thalamus [158]. Neuropsychological testing in patients with hallucination show impairments of episodic memory, confabulation, attention deficits, confusion, delusion, and misidentification for persons and places. It seems that brainstem hallucinosis may be related with the dysfunctional ascending reticular system and thalamocortical circuits [159].

Confabulations

Confabulations are often reported in patients with rostral brainstem infarcts [115]. The features are similar to what were described as Wernicke-Korsakoff psychosis.

Hemiballism and Abnormal Movements

Hemichorea or ballism may occur from infarcts affecting the subthalamic nucleus (corpus Luysii) [160]. Other movement disorders related to midbrain involvement are described above (see the section "**Midbrain Infarction**").

Other Symptoms and Signs

Occipital and thalamic infarcts are common, and relevant symptoms and signs are described in Chap. 5. Embolism may produce infarcts in the other parts of the brainstem, and the relevant symptoms and signs are described in the early part of this chapter**.**

Stroke Mechanisms and Prognosis

Occlusions of the BA tip are generally embolic [115], more often from the heart than proximal artery atherothrombosis. Although uncommon, atherothrombosis occurring in the distal BA can also result in this syndrome [161]. In patients with embolic occlusion, the embolic fragments may also occlude other vessels such as the PICA, SCA, or pontine branches before they reach to the top of BA. PCA territory infarcts are also commonly found. In patients with cardiac embolism, an embolus is frequently evanescent, and it may already be gone at the time of the angiographic study (Fig. 4.13). In this case, the patient's prognosis is generally good, although they may have residual deficits depending on already damaged structures. However, persistent BA occlusion may lead to downward extension

of thrombi to result in catastrophic bilateral brainstem infarction. The recent advent of endovascular thrombectomy is of great help in the early and successful recanalization of the occluded BA (see Chap. 11). Aside from the successful recanalization, adequate collateral system (e.g., the presence of textbook-type posterior communication artery) appears to be associated with better functional outcome in these patients [162].

References

1. Wallenberg A. Acute bulbar affection (Embolie der art. cerebellar post. inf. sinistra ?). Arch f Psychiat Nervenkr. 1895;27:504–40.
2. Norrving B, Cronqvist S. Lateral medullary infarction: prognosis in an unselected series. Neurology. 1991;41((2(Pt 1))):244–8.
3. Lewis GLN, Littman A, Foley EF. The syndrome of thrombosis of the posterior inferior cerebellar artery: a report of 28 cases. Ann Intern Med. 1952;36(2:2):592–602.
4. Peterman AF, Sieker TR. The lateral medullary (Wallenberg) syndrome: clinical features and prognosis. Med Clin North Am. 1960;44:887–96.
5. Currier RD, Giles CL, DeJong RN. Some comments on Wallenberg's lateral medullary syndrome. Neurology. 1961;1:778–92.
6. Fisher CM, Karnes WE, Kubik CS. Lateral medullary infarction-the pattern of vascular occlusion. J Neuropathol Exp Neurol. 1961;20:323–79.
7. Sacco RL, Freddo L, Bello JA, Odel JG, Onesti ST, Mohr JP. Wallenberg's lateral medullary syndrome. Clinical-magnetic resonance imaging correlations. Arch Neurol. 1993;50(6):609–14.
8. Vuilleumier P, Bogousslavsky J, Regli F. Infarction of the lower brainstem. Clinical, aetiological and MRI-topographical correlations. Brain. 1995;118(Pt 4):1013–25.
9. Kim JS, Lee JH, Lee MC. Patterns of sensory dysfunction in lateral medullary infarction. Clinical-MRI correlation. Neurology. 1997;49(6):1557–63.
10. Kim JS. Pure lateral medullary infarction: clinical-radiological correlation of 130 acute, consecutive patients. Brain. 2003;126(Pt 8):1864–72.
11. Kim JS, Lee JH, Suh DC, Lee MC. Spectrum of lateral medullary syndrome. Correlation between clinical findings and magnetic resonance imaging in 33 subjects. Stroke. 1994;25(7):1405–10.
12. Caplan LR. Posterior circulation disease: clinical findings, diagnosis, and management. Boston: Blackwell Science; 1996. p. 262–323.
13. Dieterich M, Brandt T. Wallenberg's syndrome: lateropulsion, cyclorotation, and subjective visual vertical in thirty-six patients. Ann Neurol. 1992;31(4):399–408.
14. Marx JJ, Iannetti GD, Thomke F, Fitzek S, Galeotti F, Truini A, et al. Topodiagnostic implications of hemiataxia: an MRI-based brainstem mapping analysis. NeuroImage. 2008;39(4):1625–32.
15. Meyer KT, Baloh RW, Krohel GB, Hepler RS. Ocular lateropulsion. A sign of lateral medullary disease. Arch Ophthalmol. 1980;98(9):1614–6.
16. Kwon M, Lee JH, Kim JS. Dysphagia in unilateral medullary infarction: lateral vs medial lesions. Neurology. 2005;65(5):714–8.
17. Calne DB, Pallis CA. Vibratory sense: a critical review. Brain. 1966;89(4):723–46.
18. Matsumoto S, Okuda B, Imai T, Kameyama M. A sensory level on the trunk in lower lateral brainstem lesions. Neurology. 1988;38(10):1515–9.
19. Kim JS. Sensory symptoms in ipsilateral limbs/body due to lateral medullary infarction. Neurology. 2001;57(7):1230–4.
20. Caplan L, Gorelick P. "Salt and pepper on the face" pain in acute brainstem ischemia. Ann Neurol. 1983;13(3):344–5.
21. Reutens DC. Burning oral and mid-facial pain in ventral pontine infarction. Aust NZ J Med. 1990;20(3):249–50.
22. Kuypers HG. Corticobular connexions to the pons and lower brain-stem in man: an anatomical study. Brain. 1958;81(3):364–88.
23. Fisher CM, Tapia J. Lateral medullary infarction extending to the lower pons. J Neurol Neurosurg Psychiatry. 1987;50(5):620–4.
24. Bogousslavsky J, Khurana R, Deruaz JP, Hornung JP, Regli F, Janzer R, et al. Respiratory failure and unilateral caudal brainstem infarction. Ann Neurol. 1990;28(5):668–73.
25. Opalski A. Un nouveau syndrome sous-bulbaire: syndrome partiel de l'artère vertébro-spinale postérieur. Paris Med. 1946;1:214–20.
26. Hermann DM, Jung HH, Bassetti CL. Lateral medullary infarct with alternating and dissociated sensorimotor deficits: Opalski's syndrome revisited. Eur J Neurol. 2009;16(4):e72–4.
27. Nakamura S, Kitami M, Furukawa Y. Opalski syndrome: ipsilateral hemiplegia due to a lateral-medullary infarction. Neurology. 2010;75(18):1658.
28. Carpenter MBSJ. Human neuroanatomy. 8th ed. Baltimore: Williams & Wilkins; 1983. p. 315–57.
29. Vuillier F, Tatu L, Dietsch E, Medeiros E, Moulin T. Pontomedullary sulcus infarct: a variant of lateral medullary syndrome. J Neurol Neurosurg Psychiatry. 2006;77(11):1276–8.
30. Castaigne P, Lhermitte F, Gautier JC, Escourolle R, Derouesne C, Der Agopian P, et al. Arterial occlusions in the vertebro-basilar system. A study of 44 patients with post-mortem data. Brain. 1973;96(1):133–54.
31. Caplan LR. Occlusion of the vertebral or basilar artery. Follow up analysis of some patients with benign outcome. Stroke. 1979;10(3):277–82.

32. Kim TJ, Nam H, Hong JH, Yeo MJ, Chang JY, Jeong JH, et al. Dysphagia may be an independent marker of poor outcome in acute lateral medullary infarction. J Clin Neurol. 2015;11(4):349–57.
33. Kang HG, Kim BJ, Lee SH, Kang DW, Kwon SU, Kim JS. Lateral medullary infarction with or without extra-lateral medullary lesions: what is the difference? Cerebrovasc Dis. 2018;45(3–4):132–40.
34. Kim JS, Choi-Kwon S. Sensory sequelae of medullary infarction: differences between lateral and medial medullary syndrome. Stroke. 1999;30(12):2697–703.
35. MacGowan DJ, Janal MN, Clark WC, Wharton RN, Lazar RM, Sacco RL, et al. Central poststroke pain and Wallenberg's lateral medullary infarction: frequency, character, and determinants in 63 patients. Neurology. 1997;49(1):120–5.
36. Kim SJ, Ryoo S, Bang OY, Chung CS, Lee KH, Kim GM. Perfusion-weighted MRI as a predictor of clinical outcomes following medullary infarctions. Cerebrovasc Dis. 2010;29(4):382–8.
37. Spiller WG. The symptom-complex of a lesion of the upper most portion of the anterior spinal and adjoining portion of the vertebral arteries. J Nerv Mednt Dis. 1908;35:775–8.
38. Dejerine J. Semiologie des affections du système nerveux. Paris: Masson; 1914. p. 226–30.
39. Davison C. Syndrome of the anterior spinal artery of the medulla oblongata. Arch Neurol Psychiatr. 1937;37:91–107.
40. Kim JS, Kim HG, Chung CS. Medial medullary syndrome. Report of 18 new patients and a review of the literature. Stroke. 1995;26(9):1548–52.
41. Toyoda K, Imamura T, Saku Y, Oita J, Ibayashi S, Minematsu K, et al. Medial medullary infarction: analyses of eleven patients. Neurology. 1996;47(5):1141–7.
42. Bassetti C, Bogousslavsky J, Mattle H, Bernasconi A. Medial medullary stroke: report of seven patients and review of the literature. Neurology. 1997;48(4):882–90.
43. Kumral E, Afsar N, Kirbas D, Balkir K, Ozdemirkiran T. Spectrum of medial medullary infarction: clinical and magnetic resonance imaging findings. J Neurol. 2002;249(1):85–93.
44. Park JY, Chun MH, Kang SH, Lee JA, Kim BR, Shin MJ. Functional outcome in poststroke patients with or without fatigue. Am J Phys Med Rehabil. 2009;88(7):554–8.
45. Kim JS, Han YS. Medial medullary infarction: clinical, imaging, and outcome study in 86 consecutive patients. Stroke. 2009;40(10):3221–5.
46. Ropper AH, Fisher CM, Kleinman GM. Pyramidal infarction in the medulla: a cause of pure motor hemiplegia sparing the face. Neurology. 1979;29(1):91–5.
47. Kim JS, Koh JY, Lee JH. Medial medullary infarction with restricted sensory symptom. Eur Neurol. 1998;39(3):174–7.
48. Lee SH, Kim DE, Song EC, Roh JK. Sensory dermatomal representation in the medial lemniscus. Arch Neurol. 2001;58(4):649–51.
49. Kim JS, Choi KD, Oh SY, Park SH, Han MK, Yoon BW, et al. Medial medullary infarction: abnormal ocular motor findings. Neurology. 2005;65(8):1294–8.
50. Kim JS, Moon SY, Kim KY, Kim HC, Park SH, Yoon BW, et al. Ocular contrapulsion in rostral medial medullary infarction. Neurology. 2004;63(7):1325–7.
51. Choi KD, Jung DS, Park KP, Jo JW, Kim JS. Bowtie and upbeat nystagmus evolving into hemiseesaw nystagmus in medial medullary infarction: possible anatomic mechanisms. Neurology. 2004;62(4):663–5.
52. Brown WJ, Fang HC. Spastic hemiplegia in man associated with unilateral infarct of the cortico spinal tract at the pontomedullary juncture. Trans Am Neurol Assoc. 1956;(81st Meeting):22–6.
53. Paulson GW, Yates AJ, Paltan-Ortiz JD. Does infarction of the medullary pyramid lead to spasticity? Arch Neurol. 1986;43(1):93–5.
54. Kim JS, Choi-Kwon S. Poststroke depression and emotional incontinence: correlation with lesion location. Neurology. 2000;54(9):1805–10.
55. Fisher CM, Curry HB. Pure motor hemiplegia of vascular origin. Arch Neurol. 1965;13:30–44.
56. Mizutani T, Lewis RA, Gonatas NK. Medial medullary syndrome in a drug abuser. Arch Neurol. 1980;37(7):425–8.
57. Kase CS, Varakis JN, Stafford JR, Mohr JP. Medial medullary infarction from fibrocartilaginous embolism to the anterior spinal artery. Stroke. 1983;14(3):413–8.
58. Tyler KL, Sandberg E, Baum KF. Medical medullary syndrome and meningovascular syphilis: a case report in an HIV-infected man and a review of the literature. Neurology. 1994;44(12):2231–5.
59. Meyer JS, Herndon RM. Bilateral infarction of the pyramidal tracts in man. Neurology. 1962;12:637–42.
60. Reinhold H. Beitrage zur Pathologie der akuten Erweichungen des Pons und der Oblongata. Zugleich ein Beitrag zur Lehre von der “Bulbaeren Ataxie.”. Dtsch Zeit Nervenheilk. 1894;5:351–74.
61. Babinski J, Nageotte J. Hdmiasynergie, lateropulsion et myosis bulbaires avec hemianesthesie et hemiplegie croisees. Rev Neurol (Paris). 1902;10:358–65.
62. Bassetti C, Bogousslavsky J, Barth A, Regli F. Isolated infarcts of the pons. Neurology. 1996;46(1):165–75.
63. Kumral E, Bayulkem G, Evyapan D. Clinical spectrum of pontine infarction. Clinical-MRI correlations. J Neurol. 2002;249(12):1659–70.
64. Erro ME, Gallego J, Herrera M, Bermejo B. Isolated pontine infarcts: etiopathogenic mechanisms. Eur J Neurol. 2005;12(12):984–8.
65. Kataoka S, Hori A, Shirakawa T, Hirose G. Paramedian pontine infarction. Neurological/topographical correlation. Stroke. 1997;28(4):809–15.
66. Fisher CM. Ataxic hemiparesis. A pathologic study. Arch Neurol. 1978;35(3):126–8.
67. Fisher CM. A lacunar stroke. The dysarthria-clumsy hand syndrome. Neurology. 1967;17(6):614–7.

68. Kim JS, Lee JH, Im JH, Lee MC. Syndromes of pontine base infarction. A clinical-radiological correlation study. Stroke. 1995;26(6):950–5.
69. Helgason CM, Wilbur AC. Basilar branch pontine infarction with prominent sensory signs. Stroke. 1991;22(9):1129–36.
70. Caplan LR, Goodwin JA. Lateral tegmental brainstem hemorrhages. Neurology. 1982;32(3):252–60.
71. Kim JS, Bae YH. Pure or predominant sensory stroke due to brain stem lesion. Stroke. 1997;28(9):1761–4.
72. Shintani S, Tsuruoka S, Shiigai T. Pure sensory stroke caused by a pontine infarct. Clinical, radiological, and physiological features in four patients. Stroke. 1994;25(7):1512–5.
73. Kim JS. Restricted acral sensory syndrome following minor stroke. Further observation with special reference to differential severity of symptoms among individual digits. Stroke. 1994;25(12):2497–502.
74. Combarros O, Berciano J, Oterino A. Pure sensory deficit with crossed orocrural topography after pontine haemorrhage. J Neurol Neurosurg Psychiatry. 1996;61(5):534–5.
75. Holtzman RN, Zablozki V, Yang WC, Leeds NE. Lateral pontine tegmental hemorrhage presenting as isolated trigeminal sensory neuropathy. Neurology. 1987;37(4):704–6.
76. Sunada I, Akano Y, Yamamoto S, Tashiro T. Pontine haemorrhage causing disturbance of taste. Neuroradiology. 1995;37(8):659.
77. Donaldson D, Rosenberg NL. Infarction of abducens nerve fascicle as cause of isolated sixth nerve palsy related to hypertension. Neurology. 1988;38(10):1654.
78. Fukutake T, Hirayama K. Isolated abducens nerve palsy from pontine infarction in a diabetic patient. Neurology. 1992;42(11):2226.
79. Kim JS, Kang JK, Lee SA, Lee MC. Isolated or predominant ocular motor nerve palsy as a manifestation of brain stem stroke. Stroke. 1993;24(4):581–6.
80. Kim JS. Internuclear ophthalmoplegia as an isolated or predominant symptom of brainstem infarction. Neurology. 2004;62(9):1491–6.
81. Daroff R, Hoyt W. Supranuclear disorders of ocular control systems in man. In: Bach Y, Rita P, Collins C, editors. The control of eye movements. Orlando, FL: Academic Press; 1977. p. 175.
82. Pierrot-Deseilligny C, Chain F, Lhermitte F. The pontine reticular formation syndrome. Physiopathologic data on voluntary eye movement abnormalities. Rev Neurol (Paris). 1982;138(6–7):517–32.
83. Miura K, Optican LM. Membrane channel properties of premotor excitatory burst neurons may underlie saccade slowing after lesions of omnipause neurons. J Comput Neurosci. 2006;20(1):25–41.
84. Fisher CM. Some neuro-ophthalmological observations. J Neurol Neurosurg Psychiatry. 1967;30(5):383–92.
85. Pierrot-Deseilligny C, Chain F, Serdaru M, Gray F, Lhermitte F. The 'one-and-a-half' syndrome. Electro-oculographic analyses of five cases with deductions about the physiological mechanisms of lateral gaze. Brain. 1981;104(Pt 4):665–99.
86. Fisher CM. Ocular Bobbing. Arch Neurol. 1964;11:543–6.
87. Nelson JR, Johnston CH. Ocular bobbing. Arch Neurol. 1970;22(4):348–56.
88. Newman N, Gay AJ, Heilbrun MP. Disjugate ocular bobbing: its relation to midbrain, pontine, and medullary function in a surviving patient. Neurology. 1971;21(6):633–7.
89. Caplan LR. Ptosis. J Neurol Neurosurg Psychiatry. 1974;37(1):1–7.
90. Tahmoush AJ, Brooks JE, Keltner JL. Palatal myoclonus associated with abnormal ocular and extremity movements. A polygraphic study. Arch Neurol. 1972;27(5):431–40.
91. Lapresle J, Hamida MB. The dentato-olivary pathway. Somatotopic relationship between the dentate nucleus and the contralateral inferior olive. Arch Neurol. 1970;22(2):135–43.
92. Kim JS, Lee SB, Park SK, Han SR, Kim YI, Lee KS. Periodic limb movement during sleep developed after pontine lesion. Mov Disord. 2003;18(11):1403–5.
93. Han SH, Park KY, Youn YC, Shin HW. Restless legs syndrome and akathisia as manifestations of acute pontine infarction. J Clin Neurosci. 2014;21(2):354–5.
94. Lee SJ, Kim JS, Song IU, An JY, Kim YI, Lee KS. Poststroke restless legs syndrome and lesion location: anatomical considerations. Mov Disord. 2009;24(1):77–84.
95. Egan CA, Davies L, Halmagyi GM. Bilateral total deafness due to pontine haematoma. J Neurol Neurosurg Psychiatry. 1996;61(6):628–31.
96. Cascino GD, Adams RD. Brainstem auditory hallucinosis. Neurology. 1986;36(8):1042–7.
97. Lanska DJ, Lanska MJ, Mendez MF. Brainstem auditory hallucinosis. Neurology. 1987;37(10):1685.
98. Murata S, Naritomi H, Sawada T. Musical auditory hallucinations caused by a brainstem lesion. Neurology. 1994;44(1):156–8.
99. Lee E, Sohn HY, Kwon M, Kim JS. Contralateral hyperacusis in unilateral pontine hemorrhage. Neurology. 2008;70(24 Pt 2):2413–5.
100. Fisher CM. The neurological examination of the comatose patient. Acta Neurol Scand. 1969;45(Suppl 36):1–56.
101. Kim JS. Pathologic laughter after unilateral stroke. J Neurol Sci. 1997;148(1):121–5.
102. Kim JS, Choi S, Kwon SU, Seo YS. Inability to control anger or aggression after stroke. Neurology. 2002;58(7):1106–8.
103. Andersen G, Ingeman-Nielsen M, Vestergaard K, Riis JO. Pathoanatomic correlation between poststroke pathological crying and damage to brain areas involved in serotonergic neurotransmission. Stroke. 1994;25(5):1050–2.
104. Choi-Kwon S, Han SW, Kwon SU, Kang DW, Choi JM, Kim JS. Fluoxetine treatment in poststroke

depression, emotional incontinence, and anger proneness: a double-blind, placebo-controlled study. Stroke. 2006;37(1):156–61.
105. Drake ME Jr, Pakalnis A, Phillips B. Secondary mania after ventral pontine infarction. J Neuropsychiatry Clin Neurosci. 1990;2(3):322–5.
106. Ferbert A, Bruckmann H, Drummen R. Clinical features of proven basilar artery occlusion. Stroke. 1990;21(8):1135–42.
107. Kim JS, Lee JH, Lee MC, Lee SD. Transient abnormal behavior after pontine infarction. Stroke. 1994;25(11):2295–6.
108. Kim JS, Cho KH, Kang DW, Kwon SU, Suh DC. Basilar artery atherosclerotic disease is related to subacute lesion volume increase in pontine base infarction. Acta Neurol Scand. 2009;120(2):88–93.
109. Kubik CS, Adams RD. Occlusion of the basilar artery; a clinical and pathological study. Brain. 1946;69(2):73–121.
110. Voetsch B, DeWitt LD, Pessin MS, Caplan LR. Basilar artery occlusive disease in the New England Medical Center Posterior Circulation Registry. Arch Neurol. 2004;61(4):496–504.
111. Fisher CM. The 'herald hemiparesis' of basilar artery occlusion. Arch Neurol. 1988;45(12):1301–3.
112. Ropper AH. 'Convulsions' in basilar artery occlusion. Neurology. 1988;38(9):1500–1.
113. Biemond A. Thrombosis of the basilar artery and the vascularization of the brain stem. Brain. 1951;74(3):300–17.
114. Klein IF, Lavallee PC, Schouman-Claeys E, Amarenco P. High-resolution MRI identifies basilar artery plaques in paramedian pontine infarct. Neurology. 2005;64(3):551–2.
115. Caplan LR. "top of the basilar" syndrome. Neurology. 1980;30(1):72–9.
116. Martin PJ, Chang HM, Wityk R, Caplan LR. Midbrain infarction: associations and aetiologies in the New England Medical Center Posterior Circulation Registry. J Neurol Neurosurg Psychiatry. 1998;64(3):392–5.
117. Kim JS, Kim J. Pure midbrain infarction: clinical, radiologic, and pathophysiologic findings. Neurology. 2005;64(7):1227–32.
118. Bogousslavsky J, Maeder P, Regli F, Meuli R. Pure midbrain infarction: clinical syndromes, MRI, and etiologic patterns. Neurology. 1994;44(11):2032–40.
119. Kumral E, Bayulkem G, Akyol A, Yunten N, Sirin H, Sagduyu A. Mesencephalic and associated posterior circulation infarcts. Stroke. 2002;33(9):2224–31.
120. Ogawa K, Suzuki Y, Oishi M, Kamei S. Clinical study of twenty-one patients with pure midbrain infarction. Eur Neurol. 2012;67(2):81–9.
121. Leigh RJ, Zee DS. The neurology of eye movements. 3rd ed. New York: Oxford University Press; 1999. p. 321–404.
122. Ksiazek SM, Repka MX, Maguire A, Harbour RC, Savino PJ, Miller NR, et al. Divisional oculomotor nerve paresis caused by intrinsic brainstem disease. Ann Neurol. 1989;26(6):714–8.
123. Rabadi MH, Beltmann MA. Midbrain infarction presenting isolated medial rectus nuclear palsy. Am J Med. 2005;118(8):836–7.
124. Lee DK, Kim JS. Isolated inferior rectus palsy due to midbrain infarction detected by diffusion-weighted MRI. Neurology. 2006;66(12):1956–7.
125. Halmagyi GM, Brandt T, Dieterich M, Curthoys IS, Stark RJ, Hoyt WF. Tonic contraversive ocular tilt reaction due to unilateral meso-diencephalic lesion. Neurology. 1990;40(10):1503–9.
126. Lee SH, Park SW, Kim BC, Kim MK, Cho KH, Kim JS. Isolated trochlear palsy due to midbrain stroke. Clin Neurol Neurosurg. 2010;112(1):68–71.
127. Deuschl G, Bain P, Brin M. Consensus statement of the Movement Disorder Society on tremor. Ad Hoc Scientific Committee. Mov Disord. 1998;13(Suppl 3):2–23.
128. Remy P, de Recondo A, Defer G, Loc'h C, Amarenco P, Plante-Bordeneuve V, et al. Peduncular 'rubral' tremor and dopaminergic denervation: a PET study. Neurology. 1995;45(3 Pt 1):472–7.
129. Paviour DC, Jager HR, Wilkinson L, Jahanshahi M, Lees AJ. Holmes tremor: application of modern neuroimaging techniques. Mov Disord. 2006;21(12):2260–2.
130. Deuschl G, Wilms H, Krack P, Wurker M, Heiss WD. Function of the cerebellum in Parkinsonian rest tremor and Holmes' tremor. Ann Neurol. 1999;46(1):126–8.
131. Kim DG, Koo YH, Kim OJ, Oh SH. Development of Holmes' tremor in a patient with Parkinson's disease following acute cerebellar infarction. Mov Disord. 2009;24(3):463–4.
132. Morgan JC, Sethi KD. Midbrain infarct with parkinsonism. Neurology. 2003;60(12):E10.
133. Akyol A, Akyildiz UO, Tataroglu C. Vascular parkinsonism: a case of lacunar infarction localized to mesencephalic substantia nigra. Parkinsonism Relat Disord. 2006;12(7):459–61.
134. Gonzalez-Alegre P. Monomelic parkinsonian tremor caused by contralateral substantia nigra stroke. Parkinsonism Relat Disord. 2007;13(3):182–4.
135. Kim JS, Im JH, Kwon SU, Kang JH, Lee MC. Micrographia after thalamo-mesencephalic infarction: evidence of striatal dopaminergic hypofunction. Neurology. 1998;51(2):625–7.
136. Kwon M, Lee JH, Kim J, Kim JS. Hypokinetic dysarthria and palilalia in midbrain infarction. J Neurol Neurosurg Psychiatry. 2008;79(12):1411–2.
137. Loher TJ, Krauss JK. Dystonia associated with pontomesencephalic lesions. Mov Disord. 2009;24(2):157–67.
138. Kim JS. Asterixis after unilateral stroke: lesion location of 30 patients. Neurology. 2001;56(4):533–6.
139. Park HK, Kim HJ, Kim SJ, Kim JS, Shin HW. From Jekyll to Hyde after limbic subthalamic nucleus infarction. Neurology. 2011;77(1):82–4.
140. Zakaria T, Flaherty ML. Locked-in syndrome resulting from bilateral cerebral peduncle infarctions. Neurology. 2006;67(10):1889.

141. Kobayashi K, Matsubara R, Kurachi M, Sano J, Isaki K, Yamaguchi N, et al. Locked-in syndrome with bilateral midbrain infarcts—report of an autopsy. No To Shinkei. 1983;35(2):115–21.
142. Silverman IE, Geschwind MD, Vornov JJ. Cerebellar top-of-the-basilar syndrome. Clin Neurol Neurosurg. 1998;100(4):296–8.
143. Trojanowski JQ, Wray SH. Vertical gaze ophthalmoplegia: selective paralysis of downgaze. Neurology. 1980;30(6):605–10.
144. Buttner-Ennever JA, Buttner U, Cohen B, Baumgartner G. Vertical glaze paralysis and the rostral interstitial nucleus of the medial longitudinal fasciculus. Brain. 1982;105(Pt 1):125–49.
145. Pierrot-Deseilligny CH, Chain F, Gray F, Serdaru M, Escourolle R, Lhermitte F. Parinaud's syndrome: electro-oculographic and anatomical analyses of six vascular cases with deductions about vertical gaze organization in the premotor structures. Brain. 1982;105(Pt 4):667–96.
146. Bhidayasiri R, Plant GT, Leigh RJ. A hypothetical scheme for the brainstem control of vertical gaze. Neurology. 2000;54(10):1985–93.
147. Halmagyi GM, Evans WA, Hallinan JM. Failure of downward gaze: the site and nature of the lesion. Arch Neurol. 1978;35(1):22–6.
148. Jacobs L, Anderson PJ, Bender MB. The lesions producing paralysis of downward but not upward gaze. Arch Neurol. 1973;28(5):319–23.
149. Jampel RS, Fells P. Monocular elevation paresis caused by a central nervous system lesion. Arch Ophthalmol. 1968;80(1):45–57.
150. Lessell S. Supranuclear paralysis of monocular elevation. Neurology. 1975;25(12):1134–43.
151. Thomke F, Hopf HC. Acquired monocular elevation paresis. An asymmetric upgaze palsy. Brain. 1992;115(Pt 6):1901–10.
152. Bogousslavsky J, Regli F. Upgaze palsy and monocular paresis of downward gaze from ipsilateral thalamo-mesencephalic infarction: a vertical "one-and-a-half" syndrome. J Neurol. 1984;231(1):43–5.
153. Deleu D, Buisseret T, Ebinger G. Vertical one-and-a-half syndrome. Supranuclear downgaze paralysis with monocular elevation palsy. Arch Neurol. 1989;46(12):1361–3.
154. Collier J. Nuclear ophthalmoplegia with special reference to retraction of the lids and ptosis and to lesions of the posterior commissure. Brain. 1927;50:488.
155. Seybold ME, Yoss RE, Hollenhorst RW, Moyer NJ. Pupillary abnormalities associated with tumors of the pineal region. Neurology. 1971;21(3):232–7.
156. van Bogaert L. L'hallucinose pdonculaire. Rev Neurol (Paris). 1927;43:608–17.
157. McKee AC, Levine DN, Kowall NW, Richardson EP Jr. Peduncular hallucinosis associated with isolated infarction of the substantia nigra pars reticulata. Ann Neurol. 1990;27(5):500–4.
158. Serra Catafau J, Rubio F, Peres SJ. Peduncular hallucinosis associated with posterior thalamic infarction. J Neurol. 1992;239(2):89–90.
159. Benke T. Peduncular hallucinosis: a syndrome of impaired reality monitoring. J Neurol. 2006;253(12):1561–71.
160. Martin JP. Hemichorea resulting from a local lesion of the brain (the syndrome of the body of Luys). Brain. 1927;50:637–42.
161. Mehler MF. The rostral basilar artery syndrome: diagnosis, etiology, prognosis. Neurology. 1989;39(1):9–16.
162. Ahn SH, Kim BJ, Kim YJ, Kang DW, Kwon SU, Kim JS. Patterns and outcomes of the top of the basilar artery syndrome: the role of the posterior communicating artery. Cerebrovasc Dis. 2018;46(3–4):108–17.