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# **Wernekink Commissure Syndrome secondary to A Rare “V”-Shaped Pure Midbrain Infarction: A Case Report and Review of the Literature**

**Running head: Wernekink Commissure Syndrome: A Rare Syndrome**

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## **Abstract**

**Purpose:** Wernekink commissure syndrome is a typical but extremely rare mesencephalic syndrome, and generally presents with bilateral cerebellar dysfunction, diverse oculomotor disorders, and occasionally delayed-onset palatal myoclonus or tremor. However, it has been reported infrequently. **Methods:** We report a case of a 55-year-old man who suffered an acute paramedian midbrain infarction presenting with bilateral cerebellar ataxia, bilateral anterior internuclear

ophthalmoplegia and unilateral pseudoabducens palsy, which is confirmed as Wernekink commissure syndrome by magnetic resonance imaging (MRI). We summarized the clinical data of this entity and performed a literature review of 20 previous reports of patients with this syndrome. **Results:** In combination with previous reports, we found that the most common symptom was bilateral cerebellar ataxia (100%) and other frequent symptoms were oculomotor disorders (81%), delayed palatal myoclonus or tremor (33%) and consciousness dysfunction (33%). Lesions on brain MRI of all patients affected the area of caudal paramedian midbrain (CPM). **Conclusion:** Bilateral cerebellar ataxia and lesions involved in the area of CPM on MRI are the major features of Wernekink commissure syndrome and should be the necessary conditions of diagnostic criteria. The simultaneous occurrence of bilateral cerebellar ataxia and oculomotor disorders is significant for localization diagnosis. Consciousness dysfunction is also a relatively frequent symptom of this syndrome. Moreover, pseudoabducens palsy might be attributed to a midbrain lesion. Clinicians should be familiar with and early to recognize this unique syndrome to avoid misdiagnosis.

**Keywords:** Wernekink commissure syndrome; bilateral cerebellar ataxia; internuclear ophthalmoplegia; pseudoabducens palsy; caudal paramedian midbrain infarction

## Introduction

Wernekink commissure syndrome is a typical but extremely rare mesencephalic syndrome caused by a selective lesion in the Wernekink commissure. It was originally reported by Lhermitte in 1958 and commonly characterized by bilateral cerebellar dysfunction, diverse oculomotor disorders, and occasionally delayed-onset palatal myoclonus or tremor[1]. However, it has been reported infrequently. We, herein, describe a case of this syndrome due to a unique “V”-shaped pure midbrain infarction. Besides, we also discuss the clinical manifestations and radiological features of Wernekink commissure

syndrome through a systematic review of published cases.

### Case report

A 55-year-old man with a long-term history of smoking, alcoholism, and severe hypertension and diabetes mellitus, presented with dizziness, diplopia and gait instability on awakening for 6 h. He also suffered a tendency to fall in either direction with his eyes open when he attempted to sit or stand without assistance due to his trunk imbalance. Neurological examination revealed slightly hypersomnolence, dysarthria, horizontal gaze disorders: adduction deficit of the bilateral eyes (bilateral anterior internuclear ophthalmoplegia[INO]) and abduction deficit of the left eye (probable a pseudoabducens paralysis), bilateral clockwise torsional nystagmus on leftward gaze (from the view of doctor), left-sided incomplete ptosis with normal pupillary size and reaction, severe bilateral dysmetria, and trunk ataxia. Laboratory examinations were normal except for triglycerides cholesterol of 1.75 mmol/L, glycosylated hemoglobin of 7.2%, preprandial blood glucose of 9.6mmol/L and postprandial blood glucose of 15.4mmol/L. Doppler ultrasound suggested atherosclerosis on bilateral carotid arteries. Transthoracic echocardiography and electrocardiogram were both normal. Brain magnetic resonance imaging (MRI) showed a lesion in the midline of the paramedian midbrain on the fluid-attenuation inversion recovery (FLAIR) images, resembling “V” shape (**Fig. 1 A&B**), presenting with a high signal on diffusion-weighted image (DWI) MRI (**Fig. 1 C&D**) and low signal on apparent diffusion coefficient (ADC) map MRI (**Fig. 2 A&B**), in accordance with acute infarction. The sagittal T2-weighted image of MRI showed the caudal mesencephalic lesion expanding to the superior colliculus level of the rostral midbrain (**Fig. 2 C**). MRI angiography revealed mild stenosis in the P1 segment of the posterior cerebral artery (PCA) (**Fig. 2 D**). An acute paramedian midbrain infarction presenting with Wernekink commissure syndrome was diagnosed. After the 10-day treatment of dual

anti-platelet aggregation medication, statins, cerebral circulation, and free-radical scavenger, only dizziness and hypersomnolence improved.

## Discussion

With the complex and richly supply to the midbrain, pure midbrain infarction is very rare (merely 0.6% in total ischemic stroke cases), and Wernekink commissure syndrome is even rarer[2]. Generally, there are four groups of arterial territories in the midbrain, including anteromedial (paramedian), anterolateral, lateral and dorsal arterial territory[3]. The paramedian area ranging from the thalamus to midbrain is mainly supplied by the interpeduncular fossa perforating branches that can be categorized into three groups based on the vascular supply territory[4]. The inferior paramedian mesencephalic arteries (IPMAs), one group of the interpeduncular fossa perforating branches, arising from the distal basilar arterial and proximal PCA or superior cerebellar artery, and supplying the region of caudal paramedian midbrain (CPM) including the Wernekink commissure, medial longitudinal fascicle (MLF), reticular formation and so on are commonly regarded as the culprit vessels of Wernekink commissure syndrome secondary to stroke[5, 6]. Because of the anatomic variations of IPMAs, the morphology of caudal paramedian midbrain infarction (CPMI) on MRI can be various including oval, round, and oblong shape[6]. However, in our case, an unusual “V”-shaped lesion was found. Previously, only 2 cases of Wernekink commissure syndrome with “heart or V”-shaped lesion have been reported[6, 7]. Given that a one-hit pattern of onset was presented, the probable explanation for this shape lesion was the IPMAs with the variant branches supplying bilateral CPM[6].

Wernekink commissure is firstly described as a horseshoe-shaped commissure by the German anatomist Friedrich Wernekink and actually the decussation of superior cerebellar peduncles (SCP). It mainly consists of two white matter tracts: dentato-rubro-thalamic tract and dentato-rubro-olivary

tract[1, 8]. The former pathway provides cerebrocerebellum connection by connecting the dentate nucleus through the SCP to the contralateral red nucleus and thalamus. The latter one was formed by the fibers that contacted dentate and interposed cerebellar nuclei to the contralateral red nucleus through the SCP and inferior olfactory nucleus in the medulla. The location of this commissure is anterior to the aqueduct and at the paramedian area of upper brainstem (mainly in the caudal midbrain as well as small portion in rostral pontine and midbrain)[9]. The structures adjacent to Wernekink commissure include MLF, reticular formation, trochlear nucleus (at the inferior colliculus level), and the oculomotor nuclei and fibers (at the superior colliculus level). Therefore, the classical symptoms of Wernekink commissure syndrome are described as constant bilateral cerebellar dysfunction along with commonly various ocular signs, and occasionally delayed-onset palatal myoclonus or tremor.

In our case, it is not difficult to diagnose with Wernekink commissure syndrome according to the clinical presentation and MRI imaging. Unlike previously reported cases, the lesion of our case did not limit at the caudal midbrain level, and approximately expanded to the superior colliculus level of the rostral midbrain. Consequently, the symptoms of ptosis and torsional nystagmus can be explained by the rostral extension of infarction to the portion of the oculomotor nuclei/nerves and interstitial nucleus of Cajal (INC), respectively[10]. Due to slightly deviating to the left side, the “V”-shaped lesion involved the left INC which caused ipsilesional torsional nystagmus. This sign is uncommon and can result from caudal midbrain lesion involving the INC only but sparing the rostral interstitial nucleus of MLF and posterior commissure with its nucleus[11,12]. The bilateral adduction deficit can be attributed to involving the bilateral MLF which results in a bilateral anterior INO. However, a curious ocular finding of the abduction deficit in our case was observed and provided a challenge for the topical diagnosis. Initially, we considered the neuro-ophthalmologic signs as the possibility of a

“one-and-a-half syndrome” but, there was no evidence of involvement of the pons. Why a midbrain lesion can present with “abducens paralysis”? By reviewing the literature and analyzing our imaging findings, we found that our case was similar to some prior published cases presented with pseudoabducens paralysis secondary to a lesion restricted to thalamus or midbrain[13-16]. The sign of abduction deficit in our case could be also recognized as a “pseudoabducens paralysis” which, albeit speculative, seems to be reasonable. Pseudoabducens palsy (or sixth nerve pseudopalsy) was first proposed by Fisher in 1965, later described by Caplan as “a failure of ocular abduction, which is not due to dysfunction of the sixth nucleus, fascicle, or nerve”[17,18]. The exact pathophysiology of pseudoabducens palsy is not well understood, but a widely accepted mechanism of the impairment of inhibitory convergence pathways might provide an explanation. The pathway contains two descending fibers, each of which connects the thalamus/rostral subthalamus through the midbrain-diencephalic junction to the contralateral “near response” neurons that are located within the supraoculomotor area[13,19]. While the role of projections from the near response neurons is to excite the ipsilateral medial rectus (MR) subnucleus and inhibit the ipsilateral abducens nucleus[13]. If the pathway was interrupted, inhibition on the MR muscle would be removed which results in esotropia and mimicking unilateral or bilateral abducens paralysis. Due to the decussation in pathways, an ipsilesional or contralesional abduction deficit may result from a caudal or rostral mesencephalic lesion, respectively[13]. In this case, the absent esotropia may reflect the bilateral MLF dysfunction at the midbrain level. Furthermore, another explanation might be a supranuclear horizontal gaze paresis (including abduction deficit) induced by damage to the cortical-pontine horizontal gaze pathways, which could be difficult to recognize in the setting of unilateral or bilateral third nerve paresis[13]. We are confident that pseudoabducens paralysis of this case is not secondary to the involvement of the

sixth nucleus, fascicle or nerve, and is first described in the Wernekink commissure syndrome.

Clinically, besides the only consistent symptom of bilateral cerebellar dysfunction, there are still some heterogeneities in the associated clinical features of the currently published cases on Wernekink commissure syndrome, predominantly due to variations vessels resulting in various morphology and distribution of infarction[20]. Therefore, we performed a comprehensive literature review of 20 previous reports of CPMI presenting with Wernekink commissure syndrome. Twenty-one cases with complete clinical and radiological findings, together with our case, were included in this study (Table 1) [6, 7, 20-32].

The average age was  $59 \pm 13$  years (range, 34-85 years) and thirteen patients (62%) were males. The most common symptom was bilateral cerebellar ataxia (100%,  $n=21$ ), all of which manifested as dysarthria, truncal and/or tetra ataxia. It is mainly owing to the interruption of the dentato-rubro-thalamic pathways prior to and after the decussation result in this clinical symptom. Wernekink commissure was thought to be the only anatomical structure in the brainstem to induce bilateral cerebellar ataxia [28]. The second common symptom was oculomotor disorders (81%,  $n=17$ ), including ophthalmoplegia (67%,  $n=14$ ) and nystagmus (62%,  $n=13$ ). INO (57%,  $n=12$ ) is the most frequent type of ophthalmoplegia due to the location of the Wernekink commissure is adjacent to MLF[6]. Besides, the third nerve paresis, vertical ophthalmoplegia and convergence impairment were also observed in some cases. Among the various nystagmus, horizontal nystagmus (43%,  $n=9$ ) was most common, while additional types can be comprised of vertical, seesaw and upbeat nystagmus[6,7]. It is significant for topical diagnosis by detecting the co-existence of bilateral ataxia and ocular signs, especially INO, highly indicating a lesion at the CPM, and a previous study even more accurately located the lesion just at the pontomesencephalic junction[33]. Palatal myoclonus and/or tremor, the

consequence of destroying the fibers connected with the red nucleus or the inferior olivary nucleus, cannot be observed in every case with a total rate of 33% ( $n=7$ ). One reason was ascribed to a short period of observation and disease course[29]. Moreover, the range and location of the lesion may be a different explanation. Palatal myoclonus is usually secondary to inferior olivary degeneration (IOD) which typically caused by lesions in the dentato-rubro-olivary tract that destroyed the Guillain-Mollaret triangle circuit. Therefore, a lesion, if involved in the bilateral dentato-rubro-olivary fibers at the decussation of the superior cerebellar peduncle, may result in bilateral olivary degeneration[28]. However, IOD could not always develop to palatal myoclonus. In our study, only 3 patients presented with palatal myoclonus and IOD simultaneously. We have to point out that our review mainly differs from the others not only in increasing the numbers of reviewed cases, but also finding another relatively frequent symptom. Consciousness dysfunction (33%,  $n=7$ ) was as common as palatal myoclonus and/or tremor, of which hypersomnolence (24%,  $n=5$ ) was the majority. Lesions of the Wernekink commissure may involve the reticular formation at the CPM, which would affect the sleep-wake cycle. All patients of our review underwent brain MRI and revealed that all of the culprit lesions affected the region of CPM (100%,  $n=21$ ).

In clinical practice, differential diagnosis of the bilateral ataxia should be considered, and below, we summarized some identification points of related diseases which are more easily misdiagnosed:

- **Acute cerebellitis**[34, 35]: 1) mainly occurs in children, few in adults; 2) generally with a history of viral infection; 3) the most frequent symptom is cerebellar ataxia, presenting with wide-based gait (92%), balance disturbances (68%), dysmetria (35%) and dysarthria (27%), other common signs include vomiting, fever, and headache; 4) bilateral diffuse cerebellar hemispheric increased signal intensity confirmed on T2-weighted image MRI (73%) and increased cell counts in

cerebrospinal fluid (CSF) finding may be aid for diagnosis.

- **Miller-Fisher syndrome (MFS)**[36-38]: 1) generally with a history of upper respiratory tract infection; 2) frequently started with diplopia (78%) or ataxia (46%) or both (34%); 3) bilateral ophthalmoplegia is typically the first symptom of MFS, mainly presenting with pupillary abnormalities and ptosis; 4) with a one-day interval between the onset of diplopia and ataxia on average; 5) the mechanism of ataxia in MFS has not been fully explained, whereas, is generally accepted to be sensory ataxia; 6) areflexia is also a profound clinical sign; 7) sera anti-GQ1b IgG antibodies are the specific biomarkers (detection rate of over 90%).
- **Wernicke's encephalopathy**[39]: 1) generally result from a deficiency in vitamin B1 (thiamine) caused by chronic alcoholism or gastrointestinal disorders; 2) mental status changes (82%), ocular disorders (29%) and ataxia (23%) were the common symptoms at presentation; differently, ataxia mainly present with truncal ataxia and gait incoordination, few present with dysarthria or tetra ataxia; 3) MRI may show bilaterally symmetrical increased T2 signal in the paraventricular regions of thalamus, hypothalamus, mamillary bodies, periaqueductal region, the floor of the fourth ventricle and midline cerebellum (sensitivity of 53%, specificity of 93%) .
- **Multiple sclerosis (MS)**[40, 41]: 1) generally has the dissemination in space and time, and could also be manifested as ataxia and INO, however, ataxia in MS may be various including sensory, cerebellar, and vestibular ataxia; 2) the positive CSF findings (elevated immunoglobulin G [IgG] index or 2 or more oligoclonal bands) can be important to support the diagnosis of MS.

## Conclusions

In summary, bilateral cerebellar ataxia and lesions involved CPM confirmed by MRI were the major features of Wernekink commissure syndrome and may be the necessary conditions of diagnostic

criteria. Simultaneous occurrence of bilateral cerebellar ataxia and oculomotor disorders may highly suggest lesions at the CPM. Consciousness dysfunction is also a relatively frequent symptom of this syndrome. Furthermore, pseudoabducens palsy might be attributed to a midbrain lesion and could increase the difficulty of localization diagnosis. Clinicians should be familiar with and early to recognize this unusual syndrome.

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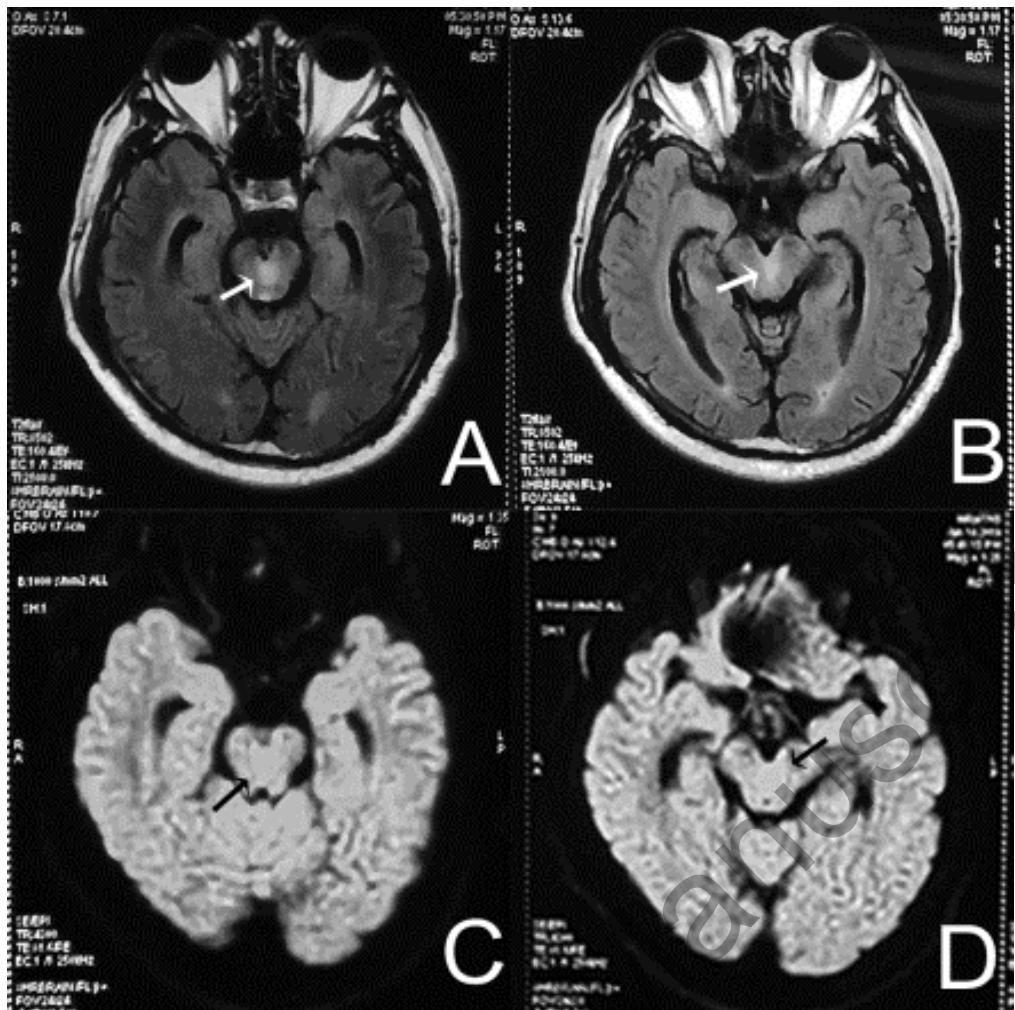


Figure 1. A&B. Axial FLAIR images revealed a “V”-shaped appearance area of increased signal located in the midline of the paramedian midbrain involving the decussation of the SCP, MLF and oculomotor nuclei (white arrow). C&D. The same region exhibited restricted diffusion with a high signal on axial DWI images (black arrow).

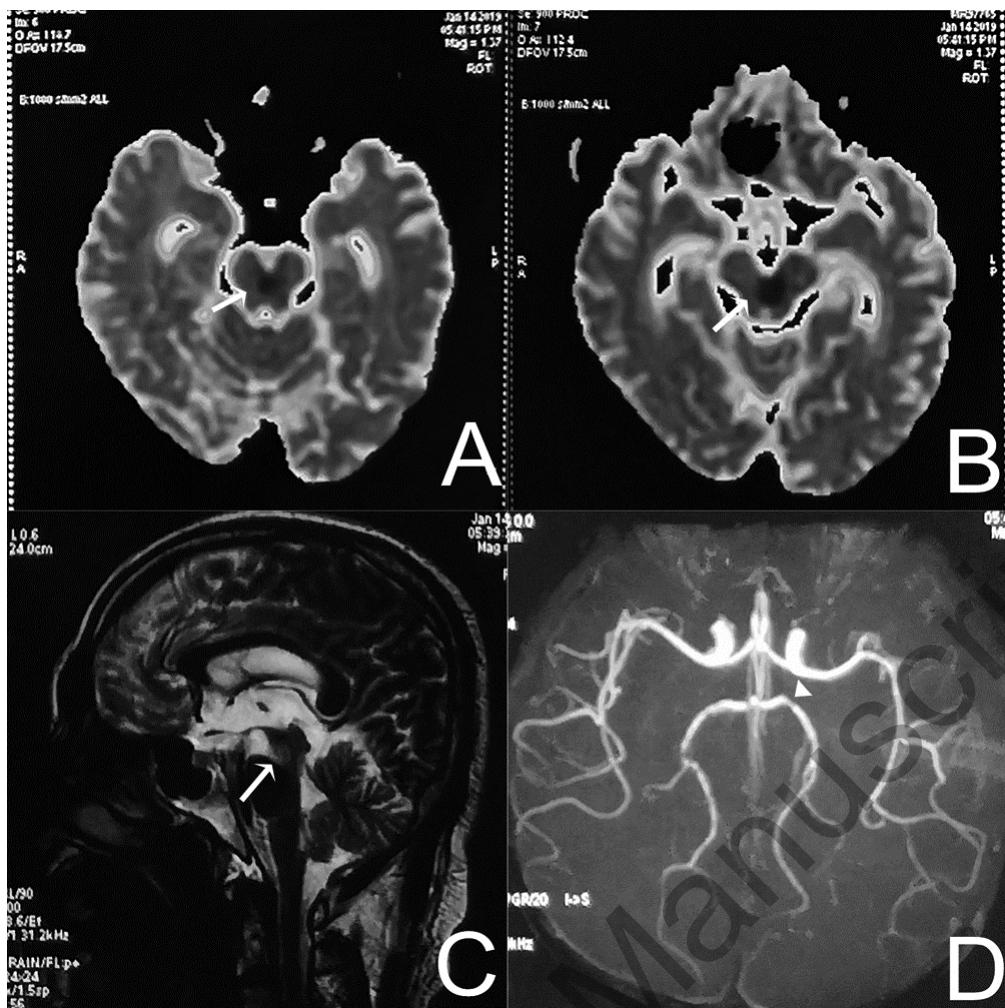


Figure 2. A&B. Axial ADC images showed low signal in the same lesion (white arrow). C. Sagittal T2-weighted image demonstrated the caudal midbrain lesion expanding to the superior colliculus level of the rostral midbrain (white arrow). D. MRI angiography image showed mild stenosis in the P1 segment of the left posterior cerebral artery (triangle).

**Table 1. Characteristics of patients with acute caudal paramedian midbrain infarction presenting with Wernekink commissure syndrome.**

No.	Age /Sex	Bi. Ataxia	Oculomotor disorders		DPM	Tremor	Other symptoms	IOD	Site of lesion	Ref
			Ophthalmoplegia	Nystagmus						
1	57/F	+	Bi. INO, upward gaze palsy+impaired convergence	Horizontal	- (5 weeks)	Head, Bi. limbs (5 weeks)	Hypersomnolence	- (5 weeks)	CPM extending to the left cerebral peduncle	[21]
2	57/F	+	Rt. INO	Upbeat	- ( no follow-up)	-	-	- ( no follow-up)	Rt. CPM	[22]
3	67/M	+	Bi INO	Horizontal	- (3 month)	Neck, Bi. upper limbs (onset)	Hypersomnolence (daytime), confusion and agitation (nighttime)	- (3 month)	Bi. CPM ventral to the aqueduct	[23]
4	64/M	+	-	-	+ (3 years)	-	-	+ (3 years)	Rt. CPM	
5	52/M	+	-	-	- (2 months)	-	-	+ (2 months)	Lt. CPM	
6	38/M	+	Upward gaze palsy, impaired convergence	Horizontal	- (7 years)	-	Headache, coma, incomplete locked-in syndrome	+ (7 years)	Lt. CPM, Lt. cerebellar hemispheric and paramedian thalamic	[20]
7	34/F	+	Rt. third nerve paresis, Rt. INO	Horizontal	- (14 months)	-	-	+ (8 months)	Rt. CPM	

8	42/M	+	Bi. third nerve paresis	-	(5 months)	-	-	(5 months)	Lt. CPM
9	70/M	+	Lt. INO	-	(2 weeks)	Jaw (onset)	Confused, disoriented and visual hallucinations	(2 weeks)	Lt. CPM [24]
10	80/M	+	-	-	(2 weeks)	Bi. upper limbs (onset)	-	(2 weeks)	Central portion of CPM [25]
11	71/M	+	-	-	(8 months)	-	Hypersomnolence	(8 months)	Central portion of CPM [26]
12	59/F	+	-	Horizontal	(12 days)	-	-	(12 days)	Central portion of CPM anterior to the periaqueductal gray [27]
13	59/F	+	-	Horizontal	(2 weeks)	-	-	(2 weeks)	Central portion of CPM ventral to the aqueduct [28]
14	71/M	+	Lt. INO	-	(2 weeks)	-	-	(2 weeks)	Lt. CPM
15	62/M	+	-	Upbeat	(1 weeks)	-	-	(1 weeks)	CPM (from right red nucleus ventrally to left superior cerebellar peduncle dorsally) [29]
16	51/M	+	Rt. INO	Horizontal	( no follow-up)	-	-	( no follow-up)	Lt. CPM [30]
17	85/F	+	Rt. INO	Horizontal	(6 weeks)	-	-	(6 weeks)	Central portion of CPM [31]

18	58/F	+	Bi. INO	-	-	(3 months)	-	-	(3 months)	Bi. CPM	[4]		
19	60/M	+	Bi. INO, impaired convergence	Horizontal and upbeat	+	(3 months)	Head	(3 months)	Hypersomnolence (daytime), aggressive (nighttime)	+	(3 months)	Bi.CPM	[3]
20	53/F	+	Rt. INO	Multidirectional	+	(onset)	-	-	-	+	(onset)	Rt. CPM	[32]
21	55/M	+	Bi. INO, Lt. third nerve and pseudoabducens paresis	Torsional	-	(10 days)	-	-	Hypersomnolence	-	(10 days)	Bi. CPM expanding to the rostral midbrain	Present case

**Abbreviations:**

Bi., bilateral; INO, internuclear ophthalmoplegia; Rt., right; Lt., left; DPM, delayed-onset palatal myoclonus; IOD, inferior olivary degeneration; CPM, caudal paramedian midbrain.