Original Article
Wernekink commissure syndrome: clinico-radiological criteria

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Abstract:
Introduction: Wernekink commissure syndrome is a rare midbrain syndrome selectively affecting the Wernekink commissure, characterized by bilateral cerebellar ataxia and eye movement disorders, especially internuclear ophthalmoplegia. This article aims at proposing clinico-radiological criteria for Wernekink commissure syndrome with review of the neural circuitary responsible, to aid in recognition and reporting.

Methods: This was a prospective study conducted at Department of Neurology, at Pushpagiri institute of medical sciences and research centre, Thiruvalla, Kerala, India, over a period of 5 years among patient with pure midbrain syndromes. All patients with pure midbrain infarction were studied. Subjects presenting with clinical features of Wernekink commissure syndrome were shortlisted and were assessed by investigators independently. Neuroradiology was assessed by investigators 1 and 2, independently. The demographic profile, risk factors, clinical features, neuroimaging findings and outcomes were analysed using SPSSv21.

Results: Details of 43 subjects with pure midbrain stroke were included in the study. 8 had clinical features of Wernekink commissure syndrome. The most common findings were bilateral ataxia and unilateral or bilateral internuclear ophthalmoplegia. None of our patients had palatal tremor. Unilateral caudal paramedical infarction was seen on MRI in 5 patients, whereas it was bilateral in 3 patients.

Conclusions: The proposed clinico-radiological criteria consisting of all of the essential criteria (Ipsilateral internuclear ophthalmoplegia, Unilateral or bilateral ataxia and Neuroradiological evidence of Caudal midbrain involvement) with or without one among the supportive criteria (Rubral Tremor, Palatal myoclonus) can safely point at a diagnosis of Wernekink commissure syndrome.

Key words: Diagnostic criteria, Internuclear ophthalmoplegia, Wernekink commissure syndrome

INTRODUCTION

Wernekink commissure syndrome is a rare syndrome , due to involvement of the midbrain and it is characterized by bilateral cerebellar ataxia, internuclear ophthalmoplegia and delayed onset palatal myoclonus.[1-3] The structures located in the medial part of midbrain include oculomotor nuclei, descending cerebellar tracts, medial longitudinal fasciculus, and central tegmental tract, and a lesion in this region can result in the clinical features described in this syndrome.[4] Wernekink commissure syndrome was first described by Lhermitte and it was named after German anatomist Friedrich Wernekink, who described it as a horseshoe-shaped commissure.[5]

Wernekink commissure syndrome is reported sparsely in literature, and the authors believe this to be a result of lack of clarity regarding the neural circuitries and possible permutations of various clinical syndromes involved, making it difficult to localize it to a single vascular territory. To the best of our knowledge this is one of the largest follow up cohorts of subjects with clinical and radiologically confirmed Wernekink commissure syndrome, with proposal of a clinico-radiological criteria as a guide for diagnosis for first contact physician and neurologist alike.

METHODS AND MATERIALS

This is a prospective hospital-based study, conducted in the Department of Neurology, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, a tertiary care centre in central Kerala, India. All subjects presenting with pure midbrain syndromes were included in the initial study group. Subjects presenting with acute onset of Ipsilateral internuclear ophthalmoplegia and unilateral or bilateral ataxia with or without palatal myoclonus, with 1.5 T MRI brain showing caudal paramedian midbrain infarction, were included in the study group and were independently assessed by investigators 1 and 2. Any discrepancy noted during the assessment was settled through an expert committee assessment including neurologists and radiologists. The demographic profile, risk factors, clinical features, neuroimaging findings and outcomes were analysed using SPSSv21. The study was conducted between 1stAugust 2014 and 30th July 2019.

RESULTS

A total of 43 patients with pure midbrain infarction were identified over this five-year period. Of these, 08 patients (18.6%%) complied with the proposed criterion for diagnosis of Wernekink commissure syndrome. Age group ranged from 34 years to 70 years, with a mean age of 55.6 $\pm$ 2.6 years. There were 5 males and 3 females. Six out of eight patients were hypertensive and diabetic with five patients having dyslipidemia. Three had pre-existing coronary artery disease and two had atrial fibrillation. Systemic lupus erythematosus related vasculitis caused infarction in patient 3.

All the eight patients had unilateral internuclear ophthalmoplegia (INO), characterized by impaired eye adduction on the side of the lesion and abducting nystagmus on the contralateral side, due to possible involvement of medial longitudinal fasciculus (Fig 1). Though described in contemporary literature, none of our patients had bilateral INO. Three had skew deviation, with ipsilateral hypertropia and vertical nystagmus. All but two patients had bilateral cerebellar signs. (Table:1) None of our patients had palatal myoclonus even at 3 months follow up. At follow up, 5 patients had a m RS score (modified Rankin score) of 1 and 3 had a score of 0 (indicating that the patient has no residual symptoms).

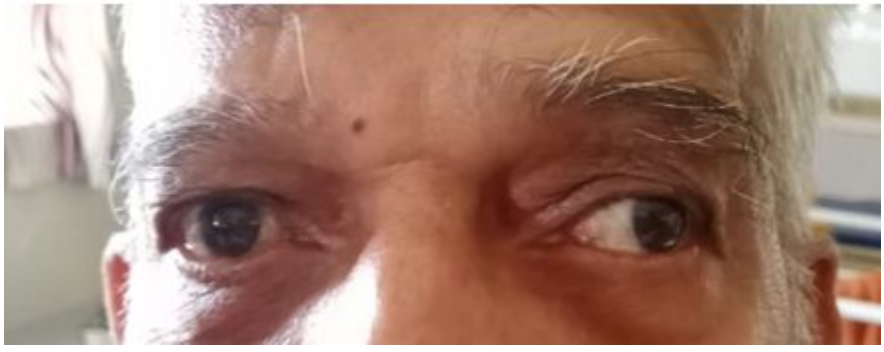

Figure 1: Impaired adduction of the right eye, on attempting gaze towards the left side. This patient had nystagmus of the abducting left eye, suggesting a right internuclear ophthalmoplegia.

All the patients underwent magnetic resonance brain imaging in 1.5 T machine. Five patients had unilateral caudal paramedian infarcts. Three had bilateral caudal paramedian infarcts (Figure 2).

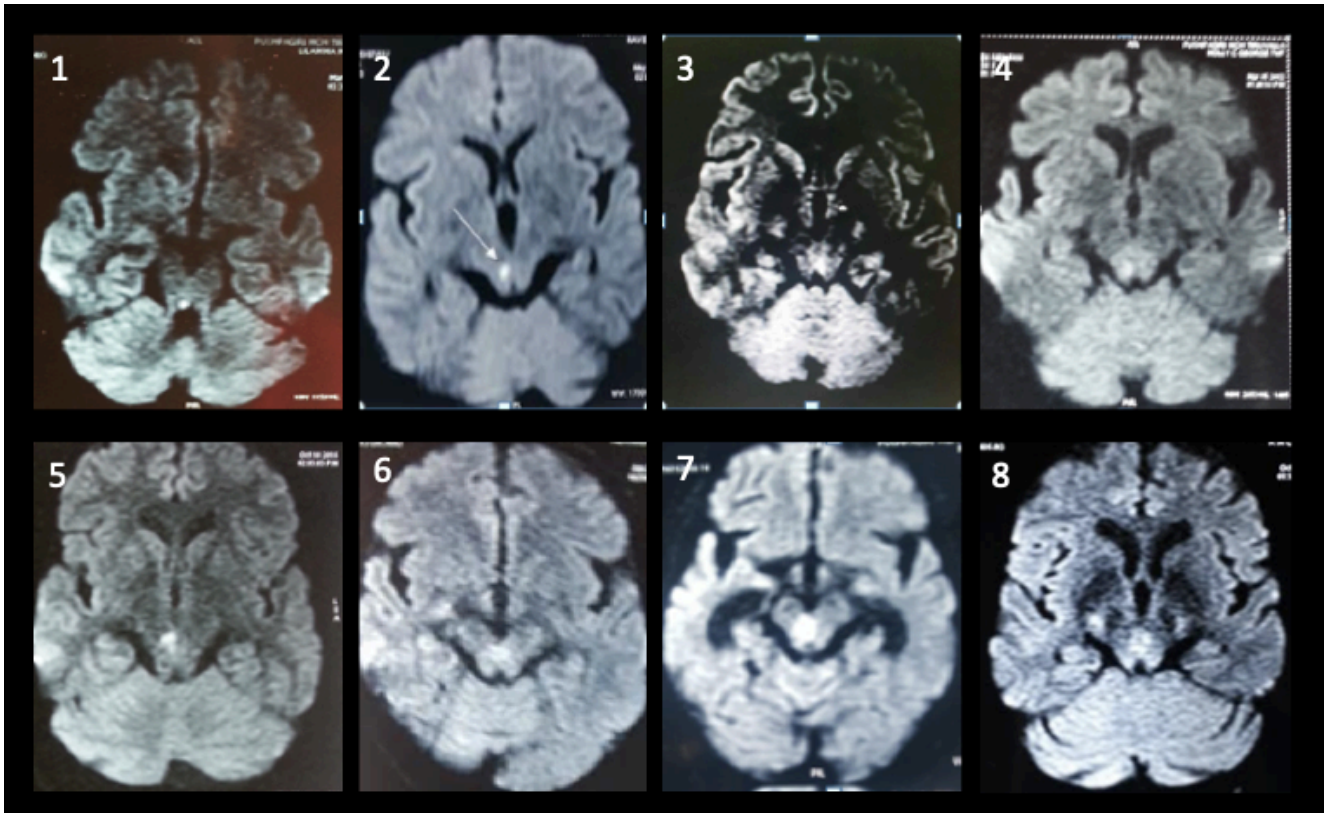

Figure 2: Magnetic resonance imaging- Diffusion weighted sequences of Patients 1 to 8 showing paramedian midbrain infarction

DISCUSSION

Wernekink commissure syndrome is a rare syndrome, which selectively involves the Wernekink commissure involving the decussation of the superior cerebellar peduncle in midbrain. It was first described by Lhermitte in 1958.[5]

Pure midbrain infarction is very rare, with a prevalence between 0.7 and 2.3%.[6] Based on the arterial territories, the midbrain can be divided into the paramedian, lateral, and dorsal territory. The paramedian area of the midbrain is supplied by the interpeduncular fossa perforating branch, which arises from the the basilar artery, superior cerebellar artery, and the pre-communicating segment of the posterior cerebral arteries. The caudal midbrain tegmentum, which includes the Wernekink commissure, medial longitudinal fascicle (MLF), anterior portion of the periaqueductual gray matter, and reticular formation, is supplied by the inferior paramedian mesencephalic arteries (IPMAs).[7-9] Hence, involvement of this artery can result in Wernekink commissure syndrome. Though classically described in midbrain infarctions, Wernekink commissure syndrome has been reported with other etiologies like haemorrhage, demyelination (multiple sclerosis, neuromyelitis optica), tumors (medulloblastoma, glioma, lymphoma), infections and vasculitis (systemic lupus erythematosus).[10-12]

Wernekink commissure refers to the decussation of the superior cerebellar peduncles, in the midbrain, before their entrance into the red nucleus.[13] This explains bilateral cerebellar dysfunction in

Wernekink commissure syndrome. Zhou et al concurs with our group in having bilateral signs of cerebellar dysfunction in all the subjects.[1] (Table 1)

	Mean age	Sex (M:F)	I/p INO	Ataxia	Nystagmus	Palatal myoclonus	Tremor	Caudal MB involvement
Sheetal et al	55.6	5:3	100%	100%	62.5%	0.0%	62.5%	100%
Aggregate of published English literature		5:0	100%	80.0%	0.0%	60.0%	40.0%	100%

Table 1. Clinical features of Wernekink commissure syndrome, noted in our study

In the Wernekink commissure syndrome, involvement of the medial longitudinal fasciculus(MLF), connecting the nucleus of the abducens nerve with the contralateral medial rectus nucleus of the oculomotor nerve, results in internuclear ophthalmoplegia.[2,10] The present study reports all the subjects to have unilateral internuclear ophthalmoplegia, whereas Zhou et al reported 42% subjects in their study group to have had INO.[1] Three (37.5 %) subjects among the study group were noted to have skew deviation with vertical nystagmus. MLF, links vestibular input with the trochlear and oculomotor nuclei, the interstitial nucleus of Cajal, and the rostral interstitial nucleus of the MLF, and hence is an important coordinator of vertical eye movements. Hence, MLF lesions can also result in skew deviations, vertical nystagmus and ocular tilt reaction.

Another symptom reported is delayed palatal tremor due to delayed inferior olivary degeneration. The Guillain– Mollaret triangle is formed by the ipsilateral red nucleus in the midbrain, the inferior olive in the medulla and the contralateral dentate nucleus in the cerebellum: together forming the dentato-rubro-olivary pathway. The inferior olivary degeneration is thought to be a consequence of destruction of this circuit resulting in disinhibition of the inferior olivary nucleus. This leads to hyperthrophy of the olivary nucleus and its rhythmical discharges may manifest clinically as oculopalatal tremor. However, palatal tremor does not develop in every patient with olivary degeneration.[14] None among the present study group developed palatal myoclonus, whereas 60.0% of the of reported cases of Wernekink Commissure syndrome had delayed onset palatal tremor as a symptom (Table 2).

Author	Age/Sex	Clinical presentation								Neuroimaging	Outcome at 3 months
		i/p INO	Nystagmus	Skew	Ataxia	Tremor	Palatal myoclonus	Dysarthria	Others		
Sheetal et al	52/M	+	-	-	Bilateral	-	-	-	-	Right caudal midbrain infarct	mRS 0
	70/F	+	Horizontal	-	Bilateral	-	-	-	Cheiro-oral parasethesia	Right caudal midbrain infarct	mRS 0
	45/F	+	Vertical	+	Bilateral	-	-	-	SLE	Central caudal midbrain	mRS 1
	59/M	+	Horizontal	-	Bilateral	+	-	-	-	Bilateral caudal midbrain	mRS 2
	60/M	+	Vertical	+	Unilateral	+	-	-	Left hemiparesis	Right caudal midbrain	mRS 1
	60/F	+	Vertical	+	Bilateral	+	-	-	-	Paramedian caudal midbrain	mRS 0
	65/M	+	-	-	Unilateral	+	-	-	-	Right caudal midbrain	mRS 1
	34/M	+	-	-	Bilateral	+	-	+	-	Paramedian caudal midbrain	mRS 1
Bolen et al	53/M	+	-	-	-	+	+	-	-	Left pontine hemorrhage extending to midbrain	-
Liu et al	71/M	+	-	-	+	-	+	+	Right hemiparesis	Left paramedian midbrain	-
Zhou et al	60/M	+	-	-	Bilateral	+	+	+	-	Bilateral caudal paramedian midbrain	-
Mullaguri et al	53/M	+	-	-	Bilateral	-	-	+	-	Right caudal midbrain infarction	-
Dai et al	70/M	+	-	-	+	-	-	+	-	Left caudal midbrain infarction	-

Table 2: Comparison of previously published studies on Wernekink commissure syndrome

Depending upon the arteries affected, MRI may reveal diverse morphology ,such as oval, round, oblong, and V shape lesions.[15,16] The oval and round lesion, sparing the ventral midbrain is thought to be due to the involvement of in the paramedian perforating arteries.[1] In the present study, two (25%) had round lesions and three (37.5%) had ovoid lesions. Three were noted to have bilateral paramedian infarction.

This study is in close agreement with the case reports published earlier (Table 2). After analysis of the clinical features of cases of Wernekink commissure syndrome published, we propose the below mentioned clinico-radiological criteria for diagnosis of Wernekink Commissure syndrome (Figure 3). This would facilitate early identification and localisation of the uncommon syndrome.

PROPOSED DIAGNOSTIC CRITERIA

Essential criteria

- *Ipsilateral internuclear ophthalmoplegia*
- *Unilateral or bilateral ataxia*
- *Neuro-radiological evidence of Caudal midbrain involvement*

Supportive criteria

- *Rubral Tremor*
- *Palatal myoclonus*

Diagnosis may be established with the presence of all three Essential criteria with or without one or both of the supportive criteria.

Figure 3. Clinico-radiological criteria for diagnosis of Wernekink Commissure syndrome

CONCLUSION

The Wernekink commissure syndrome, is classically characterized by constant bilateral cerebellar dysfunction and variable eye movement disorders of which internuclear ophtalmoplegia is the commonest. It is caused by caudal paramedian midbrain infarction.

CONFLICT OF INTEREST

Nothing to disclose

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