A Case of Wall-Eyed Bilateral Internuclear Ophthalmoplegia (WEBINO) Syndrome Caused by Pontine Infarction

Katsuhiko Ogawa, Takayoshi Akimoto, Makoto Hara, Satoshi Kamei, Hideto Nakajima, Yasuyuki Nomura and Shuntaro Shigihara

1) Division of Neurology, Department of Medicine, Nihon University School of Medicine, Tokyo, Japan
2) Department of Otolaryngology-Head and Neck Surgery, Nihon University School of Medicine, Tokyo, Japan

We report a case of a 50-year-old man with wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) syndrome caused by pontine infarction. The patient exhibited bilateral internuclear ophthalmoplegia with alternating exotropia and left hemiparesis. In an inattentive state, bilateral mild exotropia was noted. On magnetic resonance imaging, infarcts were detected in the right pontine base and the tegmentum on both sides. On electroneystagmogram of saccade, the velocity in adduction and abduction was decreased bilaterally. Furthermore, the velocity in adduction was more decreased than that in abduction bilaterally. This result indicated that the medial longitudinal fasciculus (MLF) and the bilateral paramedian pontine reticular formation (PPRF) were impaired bilaterally in predominance of the MLF. Inhibition of the lateral rectus muscle depends on inhibitory burst neurons connected to the contralateral PPRF. This inhibitory function was considered to be related to adjustment of the forward gaze in the lateral eye.

Key words: Wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) syndrome, Electroneystagmogram, Saccade, Paramedian pontine reticular formation, Medial longitudinal fasciculus

Deviation to the left side was shown during standing on the left foot and tandem gait. Sensory impairment was absent.

Data on peripheral blood and blood biochemistry were normal. Nuclear cell counts in the cerebrospinal fluid were not increased. The concentration of total protein in the cerebrospinal fluid was increased slightly to 47 mg/dl. An oligoclonal IgG band was negative. Myelin basic protein levels were within the normal range.

T2-weighted brain magnetic resonance imaging (MRI), which was performed on the day of hospitalization, showed two abnormal lesions of high intensity (Fig. 2A). One lesion was located in the upper pontine basis on the right side (Figs. 2A and B), and the other lesion spread from the right tegmentum to part of the left tegmentum (Figs. 2A and B).

The eye tracking test (ETT) and ENG in the horizontal direction were performed in a monocular manner (Figs. 3 and 4). The ETT showed stepwise pursuit which was prominent in abduction on both sides (Fig. 3). In the analysis using ENG, the velocity of saccade (VS) was measured by the visual target in the calibration of 10° (Fig. 4). Each VS in adduction and abstraction was decreased more in the right eye than the left eye. Furthermore, VS was decreased more in adduction than abstraction in each eye. Compared with the average VS (average velocity; 230°/sec. in the lateral gaze to the right (right abstraction, left adduction), 220°/sec. in the lateral gaze to the left (right adduction, left abstraction));8, 9) the VS in adduction was under 50°/sec. for the right eye (severe decrease). The VS in abstraction for the right eye was measured as under 100°/sec. and almost ranged within 50°/sec. to 100°/sec. (moderate decrease.). The VS in abstraction for the left eye was measured as under 150°/sec. and almost ranged within 100°/sec. to 150°/sec. (mild decrease.).

**Discussion**

WEBINO syndrome is characterized by bilateral internuclear ophthalmoplegia with alternating exotropia, and is usually accompanied by disturbance of convergence. In an inattentive state, mild exotropia is observed on both sides. Disorders of eye movements in our patient were consistent with the characteristics of WEBINO syndrome. Internuclear ophthalmoplegia is caused by
involvement of the MLF\textsuperscript{10}. Thus, the internuclear ophthalmoplegia is also called MLF syndrome\textsuperscript{10}. MLF exists in the region of the tegmentum that is situated in the ventromedial area from the midbrain to the medulla (Fig. 5)\textsuperscript{11}. The PPRF is located in the pontine tegmentum near the abducens nerve nucleus and is adjacent to the MLF (Fig. 5)\textsuperscript{12,14}. In conditions of mild impairment of the PPRF, paralytic nystagmus and a decrease in VS to the side of the impairment with the PPRF can occur, and lateral gaze paralysis occurs in conditions of severe impairment of the PPRF\textsuperscript{13,15}. Previously, severe impairment of the bilateral MLF was postulated in the pathogenesis of WEBINO syndrome\textsuperscript{16}. WEBINO syndrome in our patient was caused by a lesion in the bilateral tegmentum in the upper pons (Fig. 2). Other neurological findings were caused by the lesion in the upper pontine basis on the right side. In general, the laterality of symptoms is usually represented in bilateral MLF syndrome caused by cerebrovascular diseases\textsuperscript{15,17}. In our patient, the severity of disorders in eye movements was also more prominent on the right, which correlated with the spread of the lesion in the tegmentum in the upper pons (Fig. 2).

In the eye movements in the horizontal direction, especially in saccadic eye movements, the PPRF and the MLF play an important role\textsuperscript{13,18}. As a mechanism for the incidence of exotropia in WEBINO syndrome, hyperexcitation of the PPRF has been postulated in addition to severe impairment of the bilateral MLF\textsuperscript{5,7}. In order to gaze in the forward direction in this condition using the lateral eye, hyperexcitation of the contralateral PPRF is necessitated to contract the MR muscle in gazing eye through activation of the impaired MLF\textsuperscript{4,5,7}. On the other hand, non-gazing eye deviated to the lateral side by activation of the abducens nerve nucleus caused by hyperexcitation of the PPRF\textsuperscript{4,5,7}. In this hypothesis\textsuperscript{4,5,7}, the mechanism of exotropia was explained by sole impairment of the bilateral MLF. However, the data on ENG in our patient showed a decrease in the VS of bilateral abduction (Fig. 4), which indicated impairment of the PPRF on both sides. Thus, it was considered to hard to postulate

![Fig. 3 The eye tracking test (ETT) in the horizontal direction.](image)

The original wave of the smooth pursuit (a, c) (calibration: 10°) and the velocity (b, d) were shown. The ETT noted marked stepwise pursuit in bilateral abduction (arrows). Rt: Right, Lt: Left
In recent years, the presence of inhibitory neurofibers for horizontal eye movements, especially in saccadic eye movement, has been postulated (Fig. 6)\(^{13,18}\). When gazing to the right side, the right (ipsilateral) PPRF inhibits the ipsilateral oculomotor nerve nucleus (III) through the para-medial longitudinal fasciculus (para-MLF), and then the MR muscle relaxes (Fig. 6)\(^{18}\). The right (ipsilateral) inhibitory burst neurons (IBN) activated by the right PPRF inhibits the left (contralateral) abducens nerve nucleus (VI), and causes relaxation of the left (contralateral) LR muscle (Fig. 6)\(^{13,18}\). On the other hand, the right PPRF activates the ipsilateral abducens nerve nucleus (VI), and next contracts the right (ipsilateral) LR muscle. The right PPRF activates the MLF through the right (ipsilateral) abducens nerve nucleus (VI) and then contracts the left (contralateral) MR muscle as well\(^{13,18}\). Due to the hyperexcitation of the PPRF.

Fig. 4 The velocity of saccade (VS) in the horizontal direction. The original wave of saccade (a, c) (calibration: 10°) and the VS (b, d) were shown. The average VS is 230°/sec. in the lateral gaze to the right (right abduction, left adduction) and 220°/sec. in the lateral gaze to the left (right adduction, left abduction)\(^{8,9}\). The VS in abduction and adduction in both sides was decreased. Severe reduction in the VS in adduction was shown in the right eye (under 50°/sec.). The VS in abduction in the right eye and adduction in the left eye were decreased moderately (under 100°/sec.) and almost measured in the range of 50°/sec. to 100°/sec. The VS in abduction in the left was decreased mildly (under 150°/sec.) and almost measured in the range of 100°/sec. to 150°/sec.. Rt: Right, Lt: Left

Fig. 5 The schema of the upper pons (modified from the original figure of Goto\(^{12}\)). The medial longitudinal fasciculus (MLF) is located in the dorsomedial part. The paramedian pontine reticular formation (PPRF) also exists in the tegmentum and is adherent to the MLF.
contraction of the right LR muscle and the left MR muscle in addition to relaxation of the right MR muscle and the left LR muscle, the bilateral eyes deviate to the right side (Fig. 6). Based on the pathway of the horizontal gaze, which referred to the presence of inhibitory neurofibers and the mechanism of the eye movements disorder in our patient was studied (Fig. 6). In the inattentive state in WEBINO syndrome in our patient, bilateral eyes were positioned with mild exotropia because the MLF was more impaired than the PPRF on both sides, which was consistent with the result of ENG (Fig. 4). When gazing in the forward direction using the left eye, the residual function of the right PPRF excites the right (ipsilateral) abducens nerve nucleus (VI) and contracts the right (ipsilateral) LR muscle. The right PPRF also inhibits the right (ipsilateral) oculomotor nerve nucleus (III) through inhibition of the para-MLF, and then relaxes the right MR muscle (Fig. 6). As a result, the right eye deviated to the right side. In other words, the right PPRF excites the right (ipsilateral) IBN. Although activation of the right (ipsilateral) IBN was not be enough by partial impairment of the right PPRF, the residual function of the right PPRF inhibited the left (contralateral) abducens nerve nucleus (VI) through the activation of the right IBN, and then the left (contralateral) LR muscle was relaxed (Fig. 6). In contrast, the left MR made an inadequate contraction because the oculomotor nerve nucleus (III) exerted little activation on the left MR muscle by marked impairment of the left MLF (Fig. 6). To fix the left eye in the forward direction in this condition, appropriate adjustment due to relaxation of the left LR is considered to be necessary (Fig. 6). Similarly, when gazing in the forward position using the right eye, the same mechanism as the above-mentioned pathway which was mainly controlled by the residual function of the contralateral (left) PPRF was considered to be necessary in exotropia of the left eye. Accordingly, adjustment by inhibition of the LR muscle caused by activation of the contralateral residual PPRF was considered to play a crucial role in fixing the lateral eye in the forward direction with marked impairment of the MLF in WEBINO syndrome.

In conclusion, both the MLF and the PPRF were functionally involved in predominance of the MLF in WEBINO syndrome. The ENG data also supported this phenomenon in our case. To fix the lateral eye in the forward position, appropriate adjustment of the relaxation of the LR muscle, which was activated by the contralateral residual PPRF, was considered to be necessary. However, our study is limited to the analysis of the single case. Analysis of ENG data from many patients of WEBINO syndrome is necessary in the future.

**Declaration of interest**

The authors state they have no Conflicts of Interest (COI) to disclosure.

**References**


