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Case Report

Horizontal Gaze Palsy and Ipsilateral Facial Nerve Palsy in Older Patient as Initial Manifestation of Very Late-Onset Multiple Sclerosis Successfully Treated with Oral Corticosteroids: A Case Report

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Keywords
Corticosteroids · Horizontal gaze palsy · Multiple sclerosis · Neuroimaging · Very late-onset multiple sclerosis

Abstract
Introduction: Multiple sclerosis (MS) is a demyelinating condition of the central nervous system (CNS) that primarily affects young adults. Very late-onset multiple sclerosis (VLOMS) is an uncommon form of MS, accounting for only 0.5 percent of all MS patients. Eye movement impairments such as internuclear ophthalmoplegia are common in MS, while horizontal gaze palsy is an uncommon occurrence. ***Case Presentation:*** We report a case of a patient diagnosed with VLOMS who presented with left horizontal gaze palsy and ipsilateral facial nerve palsy. Brain magnetic resonance imaging showed Dawson's fingers in the left and right periventricular white matter; multiple small, round, hyperintense lesions in the left and right cortex and juxtacortical cerebellar hemisphere; and small hyperintense lesion in the left paramedian pontine reticular formation, suggesting the diagnosis of MS. Oral corticosteroids led to complete resolution of ocular movement and ipsilateral facial nerve palsy. ***Conclusion:*** We propose that neuroimaging should be performed in ophthalmoplegia with a pattern representing CNS lesion and oral corticosteroids may be an effective alternative to high-cost intravenous corticosteroids.

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Introduction

Multiple sclerosis (MS) is a chronic, immune-mediated, demyelinating condition of the central nervous system (CNS) that primarily affects young adults aged 20–40 [1, 2]. The very late-onset multiple sclerosis (VLOMS) represents only 0.5 percent of all MS diagnoses [3]. Horizontal gaze palsy is a rare MS finding, and in people over 50 years old, the etiology is usually vascular [2, 4]. Magnetic resonance imaging (MRI) is highly sensitive for detecting MS-specific CNS lesions [1], and corticosteroids can reduce the severity of clinical impairment and accelerate recovery of the deficits [5, 6]. Here, we report a case of a VLOMS presented as horizontal gaze palsy with ipsilateral facial nerve palsy that fully resolved after being treated with oral corticosteroids.

Case Report

A 63-year-old Indonesian male presented with sudden-onset binocular horizontal diplopia for 1 week that was constant and worse in left gaze, also with weakness of his left facial muscles. There was no disturbance in visual acuity, no history of similar symptoms, other neurological deficits, or trauma. No history of similar symptoms in his family. Patient had history of hypertension for 10 years and regularly takes antihypertensive medicine. He also had history of anisometropic amblyopia of the left eye (LE). The patient is a retired civil servant with no history of smoking or recreational drug use.

On physical examination, the vital signs were within normal limit. Ophthalmic examination revealed best corrected visual acuities with Snellen chart were 0.8 on the right eye (RE) and 0.08 on the LE. His primary eye position was orthotropic; however, the red glass test revealed uncrossed diplopia. There was an RE adduction deficit and LE abduction deficit on attempted left gaze (shown in Fig. 1a), and no nystagmus during saccadic eye movements. Patient had normal eyelid position. The light reflex, color vision, and visual field examination were within normal limits in both eyes. No relative afferent pupillary defect was found. Anterior segment examinations were unremarkable. Posterior segment examinations revealed a myopic fundus and optic disc with defined margin on both eyes. Neurological examination showed left facial nerve palsy (shown in Fig. 2a). The patient had incomplete closure of the left eye, unable to raise the eyebrow on the affected side, and there is forehead involvement of facial nerve palsy. The remaining of neurological examination was unremarkable.

The patient's blood glucose and lipid profile test were within normal limit. Brain MRI on T2-weighted (T2W) fluid attenuated inversion recovery (FLAIR) demonstrated hyperintense lesions in periventricular white matter perpendicular to the ventricles (Dawson's fingers) (shown in Fig. 3a), multiple small, round, hyperintense lesions the left and right cortex and juxtacortical cerebellar hemisphere with post-contrast enhancement of lesions (shown in Fig. 3b); also small hyperintense lesion in the left paramedian pontine reticular formation (PPRF) in dorsal of pons with post-contrast enhancement of lesion (shown in Fig. 3c–f), that met 2017 revised McDonald's criteria of dissemination in time and space [7], suggesting the diagnosis of MS. Hyperintensity on diffusion-weighted imaging was not caused by restricted diffusion but rather T2 shine through, supported by normal apparent diffusion coefficient (ADC) and ADC exponential not hyperintense (shown in Fig. 4), rule out the common cerebrovascular etiology in this age group. We did not perform spinal cord imaging and the test of oligoclonal bands in cerebrospinal fluid because the test was not available in our center. The patient underwent brain MRI in other hospital in our city.

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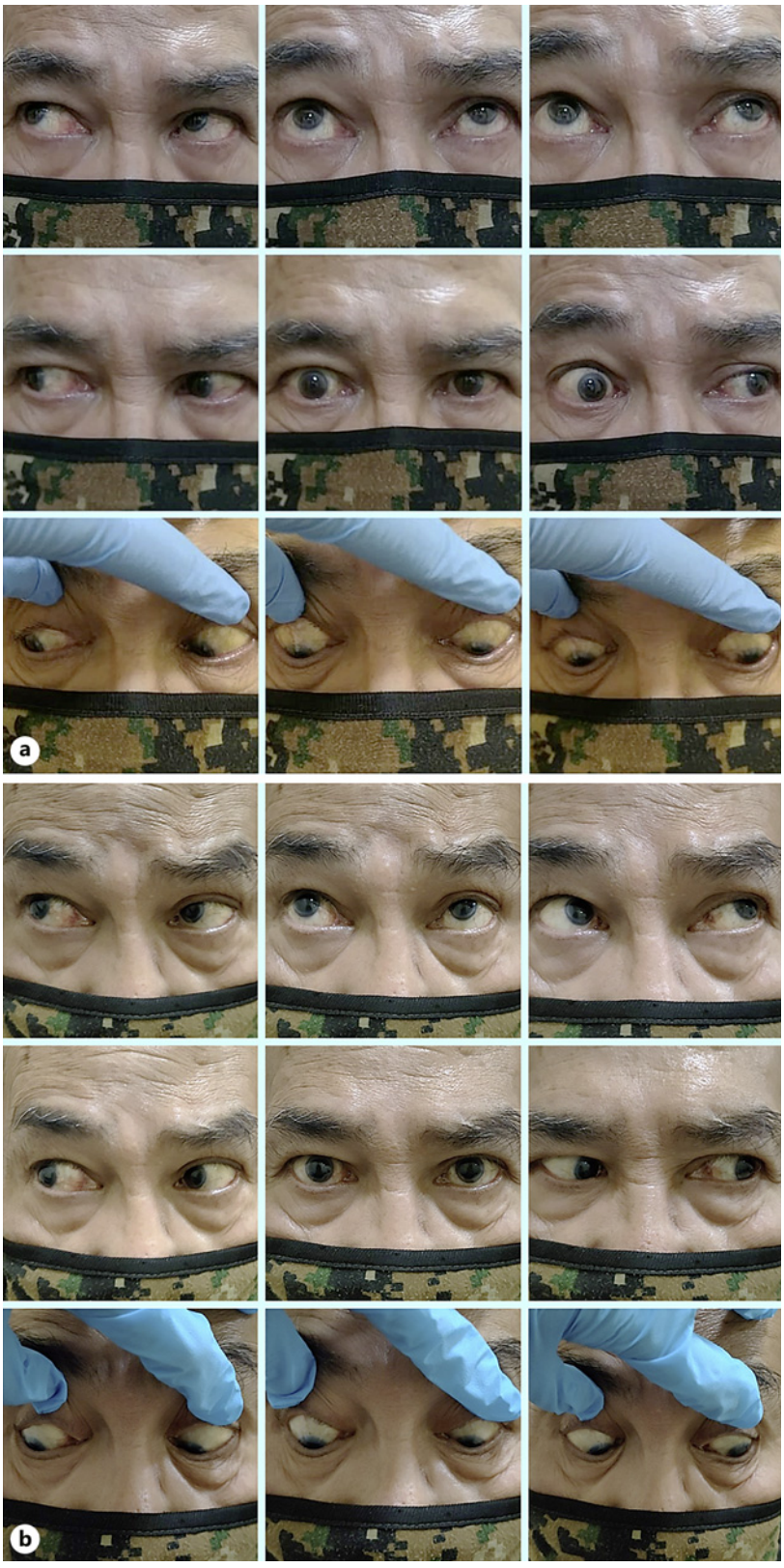

Fig. 1. Cardinal eye position. **a** Initial presentation. **b** Five weeks after treatment. The improvement of RE adduction and LE abduction.

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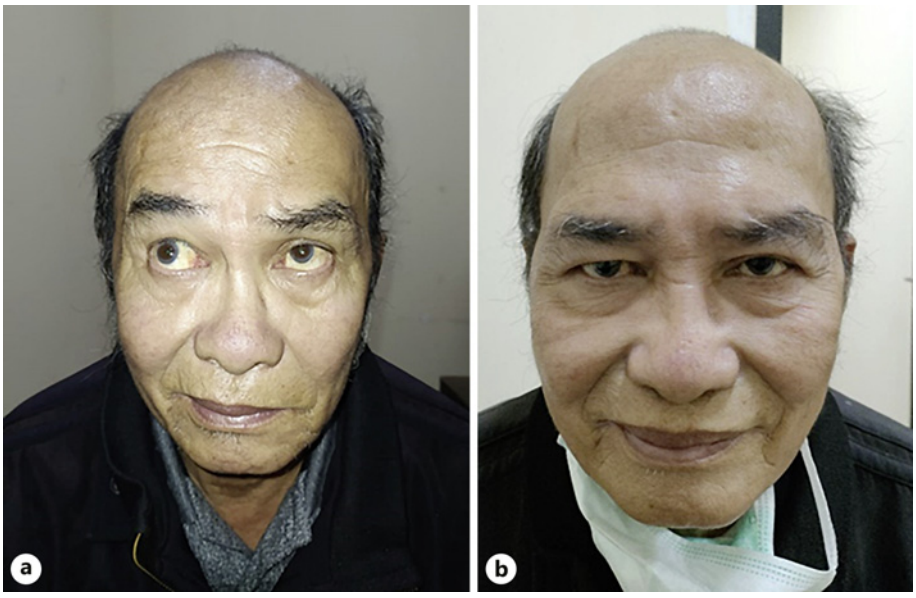

Fig. 2. Left facial nerve palsy. **a** Initial presentation. **b** Twelve weeks after treatment.

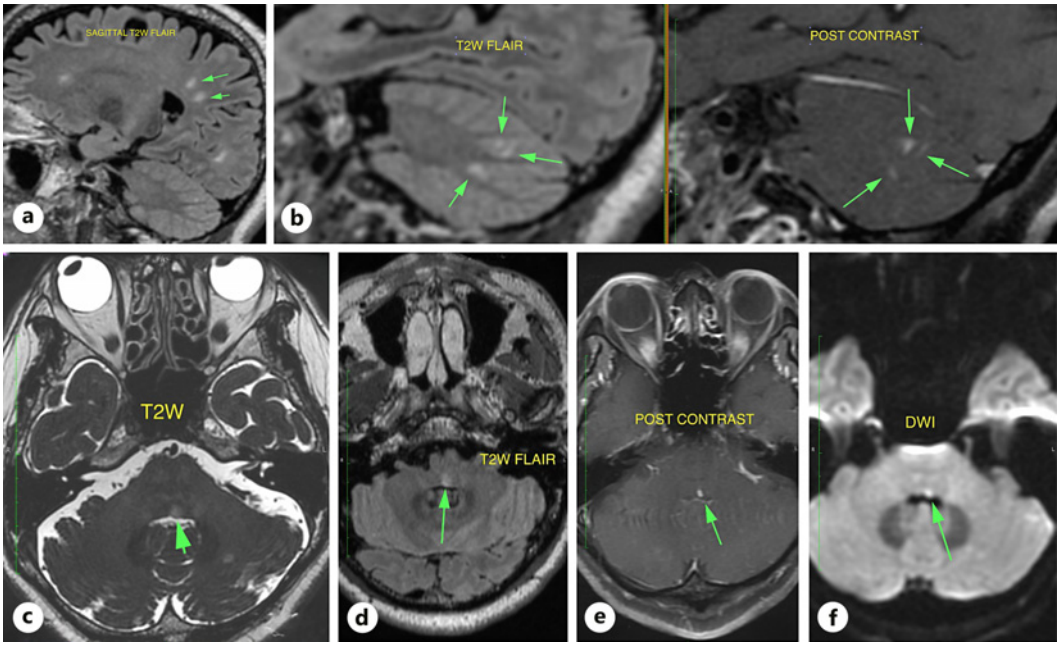

Fig. 3. Brain MRI findings support diagnostic criteria for MS. Note the arrow. **a** Sagittal T2W FLAIR MRI showing hyperintense lesions in periventricular white matter perpendicular to the ventricles (Dawson's fingers) (arrow). **b** Sagittal T2W FLAIR MRI showing multiple small, round, hyperintense lesions in the left and right cortex and juxtacortical cerebellar hemisphere. The enhancement in post-contrast images. **c–f** Axial T2W and T2W FLAIR MRI showing small hyperintense lesion in the left paramedian pontine reticular formation (PPRF) area in the dorsal of pons (arrow). The enhancement in post-contrast and diffusion-weighted imaging.

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The patient was given oral methylprednisolone 1 mg/kg daily, as well as oral citicoline 1,000 mg daily. We planned a neurologist referral for a thorough neurological examination and management. Follow-up visit was scheduled every 1 to 2 weeks. Oral methylprednisolone tapered weekly (56-48-40-32-24-16-8-4 mg). On follow-up visit 5 weeks later, there was no complaint about diplopia with complete resolution of ocular motility (shown in Fig. 1b). Ipsilateral facial nerve palsy was fully resolved at the follow-up visit in week twelve after starting the treatment. (shown in Fig. 2b). There were no ocular or systemic side effects from the drugs.

Discussion

MS can manifest in a variety of clinical manifestations [8] and presents as a diagnostic challenge, which causes delays in diagnosis, particularly in older people [2, 3]. Eye movement impairment is a common feature of MS, but horizontal gaze palsy is uncommon [8]. This patient is a 63-year-old male who has horizontal gaze palsy and ipsilateral facial palsy. Because of the higher prevalence at this age, possible similar symptoms [2], and the patient's history of hypertension, vascular disease of the CNS is the main differential diagnosis. However, brain MRI confirms the diagnosis of MS by dissemination in time and space. VLOMS, defined as MS with first symptom at 60 years or above [2, 3], accounts for only 0.5 percent of all MS diagnoses [3]. Our patient reports his first complaints related to MS at age 63-year-old, met the age criteria of the uncommon VLOMS.

Horizontal gaze palsy is caused by a variety of causes, including pontine ischemic, hemorrhagic, neoplastic, or demyelination lesions [4, 9]. Brain MRI is advised because nearly all MS patients with established disease and more than 80% of patients with clinically isolated syndrome who acquire MS have abnormal brain MRI results. Additionally, a brain MRI can reveal an alternative diagnosis [1].

Our patient's brain MRI is compatible with the diagnosis of MS according to 2017 McDonald Criteria. The MRI is highly sensitive for detecting characteristic CNS lesions. Periventricular and juxtacortical locations are typical for MS lesions [1]. We did not perform spinal cord imaging and targeted laboratory test such as oligoclonal bands in spinal fluid because the tests were not available in our center. In addition, according to Brownlee et al. [1], the diagnosis of MS is based on clinical findings alongside evidence of the dissemination of CNS lesions in space and time. Spinal cord MRI is recommended in patients with myelopathy or when MRI brain findings are not diagnostic for MS. Further targeted laboratory tests to exclude mimics of MS might be indicated if the history, examination, or MRI findings are atypical. According to Lotti et al. [2], in the LOMS population, oligoclonal bands proved not to assist in the MS diagnosis, which might be because older patients have lower levels of inflammatory and neurodegenerative biomarkers in their cerebrospinal fluid.

The horizontal gaze center is located in the dorsal tegmental pons and is made up of the PPRF, the abducens nucleus, the medial longitudinal fasciculus (MLF), and projection fibers to the contralateral oculomotor nerve medial rectus subnucleus [10]. Because the seventh nerve fascicles are so close to the sixth nerve nucleus, as well as the MLF and the PPRF, a single lesion can affect all of these structures, resulting in several variations of this finding [11]. Green et al. reported a similar case of a 62-year-old female with hypertension who developed partial right horizontal gaze palsy without internuclear ophthalmoplegia (1 ½ – ½ = 1), which was accompanied by ipsilateral fascicular seventh nerve palsy caused by ischemia. They named this pattern of MLF-sparing nuclear and seventh nerve fascicular palsy the "eight syndrome," which is a neuroanatomical variant of the eight-and-a-half syndrome [11].

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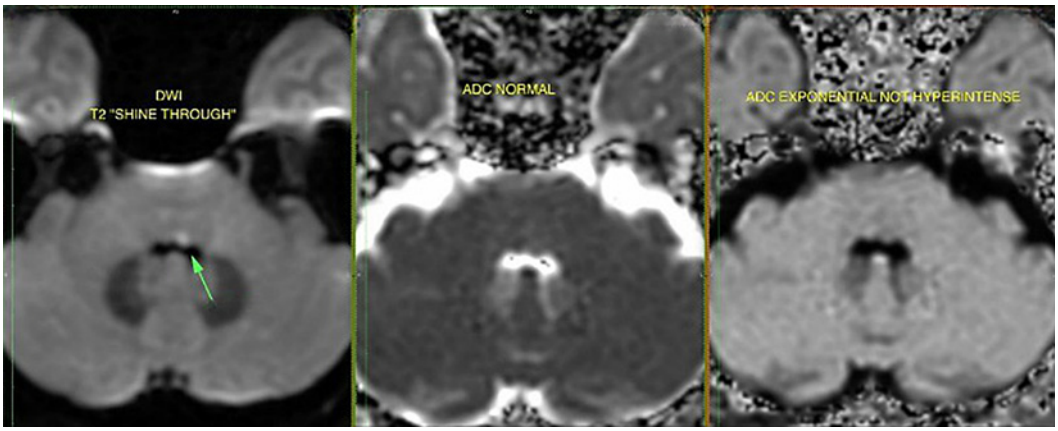

Fig. 4. Brain MRI findings rule out acute ischemia. Hyperintensity on diffusion-weighted imaging caused by T2 shine through supported by normal ADC and ADC exponential not hyperintense.

In this patient, follow-up visits were scheduled every 1 to 2 weeks, then after the fifth week, the follow-up visit was scheduled 1 month later, but the patient came again at week twelve, with fully resolved facial nerve palsy. We cannot confirm the exact time of complete resolution of the facial palsy, but we propose that the time is between 5 and 12 weeks. There was a possibility that our patient had distinct seventh nerve palsy, which led to a coincidental diagnosis of MS. But there was no lesion on the nucleus of the facial nerve in the MRI. Patient's lesion was found in the dorsal pons in the PPRF area. We proposed that the seventh nerve palsy represented the expression of the same underlying immune-pathological dysfunction of MS.

Relapsing-remitting multiple sclerosis (RRMS) is defined by acute episodes of neurological impairment followed by a recovery to baseline function [2]. Our patient had complete remission of his neurological abnormalities and did not have a relapse episode in 12 months after the diagnosis. In a meta-analysis by Naseri et al. [12], 49.80% of all late-onset multiple sclerosis (LOMS) cases, defined as disease onsets at or after the age of 50, have the RRMS pattern. However, there is an increasing concern about a more progressive form of MS [12] as well as attaining severe disability in LOMS cases [13].

Glucocorticoids are recommended as the treatment for acute MS flares. Their proven efficacy reduces the severity of clinical impairment, accelerates recovery, and lowers the risk of exacerbations [5, 6, 14]. Liu et al. [14] discovered no significant differences in clinical efficacy or adverse events between oral and intravenous methylprednisolone for treating MS relapses. Oral administration is less invasive, less expensive, and more convenient for the patient [6, 14, 15]. This patient showed complete resolution of horizontal gaze palsy and ipsilateral facial palsy after being treated with oral methylprednisolone. We also give this patient oral citicoline 1,000 mg daily. Citicoline, a neuroprotective drug, has been shown to improve and speed up remyelination in MS patients. It was found to be significantly effective in two complementary MS rodent models [16].

Managing MS in the elderly presents unique challenges. There are still no studies about the efficacy of disease-modifying therapy (DMT) for RRMS in the elderly, and patients with LOMS are less frequently exposed to DMT; therefore, little is known about its effectiveness in this population [13]. Furthermore, age-related immune system changes known as age-induced immunosenescence may affect the safety of DMT, leading to potentially severe adverse events such as progressive multifocal leukoencephalopathy and DMT-induced cancer,

which are more common in elderly patients [13]. The DMT itself was not available at our center.

In this patient, there has been no complaint of recurrence or other related symptoms over the past 12 months since his initial presentation without DMT; however, further long-term follow-up is essential considering the natural course of MS, the higher prevalence of disability, and the growing concern regarding MS progression in the elderly.

Conclusion

Horizontal gaze palsy in older people can be the first sign of VLOMS. Neurological examination is essential to localize the site of involvement and reveal other neurological findings. Regarding the greater delay in diagnosis of VLOMS, we propose that neuroimaging should be performed in ophthalmoplegia with a pattern representing a CNS lesion. Oral corticosteroids may be an effective alternative to high-cost intravenous corticosteroids. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000536639).

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Statement of Ethics

This study was approved by the Research Ethics Committee Cicendo Eye Hospital Bandung (No. LB.02.01/2.3/7505/2022). Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Tjoa Debby Angela Tjoanda designed the concept, drafted the report, and extracted data relevant to the case from the literature. Antonia Kartika designed the concept and provided the critical revision. Dianita Veulina Ginting cared for the patient and provided critical revision. Rusti Hanindya Sari and Prettyla Yollamanda provided the critical revisions. All authors approved the final version.

Data Availability Statement

All data that support the findings of this study are included in this article. Further inquiries can be directed to the corresponding author.

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