Case Report

Medial longitudinal fasciculus (MLF)-syndrome in a multimorbid patient with alcohol use disorder: a case report

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Background: Patients with multiple comorbidities can present as a diagnostic challenge as overlapping symptomatology complicates the discovery of emergent pathology. Symptoms of alcohol misuse or orthostatic hypotension may especially cloud the diagnosis of insidious neurological disease, such as posterior circulation infarct. With a growing elderly population, it is expected that the complex multimorbid patient will represent a growing challenge to prompt stroke detection and treatment.

Case Description: Herein, we present a 69-year-old male with a history of alcohol abuse, chronic obstructive pulmonary disease, type 2 diabetes mellitus, paroxysmal atrial fibrillation, and congestive heart disease. The patient arrived at our emergency department with dizziness, ataxia, and diplopia. His symptoms had a sudden onset and gradual exacerbation over a span of 2 days, notably aggravated by standing and walking, but relieved when seated or supine. Notably, a month before admission, the patient had been treated with anti-congestive medications for severe congestive heart failure leading to a weight loss of 55 lbs over period of 2 weeks. The initial differential diagnoses were orthostatism, Wernicke's encephalopathy (WE), and ischemic stroke. Magnetic resonance imaging (MRI) revealed a subacute infarct in the medial longitudinal fasciculus (MLF).

Conclusions: The case underscores the challenge in diagnosing neurological conditions in multimorbid individuals. The combination of various underlying conditions may drastically complicate the diagnosis. Successful diagnosis and treatment necessitates meticulous evaluation of clinical observations, medical history, current medications, and pertinent diagnostic evaluations to effectively narrow down the potential differential diagnoses.

Keywords: Case report; ischemic stroke; internuclear ophthalmoplegia (INO); medial longitudinal fasciculus (MLF); multimorbid

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Introduction

Medial longitudinal fasciculus (MLF) syndrome is a neurological condition characterized by the impaired coordination of eye movements caused by a lesion in the MLF. The MLF is a paired white matter tract located near the midline of the brainstem (*Figure 1*). It serves as a communication pathway between the ocular motor cranial nerves and vestibular nuclei and plays a crucial role in coordinating eye movements, such as saccades. MLF infarction may produce internuclear ophthalmoplegia (INO), manifesting as the inability to fully adduct one eye during lateral gaze, with nystagmus in the contralesional eye, although nystagmus may not always be present (1). The lesion may extend into the superior cerebellar peduncles and cause cerebellar ataxia (2).

In patients with several comorbidities, the subtle symptoms of MLF syndrome may remain undetected or be attributed to existing conditions. For example, ophthalmoplegic nystagmus, a key symptom of MLF syndrome, may also be observed in Wernicke's encephalopathy (WE). WE is associated with alcohol use disorder, and given that approximately 6% of the US population has a history of alcohol dependence, it is a critical differential diagnosis in predisposed patients presenting with ophthalmoplegia (3).

Similarly, feelings of lightheadedness, or dizziness, upon mobilization in patients with congestive heart disease could be attributed to cardiovascular insufficiency, namely orthostatic hypotension, clouding the detection of posterior circulation ischemia. Nevertheless, dizziness is common in patients with MLF syndrome as fibers from the contralateral posterior semicircular canal and the utricle travel within the MLF to reach mesencephalic ocular motor neurons responsible for the vestibulo-ocular reflex (VOR) (4,5).

Herein, we report a case of a 69-year-old multimorbid male with alcohol use disorder and a recent history of congestive heart disease presenting with symptoms of MLF syndrome. We present this case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-23-177/rc).

Case presentation

A 69-year-old Caucasian male with a history of alcohol abuse and multiple comorbidities, including chronic obstructive pulmonary disease, type 2 diabetes mellitus, paroxysmal atrial fibrillation, and congestive heart disease, presented to the emergency department with symptoms of dizziness, ataxia, and diplopia. The symptoms appeared abruptly (within hours) and progressively worsened over a 2-day period, particularly when standing or walking, but improved when sitting or lying down. One month prior to this admission, the patient had been treated for severe congestive heart failure and lost 55 lbs. of body weight over 16 days with anti-congestive medication (furosemide, and ramipril). In the 2 weeks leading up to the present case, he reported losing an additional 11 lbs. Blood samples collected during this period, including those leading up to the present admission, consistently revealed electrolyte levels near the normal range. Notably, no fast changes of sodium levels were observed.

The patient had no history of headaches, epileptic stigmata, hemiparesis, dysarthria, or aphasia, and denied having vertiginous motion illusions. He reported no chest pains, shortness of breath, or urinary or bowel symptoms, and denied having consumed alcohol in the past month. Upon admission, his vital signs were recorded as a blood pressure of 130/66 mmHg (though prehospitally 80/50 mmHg), a heart rate of 97 beats per minute, and a body temperature of 35.9 degrees Celsius. The electrocardiogram (ECG) showed atrial fibrillation, for which he was receiving anticoagulant therapy (apixaban) and a β-adrenergic antagonist (metoprolol) as per Danish guidelines (6). The patient appeared alert and oriented on physical examination, with equal and reactive pupillary responses to light. The diplopia emerged on leftward gaze, accompanied by a right eye adduction defect, but there was no nystagmus (*Figure 2*, *Video 1*). Adduction movements during convergence were preserved, however. It was unclear from the patient whether the gaze-dependent diplopia was a new occurrence or a habitual condition. The ataxia manifested as postural instability and a broad-based gait, while examination of the upper and lower extremities was otherwise normal. The patient reported dizziness only upon mobilization out of bed.

Infection and electrolyte imbalance were ruled out by the initial blood work-up, which revealed normal C-reactive protein (CRP <4 mg/L), normal complete blood count (CBC), habitual electrolyte values (potassium 4.8 mEq/L, sodium 134 mEq/L), and habitual kidney function [creatinine 1.5 mg/dL, estimated glomerular filtration rate (eGFR) 43 mL/min/1.73 m^2]. Liver parameters were within normal ranges as well [international normalized ratio (INR) 1.2, albumin 4 g/dL, alanine aminotransferase (ALAT) 68 U/L].

Thiamine supplementation was noted in the patient's medication list to which he was reportedly fully compliant.

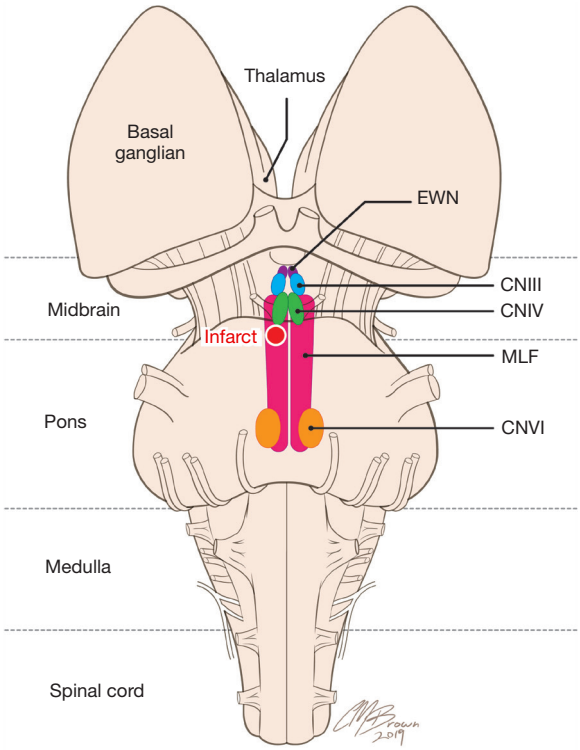
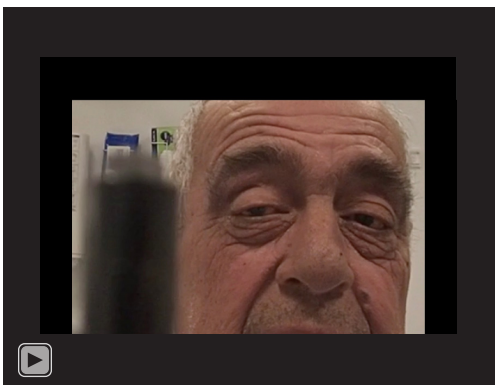


Figure 1 Neuroanatomy of MLF syndrome: the MLF is a white matter tract that interconnects the ocular cranial nerve nuclei (CNIII, CNIV, CNVI, and the EWN). The manifestation of symptoms can vary based on the precise localization of the infarct within the MLF. In this case, the patient experienced an infarct (indicated by a red-white dot) near the pontomesencephalic junction, with preserved convergence eye movements. Figure was provided by and with the permission of Christopher Brown (Indiana University School of Medicine, Department of Neurological Surgery, Indianapolis, IN, USA). EWN, Edinger-Westphal nucleus; CNIII, oculomotor nerve; CNIV, trochlear nerve; MLF, medial longitudinal fasciculus; CNVI, abducens nerve.

Orthostatic hypotension was unlikely based on the sit-to-stand test (STS) (7). Focused lung ultrasonography (F-LUS) revealed no pleural effusions or B-lines, indicating a preserved decongested state, and the inferior vena cava (IVC) diameter was normal, indication normal central hydration status.

The initial computed tomography (CT) scan revealed no evidence of acute brain pathology. To investigate the possibility of posterior circulation ischemia, a subacute non-contrast magnetic resonance imaging (MRI) was conducted the following day. The MRI revealed an apparent diffusion restriction in the tegmentum at the pontomesencephalic junction, displaying a hyperintense signal on the fluid-attenuated inversion recovery (FLAIR) sequence [diffusion-weighted imaging (DWI)-FLAIR match] and a hypointense signal on the apparent diffusion coefficient (ADC) sequence



Video 1 Internuclear ophthalmoplegia, a conjugate gaze deficit. The video sequence shows an apparent right eye adduction deficit on leftward (contra-lesional) gaze in a patient with MLF syndrome. Notably, no nystagmus is seen. MLF, medial longitudinal fasciculus.

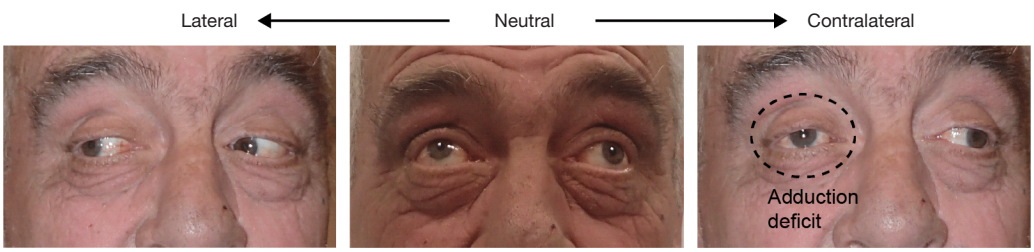


Figure 2 Internuclear ophthalmoplegia, a conjugate gaze deficit. The patient presented with a right eye adduction deficit and diplopia when looking to the left. This image is published with the patient's consent.

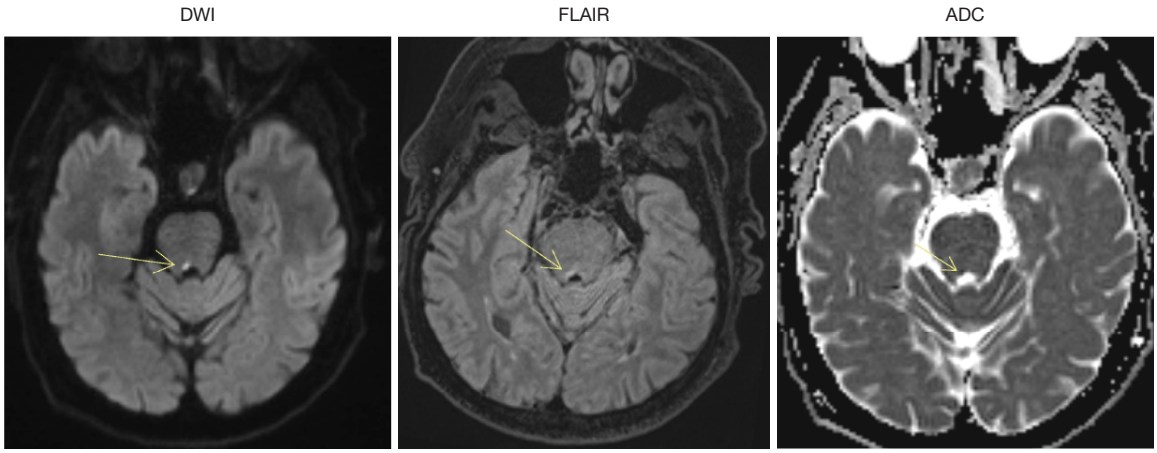


Figure 3 Non-contrast MRI with DWI, FLAIR, and ADC sequences. The yellow arrows point to an apparent diffusion restriction in the tegmentum on the border between the mesencephalon and pons with a hyperintense signal on the FLAIR sequence (DWI-FLAIR match) and hypointense signal on the ADC sequence thus representing a subacute lacunar infarct in the medial longitudinal fasciculus. DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; ADC, apparent diffusion coefficient; MRI, magnetic resonance imaging.

(*Figure 3*). This was indicative of a subacute lacunar infarct in the MLF at the level of the pontomesencephalic junction, leading to the diagnosis of MLF syndrome. Ultrasonography of the neck vessels showed moderate stenosis, while imaging of the head vessels revealed no stenosis in the vertebrobasilar system.

The patient was administered a 300 mg bolus acetylsalicylic acid (aspirin), and the habitual anticoagulant medication (apixaban) was substituted with 75 mg daily acetylsalicylic acid (aspirin) to reduce the risk of hemorrhagic complications. The patient was transferred to a specialized neurological center with high neurorehabilitation expertise and recovered well.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

The patient in this vignette presented with dizziness, ataxia, and diplopia. The patient's history of recent congestive heart failure, significant weight loss, and the multitude of comorbidities, especially alcohol use disorder, dominated the initial diagnostic workup. Through a careful diagnostic workup, the differential diagnosis was narrowed down to ischemic stroke, which was verified by MRI showing subacute MLF infarct. The MRI notably aligns with the clinical finding of INO with preserved convergence, indicating a unilateral infarction of the MLF near the pontomesencephalic junction (*Figures 1*,*3*) (4).

In patients with multiple comorbidities, diagnosing subtle neurological conditions can be challenging due to overlapping clinical features and confounding factors that may cloud symptomatology. Alcoholism, for instance, is linked to neurological complications, such as WE, which can present with abnormalities like INO. Besides, as was the case with this patient, diplopia might be discarded as a habitual symptom despite it changing key characteristics, such as attaining gaze-dependency.

In a similar vein, an increasing number of patients suffer from congestive heart disease for which they may receive loop diuretics as part of the decongestive therapy (8). Excessive decongestion can cause cerebral hypoperfusion (9), leading to symptoms that mimic neurological pathology. Therefore, it is vital to carefully differentiate between the potential causes of neurological symptoms in patients with comorbidities: A comprehensive clinical assessment, including a detailed history, physical examination, and appropriate diagnostic tests, including blood workup, is essential. Differentiating between INO related to MLF syndrome and other potential causes,

such as WE, multiple sclerosis (in younger patients) and tumors, as well as INO-mimics like myasthenia gravis and oculomotor palsy, requires careful consideration of various factors. Clinical findings, such as the presence or absence of nystagmus, headache, altered mental status, characteristic gait patterns, and muscle weakness can provide valuable clues. For example, inducible muscle weakness (such as a positive Simpson test) and slurred speech might raise suspicion of myasthenia, which could be confirmed by testing for acetylcholine antibody and by neurophysiological measurements.

Bedside tests, such as the STS, can rule out alternative diagnoses, such as orthostatism. The blood workup, together with clinical findings, might raise suspicion of vasculitis, such as periarteritis nodosa, which has been reported to cause pseudo-INO through oculomotor palsy (10). The patient's history and medication list may provide crucial information as well, such as about thiamine supplementation, recent decongestive therapy, or medications associated with INO, like propranolol and lithium (11,12). Neuroimaging, such as MRI, may help identify a specific lesion site, such as lacunar infarction of the MLF (*Figure 3*). Neuroimaging may also reveal intracranial tumors with mass effect (e.g., pseudo-INO via oculomotor palsy), or brainstem tumors or metastases disrupting ocular motor nuclei or the MLF directly (13).

Conclusions

Considering the complexity and diagnostic challenge posed by overlapping symptomatology, a multifaceted approach to the comorbid patient is needed, especially in a world with rapidly shifting population demographics (14). A multifaceted diagnostic approach could include clinical tests (e.g., the STS), lab workup (e.g., assessing ammonia levels for WE diagnosis, or investigating electrolyte derangements for related neurological deficits), targeted ultrasonographic assessments (e.g., F-LUS), diagnostic imaging (e.g., MRI).

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-23-177/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-23-177/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Virgo JD, Plant GT. Internuclear ophthalmoplegia. Pract Neurol 2017;17:149-53.
2. Sakakibara S, Sakato S, Shima T, et al. Brainstem infarcts presented medial longitudinal fasciculus (MLF) syndrome and cerebellar ataxia--report of three cases. Rinsho Shinkeigaku 1990;30:533-9.
3. Glantz MD, Bharat C, Degenhardt L, et al. The epidemiology of alcohol use disorders cross-nationally: Findings from the World Mental Health Surveys. Addict Behav 2020;102:106128.
4. Fiester P, Rao D, Soule E, et al. The Medial Longitudinal Fasciculus and Internuclear Opthalmoparesis: There's More Than Meets the Eye. Cureus 2020;12:e9959.
5. Aw ST, Chen L, Todd MJ, et al. Vestibulo-ocular reflex deficits with medial longitudinal fasciculus lesions. J Neurol 2017;264:2119-29.

6. Atrieflimren og atrieflagren [Internet]. Dansk Cardiologisk Selskab [cited 2023 Dec 4]. Available online: https://www.cardio.dk/af
7. Shaw BH, Garland EM, Black BK, et al. Optimal diagnostic thresholds for diagnosis of orthostatic hypotension with a 'sit-to-stand test'. J Hypertens 2017;35:1019-25.
8. Groenewegen A, Rutten FH, Mosterd A, et al. Epidemiology of heart failure. Eur J Heart Fail 2020;22:1342-56.
9. Rivasi G, Rafanelli M, Mossello E, et al. Drug-Related Orthostatic Hypotension: Beyond Anti-Hypertensive Medications. Drugs Aging 2020;37:725-38.
10. Kirkali P, Topaloglu R, Kansu T, et al. Third nerve palsy and internuclear ophthalmoplegia in periarteritis nodosa. J Pediatr Ophthalmol Strabismus 1991;28:45-6.
11. Cunningham GM. Drug-induced internuclear ophthalmoplegia. Can Med Assoc J 1983;128:892-3.
12. Deleu D, Ebinger G. Lithium-induced internuclear ophthalmoplegia. Clin Neuropharmacol 1989;12:224-6.
13. Cruciani A, Motolese F, Todisco A, et al. A Rare Neuro-Ophthalmological Condition in a Patient with Lung Adenocarcinoma: The Eight-and-a-Half Syndrome, Case Report and Review of the Literature. Brain Sci 2022;12:451.
14. Raveh D, Gratch L, Yinnon AM, et al. Demographic and clinical characteristics of patients admitted to medical departments. J Eval Clin Pract 2005;11:33-44.

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