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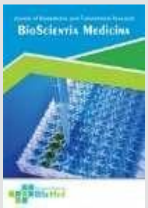

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Weber Syndrome Revisited: A Classic Midbrain Stroke Presentation Secondary to Severe Dyslipidemia

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A B S T R A C T

Background: Weber syndrome is a classic brainstem stroke syndrome resulting from an ischemic lesion in the ventral midbrain. While historically defined by its striking clinical features—ipsilateral oculomotor nerve palsy and contralateral hemiparesis—its modern relevance lies in its direct causation by common, modifiable vascular risk factors. This report uses a quintessential case of Weber syndrome as a didactic tool to illustrate the profound microvascular consequences of a specific, severe metabolic phenotype. **Case presentation:** A 60-year-old female with a history of medication non-adherence for hypertension and hypercholesterolemia presented with acute left hemiparesis, right ptosis, and diplopia. Examination confirmed a right oculomotor palsy and left hemiparesis. Her Body Mass Index was 28.5 kg/m^2. Laboratory workup revealed a severe mixed dyslipidemia (LDL-C 168 mg/dL, Triglycerides 218 mg/dL). Brain MRI confirmed an acute infarct in the right ventral mesencephalon. Vascular imaging was unremarkable, pointing towards intrinsic small vessel disease. A comprehensive, multidisciplinary management plan was initiated, focusing on aggressive medical therapy, intensive rehabilitation, and strategies to overcome barriers to medication adherence. **Conclusion:** This case highlights the elegant yet unforgiving precision of neuroanatomy and the powerful diagnostic utility of modern neuroimaging. More profoundly, it demonstrates the direct pathophysiological link between severe atherogenic dyslipidemia and the occlusion of a single, critical perforating brainstem artery. The patient's significant functional recovery underscores that a holistic approach—combining evidence-based pharmacotherapy with a robust, patient-centered rehabilitation program and a dedicated strategy to ensure long-term adherence—is paramount to optimizing outcomes after a debilitating stroke.

1. Introduction

Stroke, a sudden and devastating interruption of blood flow to the brain, remains a formidable global health challenge.[1] It stands as the second leading cause of mortality worldwide and, for those who survive, is a primary driver of long-term, often severe, adult disability. The global burden is immense and growing, particularly in low- and middle-income countries.[2] In 2021 alone, the world witnessed approximately 7.8 million new ischemic stroke cases, contributing to a staggering global population of over 93 million individuals living with the physical, cognitive, and emotional sequelae of a stroke. In regions like Southeast Asia, including Indonesia, rapid epidemiological transitions have led to a rising prevalence of key vascular risk factors, positioning stroke as a leading public health crisis that strains healthcare systems and profoundly impacts families and communities.[3]

Cerebrovascular diseases are broadly categorized based on the arterial territory affected: the anterior circulation (supplied by the internal carotid arteries) and the posterior circulation (supplied by the vertebral and basilar arteries).[4] While strokes affecting the anterior circulation—leading to the more widely recognized symptoms of hemispheric dysfunction such as aphasia and facial droop with arm weakness—are more common, posterior circulation strokes account for a significant portion of events, estimated at 20-25% of all ischemic strokes. These events, which affect the brainstem, cerebellum, and occipital lobes, present unique and often perplexing diagnostic challenges. Their clinical presentations can be notoriously variable and subtle, often manifesting with non-specific symptoms such as dizziness, vertigo, nausea, or headache, which can be easily mistaken for more benign conditions. The classic constellation of the "five D's"—dizziness, diplopia, dysarthria, dysphagia, and dystaxia—is a useful clinical heuristic, but these symptoms frequently occur in isolation or in incomplete combinations, demanding a high index of suspicion from the examining clinician.[5] Strokes specifically localized to the brainstem, the vital conduit connecting the cerebrum to the spinal cord and cerebellum, constitute approximately 10-15% of all ischemic strokes. Despite their relatively small volume, brainstem infarcts often result in disproportionately severe neurological deficits. This is a direct consequence of the extraordinary density of critical neural structures concentrated within this compact anatomical space, including the ascending and descending tracts that control all motor and sensory functions, the nuclei of ten of the twelve cranial nerves, and the intricate networks of the reticular activating system that govern consciousness, respiration, and other vital autonomic functions.

Historically, our understanding of this complex region was built upon a foundation of classic, eponymic syndromes, meticulously described by pioneering 19th and early 20th-century neurologists like Weber, Wallenberg, Millard-Gubler, and Benedikt.[6] These masters of clinical observation, working long before the advent of neuroimaging, painstakingly correlated specific clinical patterns of deficits with presumed lesion locations based on autopsy findings. These eponyms became the foundational language of clinical localization, allowing clinicians to deduce the site of a brainstem lesion with remarkable accuracy based purely on the physical examination. Among the most elegant of these is Weber syndrome, first detailed by the German physician Sir Hermann Weber in 1863.[7] It describes the eloquent clinical picture arising from a lesion in the ventral midbrain (mesencephalon) that simultaneously damages the exiting fascicles of the oculomotor nerve (CN III) and the adjacent cerebral peduncle, producing a characteristic "crossed" deficit of an ipsilateral CN III palsy and a contralateral hemiparesis. In the modern era of medicine, while these eponyms remain invaluable for rapid clinical pattern recognition, the field has evolved towards a more precise patho-anatomical and etiological classification. A diagnosis of "Weber syndrome" now serves not as an endpoint, but as a clinical starting point, prompting the crucial subsequent question: what is the underlying cause of the lesion? The answer, most often, is an ischemic infarct resulting from the occlusion of a small, perforating artery—a stark and focal manifestation of a diffuse, systemic vascular disease. The vascular supply of the ventral midbrain is particularly precarious. The region is nourished by small, terminal paramedian perforating arteries that arise directly from the P1 segment of the posterior cerebral artery (PCA) or the basilar artery bifurcation.[8] These end-arteries have minimal collateral circulation, making the tissue they supply exceptionally vulnerable to ischemic injury if the vessel becomes occluded.

The risk factors that lead to such an occlusion are well-established and largely modifiable. They are the familiar adversaries of modern vascular medicine: hypertension, diabetes mellitus, smoking, obesity, and, critically, dyslipidemia.[9] Dyslipidemia, particularly the atherogenic profile of elevated low-density lipoprotein cholesterol (LDL-C), elevated triglycerides, and low high-density lipoprotein cholesterol (HDL-C), is a primary driver of atherosclerosis. This insidious process of plaque buildup within arterial walls leads to vessel stenosis and creates a prothrombotic state, which can culminate in the occlusion of large and small vessels alike, including the delicate perforating arteries supplying the brainstem. While the link between dyslipidemia and large-vessel ischemic stroke is firmly established and widely appreciated, its direct role in precipitating specific, rare lacunar syndromes like Weber syndrome is a powerful and visceral illustration of its pathological potential.[10] The aim of this report is to present a quintessential case of Weber syndrome, meticulously correlating its classic clinical findings with definitive, multimodal neuroimaging. The novelty and primary purpose of this manuscript, however, extend beyond simple description. We aim to use this classic eponymic syndrome as a didactic tool to vividly illustrate the direct and devastating microvascular consequences of a specific, severe metabolic phenotype—in this case, untreated mixed dyslipidemia characterized by very high LDL-C and high triglycerides. By "revisiting" Weber syndrome through the lens of modern vascular neurology, we seek to reinforce the urgency of aggressive, evidence-based risk factor management. Furthermore, we aim to present a holistic narrative that encompasses not only the diagnostic process but also the critical and often overlooked challenges of therapy, multidisciplinary rehabilitation, and the promotion of long-term patient adherence to treatment, which is the ultimate determinant of future risk.

2. Case Presentation

A 60-year-old right-handed female, a retired and respected schoolteacher, was brought to the Emergency Department of Cibinong Regional General Hospital by her anxious husband and adult son. The family reported a sudden and alarming onset of neurological symptoms that had begun approximately five hours prior. The patient had been sitting and reading when she suddenly felt a "heavy, weak feeling" wash over the left side of her body. She attempted to stand but found her left leg would not support her weight, and she nearly fell. Concurrently, she developed a new and unusual headache, which she described not as a throbbing pain, but as a constant, deep, moderately severe pressure localized behind her right eye. Within minutes of the weakness, her family noticed that her right eyelid had begun to droop, and she complained of seeing "two of everything." The binocular diplopia was disorienting and nauseating. She became increasingly distressed as she found she could not voluntarily open her right eye. Her husband, recognizing the gravity of the situation, made the immediate decision to bring her to the hospital. During the journey, the patient remained fully conscious and able to communicate clearly, explicitly denying any slurring of speech, facial drooping on either side, vertigo or spinning sensations, vomiting, seizures, or sensory changes like tingling or numbness.

Her medical history was highly significant for chronic, poorly managed vascular risk factors, a story all too common in clinical practice. She had been diagnosed with hypertension and hypercholesterolemia by a primary care physician over five years prior. Despite being prescribed unspecified antihypertensive and lipid-lowering agents, she admitted to significant medication non-adherence. She explained that she would take the medications "for a week or two" after her check-ups but would then stop, citing a combination of forgetfulness, the inconvenience of a daily regimen, and, most importantly, a perceived lack of symptoms. "I felt fine," she explained, "so I didn't think I needed them." Her lifestyle was largely sedentary, a pattern that had become more entrenched since her retirement two years prior. Her diet was rich in traditional Indonesian cuisine, which she and her husband greatly enjoyed, but which was often high in saturated fats from coconut milk and fried foods, as well as high in sodium. Her family history was notable for hypertension in her father, who had passed away from a myocardial infarction in his late 70s. There was no family history of premature cardiovascular disease or stroke in first-degree relatives. The patient's detailed clinical and historical data, which provide the crucial context for her acute presentation by painting a picture of a woman with a high burden of untreated vascular risk, are summarized in Figure 1.

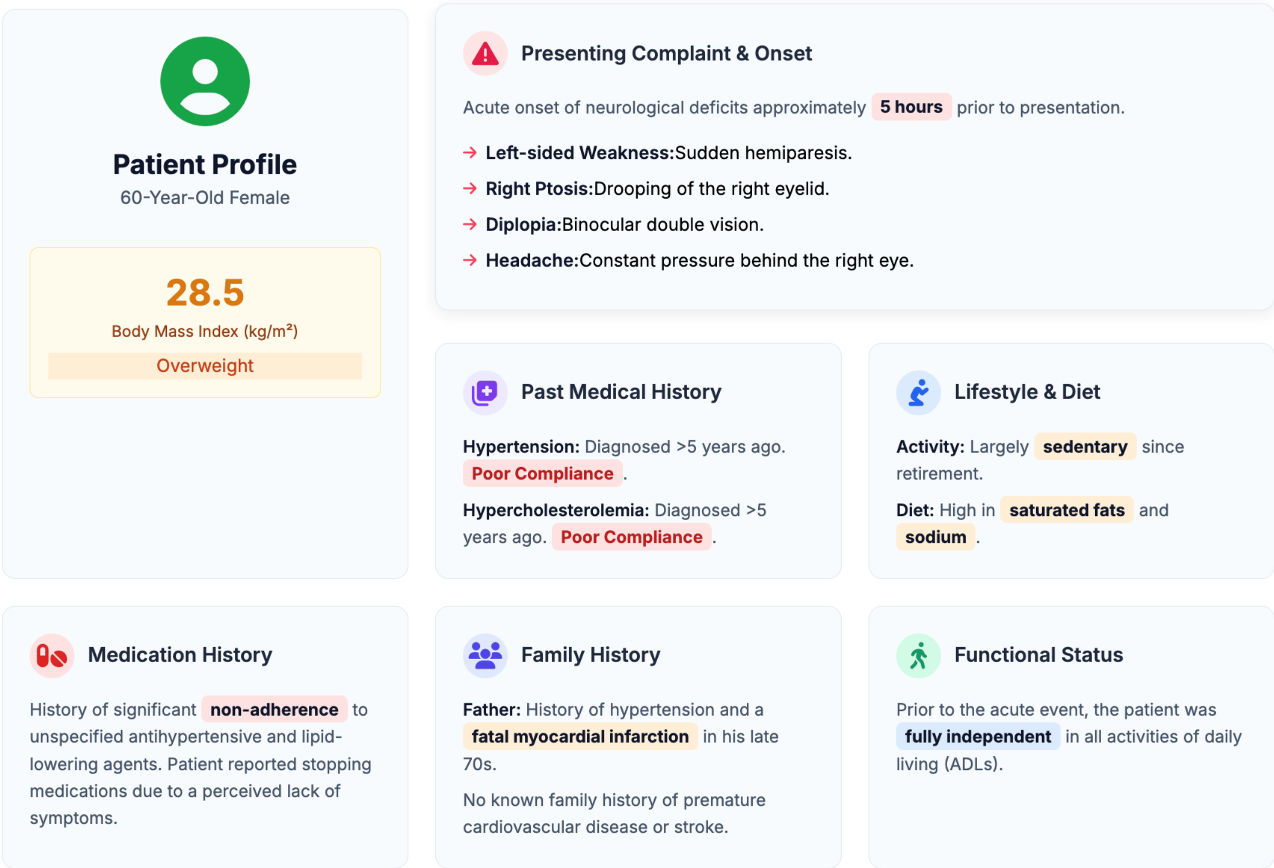

Figure 1. Patient demographics, anthropometrics, and clinical history.

Upon examination in the Emergency Department, the patient was alert, anxious but cooperative, and fully oriented to person, place, and time. Her Glasgow Coma Scale (GCS) score was 15/15. Her vital signs were notable for a significantly elevated blood pressure of 167/96 mmHg. A detailed, systematic neurological examination was performed, revealing a striking and highly localizing pattern of crossed deficits. This examination was not merely a data collection exercise; it was the first and most critical step in localizing the neurological injury and formulating a targeted diagnostic plan. The findings, summarized in Figure 2 pointed with remarkable precision to a lesion in the right ventral midbrain. The examination began with the cranial nerves. The right eye immediately drew attention. There was a severe ptosis, with the eyelid drooping to cover the superior half of the pupil. The patient could not voluntarily elevate it further. When the examiner gently lifted the lid, the underlying ocular signs became apparent. The right pupil was dilated to approximately 6 mm and was fixed, showing no direct or consensual reaction to a bright light. The left pupil was 3 mm and responded briskly. A swinging-flashlight test was performed and showed no relative afferent pupillary defect (RAPD), confirming the pupillary abnormality was purely an efferent (CN III) problem. Assessment of extraocular movements was dramatic. The right eye was deviated inferolaterally at rest—the classic "down and out" position. On command, the patient was completely unable to adduct the eye (move it inward toward her nose), elevate it, or depress it. The only movements preserved were full abduction (outward movement, confirming intact CN VI function) and a subtle intorsion (inward rotation) on attempted downward gaze (confirming intact CN IV function). In stark contrast, the left eye had a full range of motion. This constellation of findings confirmed a complete right oculomotor nerve palsy. A key component of the examination was funduscopy. Examination of the right and left optic fundi revealed Grade II hypertensive retinopathy, characterized by generalized arteriolar narrowing, focal constrictions, and arteriovenous (AV) nicking where arteries crossed over veins. This finding provided direct, objective visual evidence of chronic end-organ damage from her uncontrolled hypertension, corroborating the history. The motor examination revealed a clear left-sided hemiparesis. Strength in the left upper and lower extremities was graded at 4/5 on the Medical Research Council (MRC) scale, indicating that she could move the limbs against gravity but not against moderate resistance. Strength on the right side was full (5/5). The sensory examination was entirely normal to all modalities, including light touch, pinprick, temperature, vibration, and proprioception. Reflex testing solidified the localization. Deep tendon reflexes on the left side (biceps, brachioradialis, patellar, Achilles) were pathologically brisk (3+), while those on the right were normal (2+). The plantar response, elicited by stroking the sole of the foot, was extensor on the left (a positive Babinski sign), a clear sign of an upper motor neuron lesion. The plantar response on the right was normal and flexor. Coordination testing revealed no dysmetria, dysdiadochokinesia, or intention tremor on the non-paretic right side, making a primary cerebellar lesion unlikely.

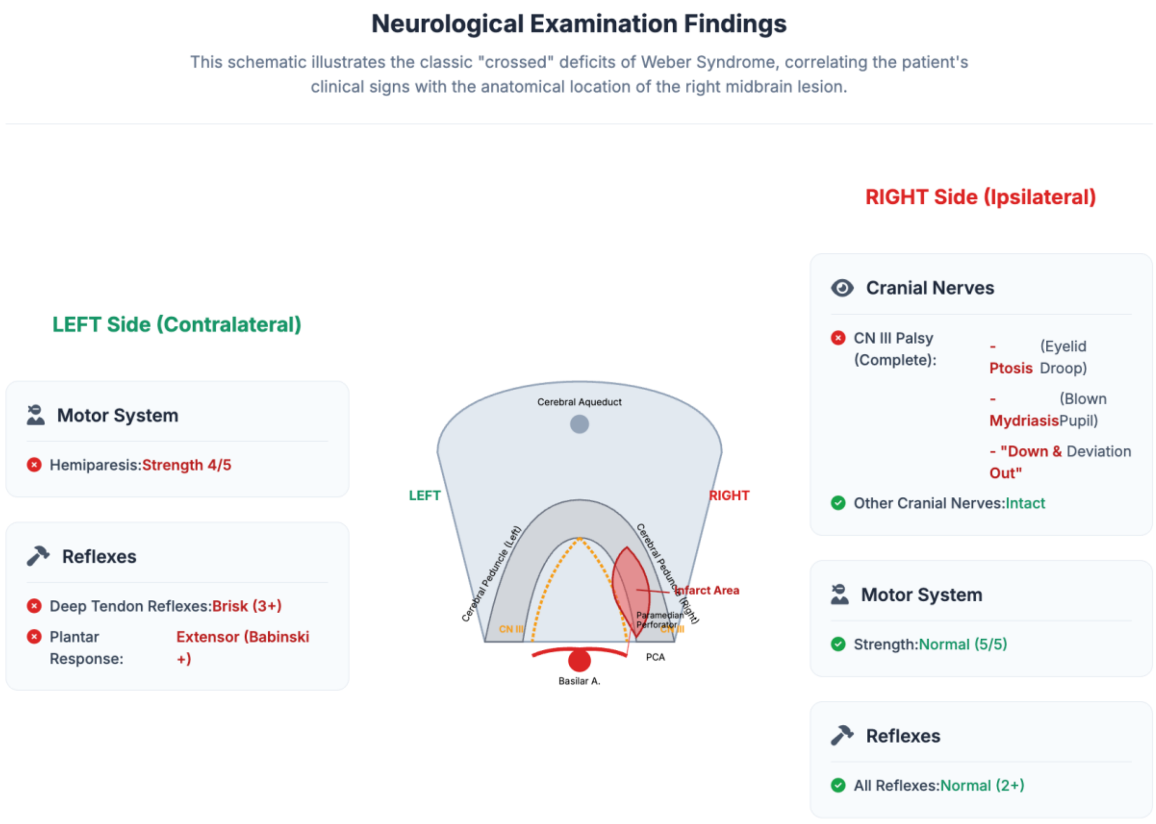

Figure 2. Neurological examination findings.

Comprehensive laboratory findings at admission provided a clear and compelling biochemical narrative that was central to understanding the etiology of the patient's acute neurological event. The patient's Total Cholesterol was markedly elevated at 242 mg/dL, significantly exceeding the desirable target of less than 200 mg/dL and immediately confirming a state of hypercholesterolemia. This was further elucidated by the LDL-Cholesterol level, which stood at a very high 168 mg/dL. This "bad cholesterol" is the primary building block of atherosclerotic plaques, and a value this high is profoundly abnormal, representing a massive burden of circulating atherogenic particles that directly contribute to vascular damage. Compounding this issue was a detrimentally low HDL-Cholesterol of 35 mg/dL, falling well below the protective threshold of 45 mg/dL. This low level of "good cholesterol" signifies a critical failure in the body's reverse cholesterol transport system—its natural mechanism for clearing excess cholesterol from the arterial walls—and a loss of HDL's crucial anti-inflammatory properties. The final component of this virulent lipid profile was the high triglyceride level of 218 mg/dL, far surpassing the target of under 150 mg/dL. This finding is not merely incidental; it is a marker of a dangerous metabolic state associated with an abundance of small, dense, and highly aggressive LDL particles that more easily penetrate the vessel lining, accelerating the atherosclerotic process. Taken together, this profile represents a perfect storm of pro-atherogenic factors. A Random Blood Glucose of 102 mg/dL, along with normal Hemoglobin and Creatinine levels, effectively ruled out uncontrolled diabetes, significant anemia, or chronic kidney disease as major contributing factors. This absence of other common confounders further sharpened the focus, implicating the severe mixed dyslipidemia not just as a risk factor, but as the principal and direct cause of the small vessel occlusion that led to the patient's debilitating stroke (Figure 3).

Figure 3. Comprehensive laboratory findings at admission.

MRI Findings in this case of Weber Syndrome beautifully illustrate the direct link between a specific vascular insult and a classic pattern of neurological deficits. The series of axial magnetic resonance images provides a definitive diagnosis of an acute ischemic stroke localized to a critical area of the brainstem. The initial T1-weighted images reveal an ill-defined, hypointense (dark) lesion within the right mesencephalon or midbrain. This subtle finding becomes conspicuously hyperintense (bright) on the T2-weighted and FLAIR sequences, a characteristic sign of vasogenic and cytotoxic edema that occurs in brain tissue following an ischemic event. The diagnosis of an acute infarction is unequivocally confirmed by the diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) map. The DWI sequence shows a prominent bright signal in the affected right midbrain, with a corresponding dark signal on the ADC map. This DWI/ADC mismatch confirms restricted diffusion of water molecules, the gold standard for identifying an acute stroke within hours of onset. The schematic of pathophysiology provides a brilliant anatomical correlation for the patient's clinical presentation of right-sided oculomotor nerve palsy and left-sided hemiparesis. The infarct area, highlighted in red on the right side of the midbrain cross-section, is precisely located in the territory supplied by the paramedian perforating branches of the posterior cerebral artery (PCA). The schematic shows this vascular occlusion, which has starved a vital portion of the midbrain of oxygen. The lesion strategically damages two crucial structures as they pass through this region. Firstly, it strikes the exiting nerve fibers (fascicles) of the right oculomotor nerve (Cranial Nerve III). This ipsilateral (same-sided) damage is responsible for the patient's difficulty opening the right eye (ptosis), double vision (diplopia), and the characteristic "down and out" deviation of the eye. Secondly, the infarct damages the adjacent cerebral peduncle, a massive bundle of motor fibers that includes the corticospinal tract. Because these motor pathways cross to the opposite side lower down in the medulla, damage here results in contralateral (opposite-sided) weakness, perfectly explaining the patient's left hemiparesis. This combination of imaging and schematic representation powerfully demonstrates how a single, small lesion can produce such distinct and "crossed" neurological signs, encapsulating the essence of Weber Syndrome (Figure 4).

The therapeutic journey for a patient recovering from a brainstem stroke is a complex, integrated process that extends far beyond the initial hospital stay. It represents a multidisciplinary covenant between the medical team, the patient, and their family, aimed at mitigating immediate harm, restoring lost function, and fortifying the patient against future vascular events. The management strategy employed in this case is a paradigm of modern stroke care, built upon three synergistic pillars: aggressive pharmacological intervention, personalized multidisciplinary rehabilitation, and a robust, patient-centered strategy for education and long-term adherence. This holistic approach recognizes that true recovery involves not only healing the brain but also empowering the individual to reclaim their life and actively participate in the lifelong management of their health. Each component is meticulously tailored to the patient's specific deficits and risk factors, creating a comprehensive roadmap from acute crisis to functional independence and sustained well-being. The first pillar, Pharmacological Intervention, forms the immediate line of defense and the foundation for secondary prevention. In the hyperacute phase of this ischemic stroke, the initiation of Dual Antiplatelet Therapy (DAPT), combining Aspirin (80mg) and Clopidogrel (75mg), was a critical first step. This combination works synergistically to prevent further platelet aggregation and thrombus formation on the ruptured atherosclerotic plaque that caused the initial occlusion, significantly reducing the high risk of a recurrent stroke in the immediate aftermath. The therapeutic focus then broadened to aggressively address the patient's underlying and profound vascular risk factors.

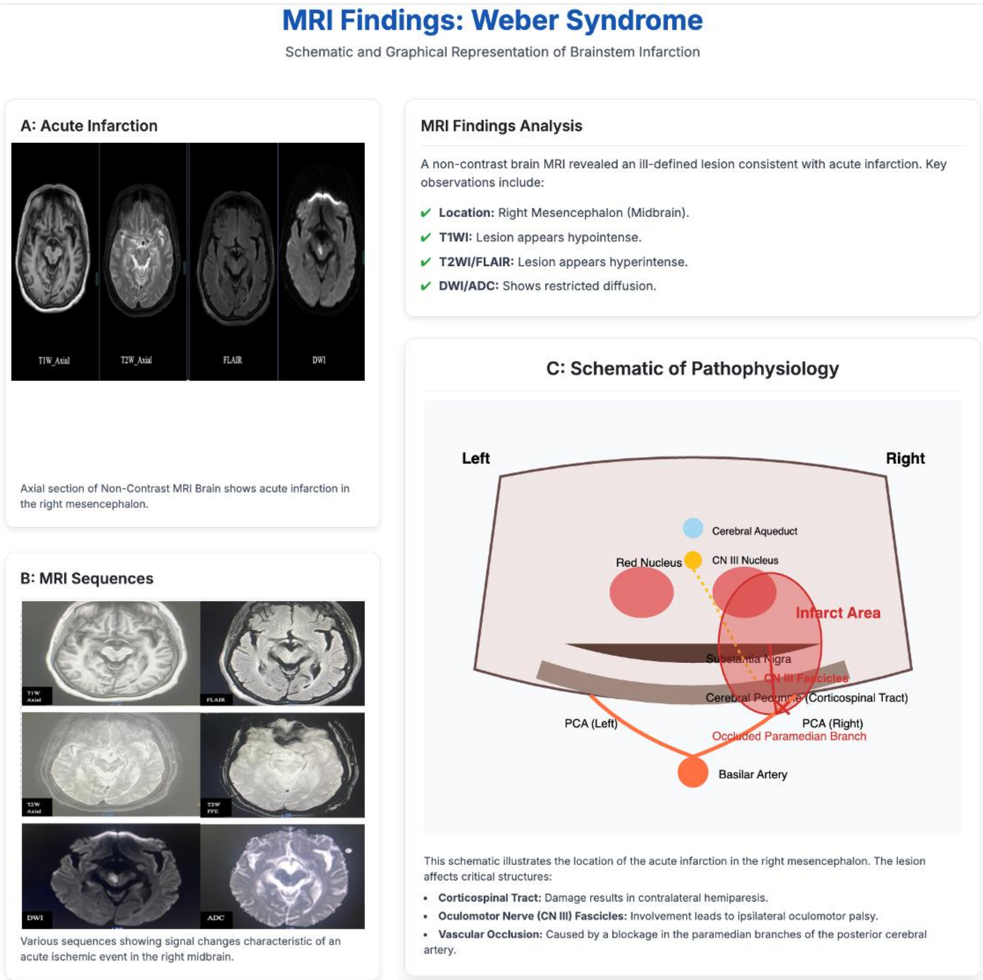

Figure 4. MRI findings analysis and schematic of pathophysiology.

Given the laboratory findings of severe hypercholesterolemia, with a total cholesterol of 242 mg/dL and an LDL-cholesterol level of 168 mg/dL, a high-intensity statin regimen with Atorvastatin was indispensable. Statins are the cornerstone of lipid-lowering therapy, proven to dramatically reduce the risk of all types of stroke by lowering LDL levels and exerting pleiotropic effects such as stabilizing existing plaques and reducing vascular inflammation. However, the patient's lipid profile was further complicated by significant hypertriglyceridemia, with a level of 218 mg/dL. This necessitated the addition of Fibrate Therapy with Fenofibrate (300mg). This targeted approach is consistent with guidelines that recommend considering a statin-fibrate combination for patients with high triglycerides, ensuring all facets of their dyslipidemia are managed. Finally, to control the patient's presenting hypertension (167/96 mmHg) and history of high blood pressure, Antihypertensive Therapy with Amlodipine (10mg) was implemented for long-term blood pressure control, reducing the chronic stress on cerebral blood vessels and lowering the risk of both ischemic and hemorrhagic events. The second pillar, Multidisciplinary Rehabilitation, shifts the focus from preventing further damage to actively restoring the functions stolen by the stroke. This highly collaborative effort began immediately to capitalize on the brain's capacity for neuroplasticity. Physical Therapy (PT) directly targeted the patient's left hemiparesis, a consequence of the damage to the right corticospinal tract. Therapists employed task-specific training, balance exercises, and intensive gait retraining to help the patient regain motor control, improve stability, and restore their ability to walk safely. Working in concert, Occupational Therapy (OT) aimed to translate these regained motor skills into functional independence in Activities of Daily Living (ADLs). This involved retraining for tasks like dressing and grooming, as well as assessing the home environment to recommend modifications that would ensure safety and maximize the patient's autonomy. The rehabilitation was further specialized to address the unique deficits of Weber Syndrome. A Speech-Language Pathologist (SLP) performed a crucial bedside swallow evaluation to rule out dysphagia. Although the patient did not report speech difficulties, brainstem strokes can subtly impair swallowing, and this proactive measure was vital to prevent aspiration pneumonia, a potentially lethal complication. Perhaps most specific to this case was the intervention by Neuro-Ophthalmology. The patient's debilitating diplopia (double vision), caused by the ipsilateral oculomotor nerve palsy, presented a major barrier to recovery. The trial of a Fresnel prism, a thin, flexible press-on lens, was an elegant solution. This prism optically realigns the discordant images, improving visual comfort and allowing the patient to participate more fully and effectively in all other aspects of their rehabilitation. The final and arguably most critical pillar is the Adherence and Education Strategy, which bridges the transition from hospital care to lifelong self-management. The medical team initiated Intensive Patient Education, conducting multiple sessions with the patient and their family. The primary goal was to forge a clear, undeniable link between the patient's "silent" risk factors—hypertension and hypercholesterolemia—and the tangible, disabling stroke they had just experienced. This understanding is fundamental to fostering the motivation required for lifelong adherence. To overcome the complexity of the multi-drug regimen, Regimen Simplification was prioritized, aiming for once-daily dosing where possible to reduce the cognitive burden and improve ease of use. This was supported by practical Empowerment Tools. A simple 7-day pill organizer was provided to serve as a physical daily reminder, and the patient's husband was engaged as a "medication partner," creating a supportive system of shared responsibility. Finally, the strategy was solidified through Reinforced Follow-Up. The patient was scheduled for regular appointments with both their neurologist and primary care physician to ensure continuity of care, monitor progress, and continually reinforce the importance of their management plan. This structured follow-up closes the therapeutic loop, transforming the journey from a passive treatment experience into an active, collaborative partnership for health (Figure 5).

3. Discussion

This case is a masterclass in neurological localization, a skill that remains the bedrock of clinical neurology even in the age of advanced imaging. The ventral midbrain represents a region of what can be termed "elegant vulnerability"—a tiny anatomical area where a focal lesion can produce a profound and predictable constellation of deficits.[11] The co-occurrence of the corticospinal tract and the exiting CN III fascicles within the cerebral peduncle creates the substrate for Weber syndrome. The lesion's location explains not just the presence of the deficits, but their specific character. It is a testament to the intricate and unforgiving precision of the brain's architecture. The hemiparesis was uniform, affecting the arm and leg similarly.[12] This is consistent with a lesion in the body of the peduncle, where the corticospinal fibers are tightly packed. This concept of somatotopy within the peduncle highlights the precision of the brain's wiring. A lesion slightly more medial might have disproportionately affected the corticobulbar fibers (potentially causing severe dysarthria or dysphagia), while a more lateral lesion might have preferentially affected fibers destined for the leg.[13] The patient's specific pattern of weakness allowed for a refined localization even before the MRI was performed.

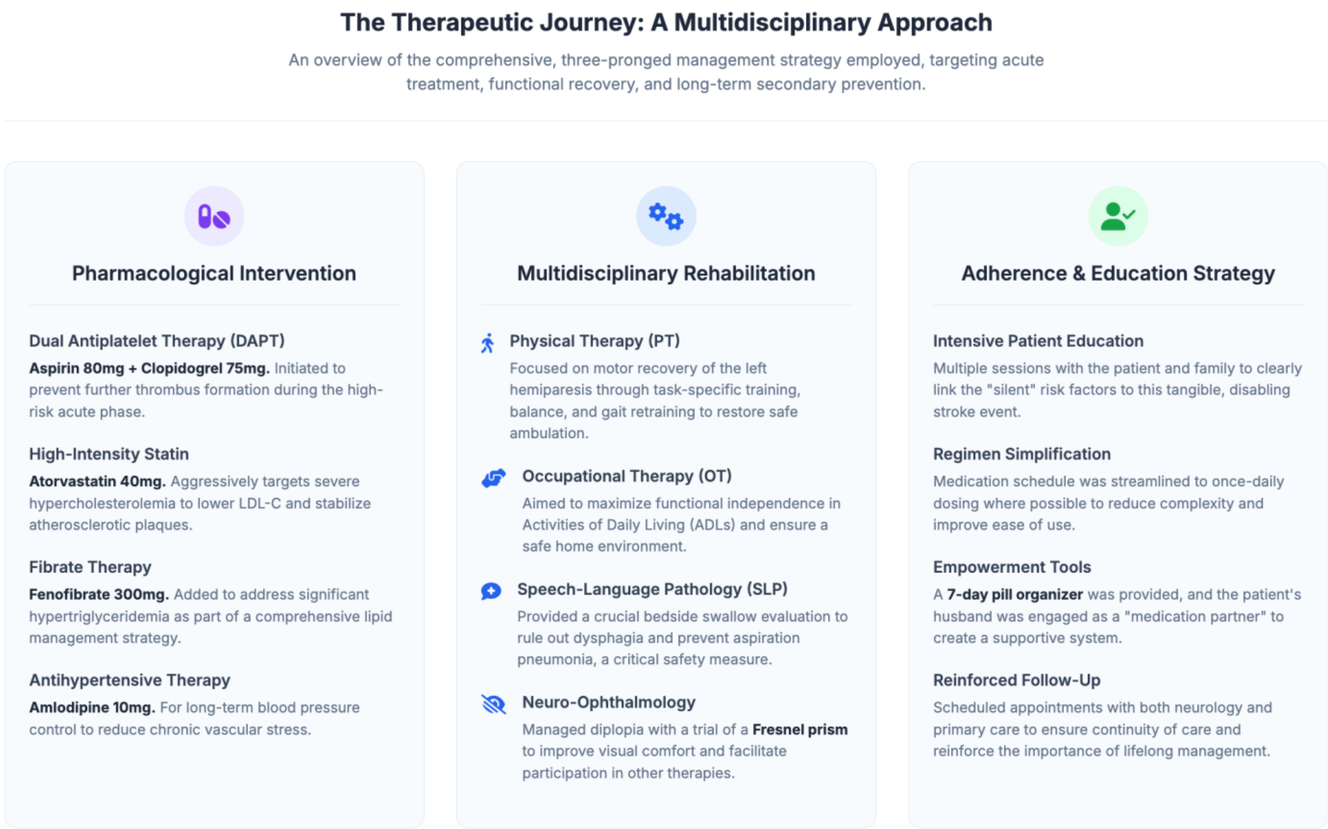

Figure 5. The therapeutic journey: A multidisciplinary approach.

Furthermore, the nature of the oculomotor palsy itself is highly localizing. CN III palsies can be nuclear, fascicular, peripheral, or compressive. A nuclear lesion is exceptionally unlikely here. The subnucleus for the superior rectus muscle is unique in that it supplies the contralateral muscle. Additionally, the subnucleus for the levator palpebrae is a shared, midline structure. Therefore, a unilateral nuclear lesion would cause a contralateral superior rectus weakness and bilateral ptosis—a clinical picture entirely different from our patient's. Her complete, unilateral palsy involving both somatic motor functions (extraocular muscles, eyelid) and parasympathetic pupillary fibers is the classic signature of a fascicular lesion.[14] This indicates damage to the nerve bundle as it courses ventrally through the midbrain parenchyma, after the fibers have organized but before they exit the brainstem. This clinical deduction was then perfectly corroborated by the MRI, showcasing a beautiful synergy between the clinical examination and advanced technology.[15]

While the clinical examination pointed to the diagnosis, modern neuroimaging provided irrefutable confirmation and, crucially, etiological insight. The DWI/ADC sequences on MRI confirmed the acute infarct with exquisite sensitivity. In the past, a CT scan might have been negative, leaving a degree of uncertainty. The MRI, however, transformed clinical suspicion into diagnostic certainty. However, the diagnostic process did not end there. The addition of MRA of the head and neck was a methodologically critical step. In any patient with a stroke, it is imperative to assess the entire vascular tree. The MRA's purpose was to search for a more proximal cause, such as a significant stenosis in the basilar artery or posterior cerebral artery from which an artery-to-artery embolism could have occurred.[16] Other possibilities, like a vertebral artery dissection or a vasculitic process, could also be considered. By demonstrating patent large vessels, the MRA allowed us to confidently exclude these alternative etiologies. This negative finding significantly strengthens the diagnosis of a lacunar infarct secondary to intrinsic small vessel disease. It allowed the therapeutic focus to shift squarely and confidently onto the management of the patient's intrinsic metabolic risk factors. In this context, the funduscopic findings of hypertensive retinopathy were not an incidental finding; they were a powerful, low-tech corroboration of the same conclusion, providing a direct window into the chronic, systemic state of the body's microvasculature.

This patient's stroke was not a random event; it was the final, predictable chapter of a long story written in her lipid profile. The discussion of the pathophysiology must go beyond a simple mention of atherosclerosis and delve into the specific nature of her severe mixed dyslipidemia, as this provides the entire rationale for the therapeutic strategy. The primary mechanism of her small vessel occlusion was likely microatheromatosis. This is the formation of a true, albeit tiny, atherosclerotic plaque at the origin of a small (50-200 μm) perforating artery from its much larger parent vessel (in this case, the PCA). This is distinct from the other primary mechanism of small vessel disease, lipohyalinosis, which is a degenerative, non-atherosclerotic hyaline thickening of the vessel wall more commonly associated with pure, severe hypertension. This patient's specific lipid profile, with its very high LDL-C and inflammatory state (evidenced by the high hs-CRP), strongly favors microatheroma as the underlying culprit. High LDL-Cholesterol (168 mg/dL) provided the raw substrate for plaque formation. LDL particles are the primary carriers of cholesterol to the arterial wall. High triglycerides (218 mg/dL), a marker for an abundance of triglyceride-rich lipoproteins (TRLs) and their metabolic byproducts, known as remnant cholesterol.[17] This remnant cholesterol is now understood to be a direct, causal factor in atherosclerosis, as these particles, like LDL, can penetrate the endothelial wall and deposit cholesterol, fueling inflammation. Furthermore, high triglycerides are a hallmark of a metabolic state that favors the formation of small, dense LDL (sdLDL) particles. These particles are particularly insidious because their small size allows for easier endothelial infiltration, they have a higher affinity for proteoglycans in the arterial wall (trapping them there), and they are more susceptible to oxidation, which is a key step in accelerating the inflammatory cascade and foam cell formation. HDL is often called "good cholesterol" for a reason. Its primary function is reverse cholesterol transport—the crucial process by which HDL acts like a garbage truck, removing excess cholesterol from plaques and transporting it back to the liver for disposal.[18] Low HDL signifies a failure of this vital cleanup process. But the detriment of low HDL goes further; HDL particles also have critical anti-inflammatory, anti-oxidant, and anti-thrombotic properties. A low HDL level, therefore, represents a state of impaired defense and heightened vulnerability. The patient's hypertension acted as a powerful accomplice in this process. The chronic high pressure inflicted constant biomechanical shear stress on the endothelium of her perforating arteries, creating micro-injuries—the "first hit." This damaged, dysfunctional endothelium became more permeable, allowing the flood of atherogenic lipoproteins from her dyslipidemia to invade the vessel wall—the "second hit." This synergy of hypertension and dyslipidemia created a perfect storm for the rapid development of the occlusive microatheroma that caused her stroke.

The choice of Atorvastatin 40 mg reflects current guideline recommendations for high-intensity statin therapy in secondary stroke prevention, which aim for a ≥50% reduction in LDL-C. An initial dose of 20 mg was considered but was deemed insufficient to achieve this target given her very high baseline LDL-C of 168 mg/dL. The long-term goal for this patient, who now has established atherosclerotic cardiovascular disease, is an LDL-C level well below 70 mg/dL, and for patients at very high risk, the target is now approaching 55 mg/dL. Her follow-up management must include lipid panel monitoring within 4-6 weeks to ensure this target is being approached, with a clear plan for potential dose titration to Atorvastatin 80 mg or the addition of a second agent like ezetimibe if the goal is not met. This "treat-to-target" approach is a cornerstone of modern lipid management. The addition of Fenofibrate was a considered clinical decision based on the severity of her hypertriglyceridemia. This represents a personalized approach to her specific metabolic phenotype. However, it is essential to acknowledge the evidence base with intellectual honesty. While logical from a pathophysiological standpoint (targeting TRLs and remnant cholesterol), large clinical trials like ACCORD-Lipid and FIELD have not consistently shown a benefit for fibrates in reducing major cardiovascular events when added to a statin in broad populations. Therefore, this decision was made by weighing the potential, albeit not definitively proven, benefit of lowering her very high TRL remnants against the small but real increased risk of myopathy from combination therapy. The patient was thoroughly counseled on this risk-benefit profile and was instructed to report any new or worsening muscle pain immediately.

The patient's remarkable recovery was not a passive process of waiting for the brain to heal; it was actively driven by an intensive, multidisciplinary rehabilitation program. The goal of rehabilitation is to harness the brain's incredible innate capacity for neuroplasticity.[19] The foundation of her motor recovery was task-specific, high-repetition training. Simply moving the limb is not enough; the brain must be retrained to perform functional tasks. By repeatedly practicing reaching for and grasping objects, the patient's brain was forced to find new neural pathways to accomplish the goal. This type of training is a powerful driver of cortical remapping, where adjacent, undamaged areas of the motor cortex can reorganize and take over the function of the damaged corticospinal tract. The management of her diplopia was a critical early step. The use of a temporary, stick-on Fresnel prism is a key intervention in neuro-rehabilitation. It works by bending light before it enters the eye, optically realigning the two disparate images and eliminating double vision in primary gaze. This simple tool had a profound effect: it not only improved her comfort but, by providing her with a single, clear visual world, it allowed her to engage more fully and safely in all other therapies, especially balance and gait training. In addition to this passive correction, active oculomotor exercises, such as tracking and convergence tasks, were initiated to strengthen the recovering muscles and promote central adaptation to the palsy. A stroke of this nature requires a team. The involvement of Speech-Language Pathology (SLP) to perform a formal bedside swallow evaluation was a critical safety measure. Brainstem strokes carry a high risk of silent aspiration, and ruling out dysphagia early prevents the catastrophic complication of aspiration pneumonia. The Occupational Therapist (OT) played a vital role in translating motor gains into functional independence, teaching one-handed strategies for dressing and eating, and ensuring the home environment was safe for her return.[20] This integrated team approach is the hallmark of modern, effective stroke rehabilitation. The most significant long-term threat to this patient's health was not the residual effects of her stroke, but the behavioral patterns that led to it. Her history of medication non-adherence had to be addressed as aggressively as her cholesterol levels. A stroke can serve as a powerful, life-altering "teachable moment," and the clinical team leveraged this. The therapeutic strategy explicitly included intensive education and empowerment tools (the pill organizer, engaging her husband as a "medication partner") to transform her relationship with her health from one of passive non-compliance to active, engaged self-management. This focus on adherence is the true cornerstone of secondary prevention; the best drugs in the world are ineffective if they are not taken.

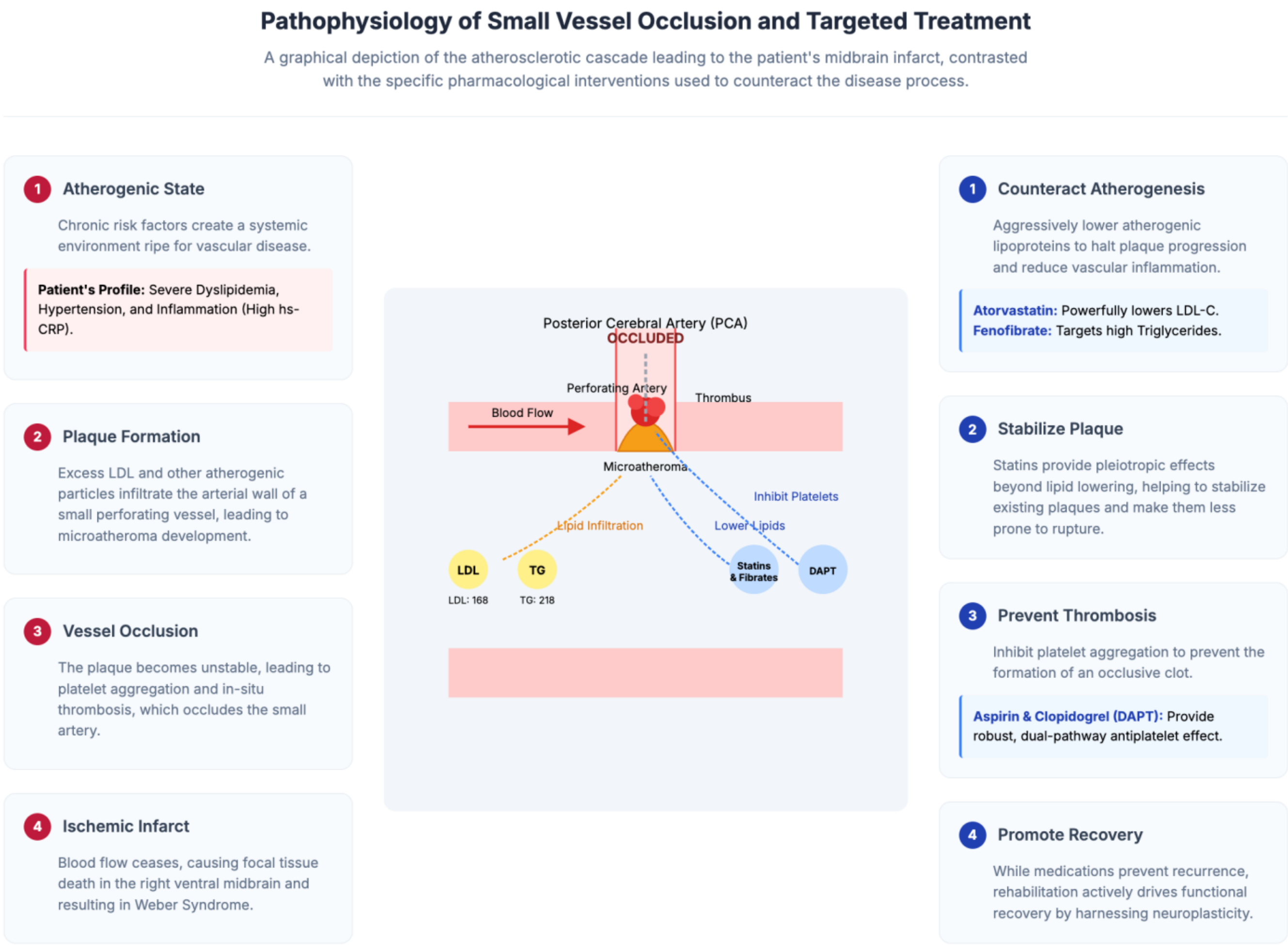

Figure 6. Pathophysiology of small vessel occlusion and targeted treatment.

Pathophysiology of small vessel occlusion and targeted treatment is a compelling narrative of a microscopic battle with macroscopic consequences, elegantly illustrating the insidious cascade from systemic risk to focal neurological devastation and the precisely targeted pharmacological counter-attack, Figure 6. This process begins not with a sudden event, but with a chronic, underlying atherogenic state. The patient's body existed in a systemic environment ripe for vascular disease, fueled by a dangerous combination of severe dyslipidemia, hypertension, and inflammation. This hostile internal milieu, characterized by a high LDL cholesterol of 168 mg/dL and triglycerides of 218 mg/dL, created the perfect conditions for the initiation of atherosclerosis, not just in large vessels, but in the brain's most delicate and vital perforating arteries. This systemic state inexorably leads to the second stage: localized plaque formation. As depicted in the central diagram, excess atherogenic lipoproteins, particularly LDL cholesterol, began to infiltrate and become trapped within the arterial wall of a small perforating artery branching from the posterior cerebral artery (PCA). This lipid infiltration triggers an inflammatory response, leading to the gradual development of a microatheroma—a small, silent plaque that progressively narrows the vessel's lumen. For a long time, this process is asymptomatic, a hidden threat growing within the critical vascular highways of the midbrain. The journey toward catastrophe accelerates at the third stage, vessel occlusion. The microatheroma, once stable, becomes vulnerable and ruptures. This rupture exposes the plaque's thrombogenic core to the bloodstream, triggering a rapid and aggressive hemostatic response. Platelets rush to the site of injury, adhering and aggregating to form an in-situ thrombus. In a small-caliber perforating artery, this clot quickly grows to become fully occlusive, completely blocking the flow of blood. This sudden blockade marks the final, devastating step: the ischemic infarct. With its blood supply cut off, the downstream brain tissue in the right ventral midbrain is starved of oxygen and vital nutrients, leading to rapid cell death. This focal infarction is the direct cause of the patient's clinical presentation with Weber Syndrome—ipsilateral oculomotor palsy and contralateral hemiparesis.[19] In response to this pathological cascade, a multi-pronged therapeutic strategy is deployed, with each medication targeting a specific step in the disease process. The primary goal is to counteract atherogenesis at its source. A high-intensity statin, Atorvastatin, is administered to powerfully lower the patient's high LDL-C levels, thereby reducing the primary building block of atherosclerotic plaque. Simultaneously, Fenofibrate is used to specifically target the high triglycerides, addressing the full spectrum of the patient's dyslipidemia and halting the progression of the underlying disease. Beyond just lowering lipids, the therapy aims to stabilize existing plaque. Statins possess crucial pleiotropic effects that help to strengthen the fibrous cap of any remaining atheromas, making them less prone to future rupture and preventing a recurrent event. To address the immediate cause of the infarct—the thrombus—the strategy must prevent thrombosis. Robust, dual-pathway antiplatelet therapy with Aspirin and Clopidogrel (DAPT) is initiated to potently inhibit platelet aggregation, directly preventing the formation of another occlusive clot.[20] Finally, while this powerful pharmacological arsenal works to prevent recurrence, the journey concludes by looking beyond prevention to promote recovery. The medications create a stable environment for the brain to heal, but it is intensive rehabilitation that actively drives functional recovery, harnessing the remarkable power of neuroplasticity to help the brain rewire itself and reclaim lost abilities. This comprehensive approach, therefore, does not just treat the stroke; it systematically dismantles the pathway that led to it.

4. Conclusion

This case of Weber syndrome serves as a powerful, multifaceted lesson in modern neurology. It is a testament to the enduring value of classic clinical localization, a demonstration of the definitive power of advanced neuroimaging, and a stark illustration of the direct, causal pathway from systemic metabolic disease to focal neurological devastation. The journey of this patient from acute disability to significant functional recovery highlights that the triumph of modern stroke care lies not in a single intervention, but in a holistic, integrated, and patient-centered approach. It emphatically concludes that aggressive, evidence-based pharmacotherapy is essential, but its success is entirely contingent upon a robust rehabilitation program to harness neuroplasticity and, most critically, a dedicated, compassionate strategy to empower the patient for a lifetime of adherence and secondary prevention. This case revisits a classic syndrome to teach a modern lesson: we treat not just the lesion, but the patient in whom it resides.

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