# El curso clínico y los desafíos de la Lesión Axonal Difusa (LAD) en un traumatismo craneoencefálico severo: Reporte de un caso

## *The clinical journey and challenges of Diffuse Axonal Injury (DAI) in a severe traumatic brain injury – A case report*

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## ABSTRACT

Diffuse axonal injury (DAI) arises as a severe consequence of traumatic brain injury (TBI), characterized by axonal misalignment, stretching, or shearing. These events trigger pathophysiological cascades, including axonal depolarization, metabolic perturbations, cellular swelling, cytotoxic edema, and apoptosis. While DAI typically involves multifocal brain damage, it predominantly affects the central third of the brain, with the corpus callosum and brainstem being especially prone to injury. Clinically, DAI presents a heterogeneous spectrum of manifestations, from acute loss of consciousness to cognitive deficits and persistent coma. Predicting outcomes remains challenging, and no standardized treatment protocol has been established.

The authors report a case of a 23-year-old male victim of a high-speed traffic accident, who progressed to a comatose state and was diagnosed with grade III DAI. Subsequently, the patient underwent successful extubation and showed favorable recovery progress.

**Keywords:** Axon, axonal pathology, diffuse axonal injury, traumatic brain injury, neurodegeneration.

## RESUMEN

La lesión axonal difusa (LAD) surge como una consecuencia grave del traumatismo craneoencefálico (TCE), caracterizada por el desalineamiento, estiramiento o cizallamiento de los axones. Estos eventos desencadenan cascadas fisiopatológicas, incluyendo despolarización axonal, perturbaciones metabólicas, hinchazón celular, edema citotóxico y apoptosis. Aunque la LAD típicamente implica daño cerebral multifocal, afecta predominantemente al tercio central del cerebro, siendo especialmente propensos a la lesión el cuerpo calloso y el tronco encefálico. Clínicamente, la LAD presenta un espectro heterogéneo de manifestaciones, desde pérdida aguda de la conciencia hasta déficits cognitivos y coma persistente. Predecir los resultados sigue siendo un desafío y no se ha establecido un protocolo de tratamiento estandarizado.

Los autores reportan el caso de un hombre de 23 años, víctima de un accidente de tráfico a alta velocidad, que progresó a un estado comatoso y fue diagnosticado con LAD de grado III. Posteriormente, el paciente fue extubado exitosamente y mostró un progreso de recuperación favorable.

**Palabras clave:** Axón, patología axonal, lesión axonal difusa, traumatismo craneoencefálico, neurodegeneración.

## CLINICAL CASE

A 23-year-old male arrived at the emergency room following a high-speed traffic accident. He sustained a traumatic brain injury (TBI) with excoriations on the right parietal side and evident bilateral leg fractures, including an exposed right femur. At the scene, his initial Glasgow Coma Scale (GCS) was 14. However, after receiving sedation with benzodiazepines and opioids for pain control, his GCS decreased to 11 upon admission to the hospital. He also exhibited disorientation and aggressiveness.

The exposed femur fracture needed immediate reduction, requiring intensive pain management and prolonged sedation, which prevented an accurate reassessment of his level of consciousness. Laboratory tests showed moderate rhabdomyolysis and mild renal injury. A full-body CT scan, including a brain CT scan, revealed bilateral pulmonary contusions and confirmed the suspected femur fractures, with no other abnormalities. Within the initial 24 hours, in the intensive care unit (ICU), he exhibited a diminished level of consciousness and conjugate eye deviation to the right, without myoclonic jerks, requiring orotracheal intubation.

Upon cessation of sedation, 48 hours later, his GCS had decreased to 8. A repeat brain CT scan revealed no changes and central nervous system infection was ruled out. A brain MRI was performed and unveiled numerous areas of T2/FLAIR hyperintensity distributed across various brain regions, including the hemispheres, cerebellar peduncles, thalamic-capsular areas, corpus callosum, and internal and external capsules, along with associated hemorrhagic foci, indicative of grade III DAI (see Figures 1 and 2).

Dysautonomic changes such as fever and tachycardia were observed and managed. The patient exhibited progressive neurological recovery and, after 12 days, was successfully extubated. He progressively began to communicate and respond to simple commands. He was admitted to a rehabilitation facility, showing continued improvement in neurocognitive and physical functions.

## DISCUSSION

Traumatic brain injury (TBI) is a multifaceted condition with various causes and mechanisms, resulting in distinct clinical pathologies categorized as focal or diffuse[1,2]. Focal brain injury refers to localized damage in specific brain regions leading to identifiable lesions and focal neurological deficits. Conversely, diffuse brain injuries involve wide-

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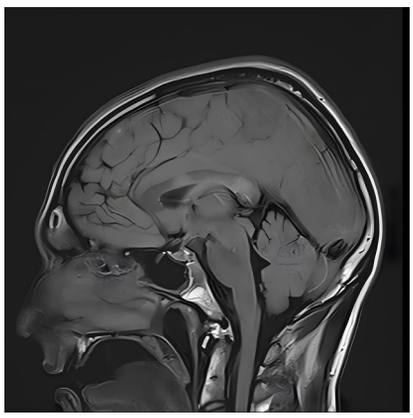

Figure 1

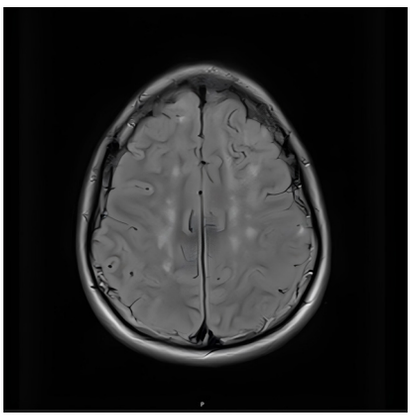

Figure 2

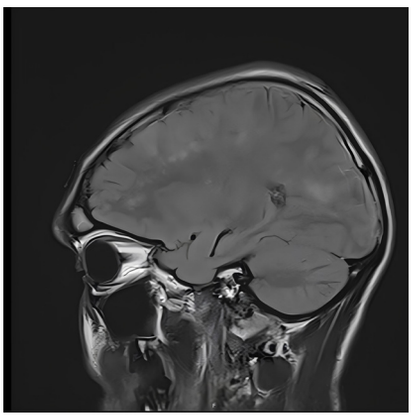

Figure 3

spread disruption of neurological function across multiple brain regions, typically lacking macroscopic lesions.

Diffuse axonal injury (DAI) is characterized by a prolonged post-traumatic coma lasting over six hours, without demonstrable mass lesions, increased intracranial pressure, or ischemia. The mechanical forces that precipitate DAI often include abrupt acceleration, deceleration, or rotation of the brain due to unrestricted head movements during trauma, as observed in our case where the patient experienced a high-energy impact. These forces induce tissue injury characterized by axonal stretching, disruption, and eventual separation of nerve fibers.

An accurate diagnosis of DAI requires a histopathological analysis of brain tissue, typically obtained post-mortem, which is not feasible in living patients. Therefore, clinical presentation and conventional brain MRI results are used to support the diagnosis, although such findings are detected in only 50% of cases[1-5]. Traditionally described as a "diffuse lesion", DAI is multifocal, affecting specific brain regions like the corpus callosum, brainstem, and cerebellum, especially at the junction of cortical gray matter and white matter.[1-7]

Some researchers question the six-hour coma threshold for DAI, noting cases of DAI in patients with mild TBI and the challenge of assessing wakefulness, especially with prolonged sedation[4], as seen in our patient. DAI severity is classified into three grades: Grade I involves widespread axonal damage in the cerebral hemispheres, Grade II exhibits similar abnormalities in the corpus callosum with tissue tear hemorrhages, and Grade III extends to the rostral brainstem with tissue tear hemorrhages.[2,3]

Standard non-invasive techniques such as brain CT or MRI often lack the sensitivity required for accurate clinical diagnosis[4,7]. However, advanced neuroimaging techniques like diffusion tensor imaging (DTI) show promise for *in vivo* assessment of white matter integrity, though further validation is needed.[7]

Fortunately, in our case, the brain MRI was enough to diagnose and grade this injury. DAI stands as a substantial subtype of TBI, encompassing 40 to 50% of cases. Classic literature still links injury severity and prognosis to the extent of axonal damage[2,3,4]. However, despite ongoing efforts to grade DAI for prognostic insights, it fails to consistently align with outcomes. This implies that DAI grading may overlook key factors influencing recovery, as illustrated by our patient's remarkable turnaround despite initially bleak prognostic expectations. Furthermore, some researchers suggest that the mean GCS at presentation might offer superior outcome prediction compared to DAI grading[3,8]. Nonetheless, DAI's presence remains a crucial contributor to TBI patient morbidity and mortality, often leading to posttraumatic coma, disability, and persistent vegetative states.[5,6]

Traditionally, post-traumatic brain damage has been perceived as an acute or subacute phenomenon. However, emerging evidence advocates that axonal degeneration might manifest years after the initial trauma, hinting at the potential initiation of a progressive neurodegenerative process following TBI. Intracellular ionic alterations instigate a cascade of events that could prove detrimental to cells, with the cellular response to traumatic calcium influx playing a fundamental role in influencing the neurological injury's outcome.[1]

In DAI, morphologically altered axons due to impaired transport or functionally disrupted yet structurally intact axons, may contribute to the chronicity of the neurological dysfunction[7]. While neural plasticity holds promise for brain tissue to regain normal function when functionally impaired but not destroyed, cognitive, physical, and behavioral changes frequently endure beyond the acute traumatic event. Despite advancements in imaging techniques, grading systems, and understanding of pathophysiological mechanisms, predicting outcomes remains difficult due to the diversity of injury presentations and recovery paths. Further research and clinical endeavors are imperative to enhance diagnostic accuracy, develop targeted therapies, and optimize long-term management strategies.[5-7]

**CONFLICT OF INTEREST**
There are no conflicts of interest.

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**ETHICAL CONSIDERATIONS**
The authors confirm that they have obtained the necessary authorization and adhered to the Helsinki ethical guidelines in conducting the research and writing this scientific article.

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