

Disputes & Debates: Editors' Choice

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Editors' Note: Scan-Negative Cauda Equina Syndrome: A Prospective Cohort Study

Using prospectively collected data from their neurosurgical referral center, Dr. Hoeritzauer et al. summarize their observations regarding patients with cauda equina syndrome (CES), with and without imaging confirmation. Among patients in this cohort, 69% lacked radiographic evidence of cauda equina compression and were referred to as “scan-negative” (normal MRI) or “mixed” (root enhancement without cauda compression). History or presence of functional symptoms, along with normal patellar reflexes, more severe pain, and panic attack at presentation were associated with a “scan-negative” condition. It is of interest that disturbances of urine or bowel function were no less common among patients with “scan-negative” CES. Dr. Amelot and colleagues highlight the importance of follow-up and education for patients at risk of CES (e.g., those with pre-existing disk disease). They also suggest that patients with scan-negative CES may be vulnerable to underlying somatization or anxiety over the threat of possible neurologic dysfunction. In response, Dr. Hoeritzauer et al. affirm that even patients with “scan-negative” CES were followed for several years after their initial presentation to evaluate the cause of their symptoms. Furthermore, the investigators maintain the objective of their study was to determine risk factors for “scan-negative” vs “scan-positive” CES, which includes functional neurologic disease, medications, pain, and panic. The investigators have referred clinicians and patients to their fact sheet on “scan-negative” CES for more information. Professor Beucler also emphasizes the clinical presentation of CES typically begins with radicular pain, followed by motor and later bowel or bladder symptoms.

James E. Siegler III, MD, and Steven Galetta, MD
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Reader Response: Scan-Negative Cauda Equina Syndrome: A Prospective Cohort Study

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We read with great interest the article by Hoeritzauer et al.¹ This work could develop into both a reference and a warning concerning the difficulty in approaching a CES diagnosis. The preeminent result was that only 24% of their patients had a “scan-positive” CES.

In fact, to suggest a potential alternative explanation for “scan-negative CES,” we believe that it would be interesting to determine the proportion of patients who were followed by a spine specialist (81% of the patients in their series suffered from pain or lower back pain). Indeed, a CES prognosis is dramatic, with highly disabling long-term dysfunction sequelae,² and is feared by all specialists. Furthermore, it develops in most of cases from pre-existing vertebral disk disease.³

Author disclosures are available upon request (journal@neurology.org).

Although emergency interventions are in favor of improved outcomes, the only true effectiveness on outcome lies within the education and prevention of patients concerning the clinical signs that should be tracked down and consulted for the slightest appearance of deficit, genitosphincter disorders, or hyperalgesia.

We believe that for patients who are psychiatrically vulnerable (>80% in the “scan-negative CES” group of Hoeritzauer et al.), living in a climate of anxiety and hyperawareness of the threat that CES represents may promote somatization and other mental health manifestations. In this group, it would not be surprising to identify patients presenting several “scan-negative CES” alerts.

1. Hoeritzauer I, Carson A, Statham P, et al. Scan-negative cauda equina syndrome: a prospective cohort study. *Neurology*. 2021;96(3):e433-e447.
2. Korse NS, Veldman AB, Peul WC, Vleggeert-Lankamp CLA. The long term outcome of micturition, defecation and sexual function after spinal surgery for cauda equina syndrome. *PLoS One*. 2017;12(4):e0175987.
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Author Response: Scan-Negative Cauda Equina Syndrome: A Prospective Cohort Study

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We thank Dr. Amelot et al. for the response to our article.¹ We are aware that in other centers only patients with positive scans are referred to neurosurgeons. In our center, and in most of the UK National Health Service system, “suspected cauda equina syndrome (CES)” cases are seen by out-of-hours neurosurgery services for urgent transfer and MRI scanning. The proportion of patients with a scan-positive CES (47/198 or 24%) was consistent with a systematic review (19%)² and our retrospective study (28%).³

We think the authors have possibly misunderstood the primary purpose of our study which was especially focused on describing what is wrong with the large majority of such patients with “scan-negative” CES presentations.⁴

We do not agree that follow-up with a specific spinal specialist might have altered our outcome data. All patients were referred to a neurosurgeon who assessed their clinical and radiologic findings for evidence of “scan-positive” CES. The 137 patients in the mixed and “scan-negative” CES groups had follow-up for an average of 24 months, looking for any new neurologic or neurosurgical diagnoses that fully or partially explained their CES symptoms. Our patients with persisting neurologic symptoms continued to have spinal specialist input from a neurosurgeon or neurologist. No patients in the mixed or “scan-negative” CES groups had a presentation with “scan-positive” CES during follow-up, which is meaningful given that nearly all patients would present to local NHS services.

We do not agree with the framing of functional neurologic disorder or somatization as reattributed distress. Functional disorders are distinct entities in their own right, to which pathophysiologic and predictive cognitive processes, medications and iatrogenic factors contribute.^{5,6}

In our article, we hypothesize that pain, panic, medications, previous bladder dysfunction, or functional neurologic disorders may cause patients to present with “scan-negative” CES.

We recently created a patient factsheet, available on neurosymptoms.org (see bladder symptoms), that explains our current thinking about “scan-negative” CES. This may be helpful for patients who are left wondering what has caused their symptoms when their scans are normal.

Further research into this neglected group is required. We are glad to have interest from neurosurgeons because we try to increase awareness and optimize treatment of this group.

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Reader Response: Scan-Negative Cauda Equina Syndrome: A Prospective Cohort Study

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Hoeritzauer et al.¹ prospectively investigated the clinical presentation of 184 patients admitted for clinical suspicion of CES, among which 47 (25%) suffered from cauda equina (CE) compression on MRI, whereas 76 (41%) only showed single nerve root compression and 61 (33%) did not show any sign of compression. I congratulate the authors as they showed that approximately one-third of the patients (33%, 61/184) admitted for suspicion of CES possibly suffer from multifactorial pre-existing organic and functional disorders, including bladder dysfunction.

I would like to clarify the clinical presentation of CES. Unilateral or bilateral sciatica is usually the first symptom, followed by neurologic deficits of the lower limbs.^{2,3} Saddle anesthesia and urinary or fecal incontinence are delayed symptoms and are usually associated with a worse prognosis.^{2,3} This published study is in line with previous reports that patients with CE compression on MRI were more likely to present sciatica (83% vs 44%) and bilateral reduced or absent ankle jerk reflexes (78% vs 12%), equally likely to present perineal symptoms, and less likely to present uncontrollable back pain (41% vs 70%) or symptoms of panic attack (37% vs 70%) compared with patients with no CE compression on MRI.

Alongside clinical presentation suggestive of CES, an emergency MRI of the lumbosacral spine remains necessary to assess any mechanical cause for the symptoms.⁴ Nevertheless, in my opinion, clinicians should be taught to give rise to the diagnosis of CES in face with bilateral sciatica, with or without neurologic deficits or perineal symptoms.

1. Hoeritzauer I, Carson A, Statham P, et al. Scan-negative cauda equina syndrome: a prospective cohort study. *Neurology*. 2021;96(3):e433-e447.
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Editors' Note: Association of Age at Onset and First Symptoms With Disease Progression in Patients With Metachromatic Leukodystrophy

Metachromatic leukodystrophy is a neurodegenerative condition with a variable rate of progression that warrants more systematic investigation. In their natural history study of 98 patients with metachromatic leukodystrophy, Dr. Kehrer et al. summarize the prominent symptoms and age of symptom onset according to various forms of the illnesses (late infantile, early juvenile, late juvenile, and adult). In younger persons (under age 6 years), motor manifestations with or without cognitive impairment were common, whereas in late juvenile and adult forms, cognitive symptoms became increasingly common. Patients with earlier disease onset experienced more rapid progression. Dr. Michell-Robinson and Lépine hypothesize that arylsulfatase A activity (the defective enzyme in metachromatic leukodystrophy) and therefore buildup of toxic sulfatide levels might be related to the severity or progression of the illness. Because some older patients may also experience rapid declines, the investigators do not believe sulfatide toxicity to be the primary mediator of disease severity. They also emphasize the importance of motor system involvement as a driver of neurologic deterioration. Although there is much more to understand about this condition, it is clear now that motor symptom manifestations typically precede rapid disease progression.

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Reader Response: Association of Age at Onset and First Symptoms With Disease Progression in Patients With Metachromatic Leukodystrophy

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Kehrer et al.¹ categorized different onset forms of metachromatic leukodystrophies based on first symptoms at onset and disease progression. The genotypes associated with each of these categories seem to indicate that earlier symptom onset is associated with more severe arylsulfatase A (ARSA) deficiency.

Based on the findings of Kehrer et al., we wonder whether ARSA activity is the factor specifying disease onset based on the rate of sulfatide accumulation in tissues, whereas the neurologic manifestations at onset are determined by the system that is most vulnerable when these levels have reached some threshold. Late infantile and early juvenile stages were associated with a higher proportion of patients presenting with motor features at onset, whereas late juvenile and adult forms were associated with higher proportions of patients presenting with cognitive features at onset. In the earlier stages, motor systems are in a critical period of development, whereas cognitive development becomes increasingly important in later stages. Both processes are associated with myelination as an important factor—a process that is known to be affected by the accumulation of sulfatides in the brain. We hoped the authors would comment on this hypothesis based on their understanding of the data.

1. Kehrer C, Elgün S, Raabe C, et al. Association of age at onset and first symptoms with disease progression in patients with metachromatic leukodystrophy. *Neurology*. 2021;96(2):e255-e266.

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Author Response: Association of Age at Onset and First Symptoms With Disease Progression in Patients With Metachromatic Leukodystrophy

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We are grateful for the interest in our article.¹ Michell-Robinson and Lépine suggest that the different types of symptoms at disease onset might partly be explained by an age- or maturation-specific vulnerability of motor and cognitive brain networks, for example, their myelination. Indeed, myelination of short-range fibers happens later than of long range.² However, this does not explain the finding in our study that a disease course with a motor onset and rapid progression can occur at all ages, including late-juvenile and adult forms.

In addition, in patients with cognitive onset type and slower disease progression, we have previously shown that there is widespread deep white matter involvement at the time of diagnosis, thus involving long-range fibers but sparing the central region with the primary motor system.³ This would argue for a differential involvement of the motor system in these 2 forms of metachromatic leukodystrophies. Once the motor network is primarily affected, rapid neurologic deterioration occurs, which then includes the cognitive system—this seems independent of age of disease onset. The origin of this differential involvement remains unclear, yet our data indicate that a genetic basis could play a role.

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CORRECTION

Opinion and Special Articles: Remote Evaluation of Acute Vertigo Strategies and Technological Considerations

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The article “Opinion and Special Articles: Remote Evaluation of Acute Vertigo: Strategies and Technological Considerations” by Green et al.¹ was published under the wrong section and should have been published in the Resident & Fellow Section. The publisher regrets the error.

Reference

1. Green KE, Pogson JM, Otero-Millan J, et al. Opinion and Special Articles: Remote evaluation of acute vertigo: strategies and technological considerations. *Neurology*. 2021;96(1):34-38.

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Opinion and Special Articles: Remote Evaluation of Acute Vertigo: Strategies and Technological Considerations

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