Late-Onset Presentations: When Adult Symptoms Mask Childhood Conditions

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Clinicians often compartmentalise conditions by age of onset, assuming early-onset disorders resolve or present definitively in childhood. But a growing body of evidence challenges this, revealing that many conditions, from visual impairments to immunodeficiencies, manifest or persist with distinct patterns in adulthood, often mimicking other pathologies. This requires a shift in diagnostic thinking, moving beyond rigid age-based classifications to consider a broader differential.

KEY TAKEAWAYS

- The Pivot: Conditions previously considered childhood-exclusive, like Cerebral Visual Impairment, persist into adulthood with unique presentations, and late-onset brain injuries can mimic these.
- The Data: The HVFQI-59Q effectively detected higher visual function deficits in adults with early-onset CVI and those with late-onset brain injury, with the latter showing a broader range of deficits and lower median values.
- The Action: Clinicians should consider a wider differential for adult-onset symptoms, including conditions typically associated with childhood or rare late-onset manifestations of genetic or acquired disorders.

The assumption that conditions with early-onset origins remain confined to paediatric practice is increasingly untenable. Cerebral Visual Impairment (CVI), for instance, has historically been studied predominantly in children, despite being recognised as a lifelong condition. A recent prospective controlled study published in PLoS One investigated higher visual function deficits (HVFDs) in adults with early-onset CVI, comparing them to neurotypical adults and a cohort of children with CVI.1

The study enrolled 67 neurotypical adults (ANTs) to assess the feasibility of an adapted HVF Question Inventory (HVFQI-59Q) for detecting HVFDs. Researchers then compared HVFD patterns in 29 adults with early-onset CVI (A-Early Onset) and 22 adults with late-onset brain injury (A-Late Onset) against a previously interviewed cohort of 92 children with CVI and 120 child neurotypicals. Chandna and colleagues used the HVFQI-59Q to evaluate the spectrum and severity of HVFDs across the adult groups.1

Visual Deficits Persist and Evolve

HVFDs are indeed present in adults with early-onset CVI, showing both similarities and distinct differences compared to children. The A-Early Onset group demonstrated persistent deficits. But the A-Late Onset group exhibited a broader range of deficits and lower median values, indicating greater variability in visual impairments.1 These findings challenge previous assumptions about localised effects of brain injury and highlight the need for a review of terminology for A-Late

Onset presentations.1 The HVFQI-59Q proved an effective clinical tool for detecting HVFDs, supporting continuous CVI evaluation across the lifespan.1

This re-evaluation of CVI in adults highlights a broader theme: conditions with a clear paediatric presentation can manifest or persist in adult life with altered characteristics. Clinicians should not dismiss visual complaints in adults as purely age-related without considering underlying neurological causes, especially given the potential for late-onset brain injuries to mimic CVI. The Oxford Handbook of Neurology offers a practical quick-reference for such complex neurological presentations.

Immunodeficiency Unmasked Decades Later

Another striking example of late-onset presentation comes from the field of immunology. A case report published in Cureus detailed a patient diagnosed with cryptococcal meningitis, which ultimately revealed a late-onset combined immunodeficiency after two decades of recurrent infections.2 This patient's history of chronic, unexplained infections should have raised red flags earlier, but the diagnosis of a primary immunodeficiency was delayed until a severe, opportunistic infection forced a deeper investigation.2

The patient's journey highlights a critical diagnostic gap: recurrent infections in adults, even if seemingly managed, warrant thorough immunological workups, not just symptomatic treatment. The case shows that immunodeficiencies are not exclusively paediatric conditions; they can smoulder for years, only to erupt dramatically in adulthood. This mirrors the challenges in diagnosing dementia in older adults, where early, subtle signs are often overlooked or attributed to normal aging.

Hyperammonemia: A Metabolic Surprise

Metabolic disorders, too, can present unexpectedly in adulthood. Adult-onset hyperammonemia, a condition often associated with paediatric inborn errors of metabolism, was the subject of a case report and literature review in Case Reports in Gastroenterology.3 The authors, Naseem and colleagues, described a patient presenting with neurological symptoms that, upon investigation, were linked to elevated ammonia levels.3

Hyperammonemia in adults can stem from various causes, including liver disease, drug-induced toxicity, or, less commonly, late-onset presentations of urea cycle disorders. The case report emphasised the importance of considering hyperammonemia in the differential diagnosis for adults with unexplained encephalopathy, even in the absence of overt liver failure.3 This is particularly relevant when considering the risk factors for cognitive decline, where metabolic disturbances can play a significant role. The diagnostic challenge lies in the non-specific nature of the neurological symptoms, which can easily be misattributed to more common conditions.3

The Broader Implications for Adult Practice

These cases collectively argue for a more expansive diagnostic approach in adult clinics. The traditional boundaries between paediatric and adult medicine, particularly for conditions with a genetic or developmental origin, are blurring. Clinicians must maintain a high index of suspicion for rare or late-onset presentations of conditions typically considered outside their immediate specialty. This means moving beyond the immediate, obvious diagnosis and considering the patient's full medical history, including any unexplained symptoms or recurrent issues from childhood or adolescence. The HVFQI-59Q, for example, offers a structured approach to visual assessment that could be integrated into adult neurological evaluations.1

The variability seen in the A-Late Onset CVI group suggests that brain injury at different developmental stages or from different etiologies can lead to a diverse array of visual deficits.1 This complexity demands a more individualised assessment rather than a one-size-fits-all diagnostic label. Similarly, the immunodeficiency case highlights the need for vigilance in patients with a long history of infections, even if they appear to be managing.2 The cryptococcal meningitis was not an isolated event but the culmination of decades of an underlying, undiagnosed issue.2

The hyperammonemia case reinforces that metabolic pathways, even those with clear genetic underpinnings, can decompensate later in life, often triggered by stressors like infection, surgery, or certain medications.3 These late-onset presentations are not anomalies but rather a demonstration of the complex relationship between genetics, environment, and the aging process. The challenge for general practitioners and specialists alike is to recognise these subtle cues and pursue further investigation, rather than defaulting to the most common diagnoses. This often requires a deeper dive into patient history and a willingness to consult across specialties, akin to the multidisciplinary approach needed for complex cognitive decline in super-agers.

The open-label design of the CVI study is an obvious caveat, as patient-reported outcomes can be influenced by awareness of their condition. But the consistency of the HVFQI-59Q across different adult groups still provides valuable insights. The case reports, by their nature, offer limited generalisability, but they serve as important reminders of diagnostic possibilities often overlooked in busy clinical settings. The lack of extensive longitudinal data on early-onset CVI into older adulthood remains a gap. Future research needs to track these patients to understand the full trajectory of their visual function and how it impacts quality of life over decades. This will further refine our understanding of how conditions evolve and present across the lifespan.

CLINICAL IMPLICATIONS

Clinicians must abandon the rigid notion that certain conditions are strictly paediatric. The evidence is clear: early-onset CVI persists, and late-onset brain injuries can mimic it, demanding a more comprehensive visual assessment in adults. The HVFQI-59Q is a tool that should be in every neurologist's arsenal, not just paediatric ophthalmologists.

The immunodeficiency and hyperammonemia cases are stark reminders that recurrent infections or unexplained encephalopathy in adults are not always straightforward. They can be the tip of an iceberg, revealing decades-long underlying conditions that have finally decompensated. A thorough history and a willingness to investigate beyond the obvious are paramount.

This shift requires a broader differential diagnosis and a greater readiness to consult with specialists in genetics, immunology, and metabolic medicine, even for seemingly common adult presentations. The cost of delayed diagnosis in these late-onset cases is significant, both for patient morbidity and healthcare resources. We must train ourselves to look for the unusual within the usual.

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