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A Clinical Perspective on Adult Cerebral Atrophy in Chronic Alcohol Use: Considering the Role of Neurotropic TORCH-Related Viruses (CMV, HSV-1, and Rubella)

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Abstract

Chronic alcohol use is a well-recognized cause of cerebral atrophy and ventricular enlargement in adults. Neurotropic viral infections, including cytomegalovirus (CMV), herpes simplex virus type 1 (HSV-1), and rubella virus—pathogens traditionally grouped within the TORCH framework—may also contribute to central nervous system injury, particularly in states of immune dysfunction. This descriptive observational study draws on routine clinical observations of eight adults aged 42–65 years with long-standing alcohol use who presented with neurological symptoms at a district-level hospital with referral access to tertiary care. Non-contrast computed tomography imaging demonstrated diffuse cerebral atrophy with proportional ventricular enlargement consistent with hydrocephalus ex vacuo rather than true hydrocephalus. Clinical history and available serological data suggested prior exposure to CMV, HSV-1, and/or rubella in several patients, without evidence of acute viral encephalitis. Integrating these observations with a narrative review of the literature, this article explores plausible mechanisms through which alcohol-related neurotoxicity, immune dysregulation, and latent or prior neurotropic viral exposure may interact to accelerating neuronal injury, with particular vulnerability of temporal lobe structures. These mechanisms are discussed as hypothesized associations rather than proven causal relationships. Recognition of these interactions is clinically relevant for practitioners evaluating alcohol-exposed adults with cerebral atrophy and ventricular enlargement, especially in resource-limited settings where advanced neuroimaging and molecular viral diagnostics are not readily available.

Keywords*: Chronic Alcohol Use, Cerebral Atrophy, Cytomegalovirus, Herpes Simplex Virus Type 1, Hydrocephalus Ex Vacuo, Rubella, TORCH Infections.*

Introduction

Chronic alcohol use is a well-established cause of structural and functional brain injury in adults, frequently manifesting as diffuse cerebral and cerebellar atrophy accompanied by ventricular enlargement on neuroimaging [1, 2]. Clinically affected individuals may present with cognitive impairment, gait disturbance, seizures, or neuropsychiatric symptoms, while radiological findings may raise concern for hydrocephalus. In many cases, however, ventricular enlargement reflects loss of surrounding brain parenchyma rather than disturbed cerebrospinal fluid (CSF) dynamics, a phenomenon referred to as hydrocephalus ex vacuo [3]. Differentiating these entities remains a diagnostic challenge, particularly in district-level and resource-limited settings where computed tomography (CT) predominates.

Neurotropic viral infections represent an additional, often under-recognized contributor to adult central nervous system (CNS) injury. Several pathogens traditionally grouped under

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the TORCH acronym—Toxoplasma gondii, Other (including syphilis), Rubella virus, Cytomegalovirus (CMV), and Herpes simplex virus (HSV)—are classically associated with congenital neurological disease but are also capable of causing CNS pathology later in life, particularly in immunocompromised hosts [4]. Among these, CMV and herpes simplex virus type 1 (HSV-1) are notable for their ability to establish lifelong latency within neural tissue, with potential for reactivation under conditions of impaired cell-mediated immunity [5, 6].

HSV-1 is highly prevalent globally and remains the most common cause of sporadic viral encephalitis in adults. Even in the absence of fulminant encephalitis, HSV-1 infection has been associated with persistent neuroinflammation, residual cerebral atrophy, and long-term cognitive sequelae following clinical or subclinical CNS involvement [7]. Similarly, CMV infection in adults—particularly when reactivated—may result in encephalitis, ventriculoencephalitis, or chronic inflammatory processes that contribute to neuronal loss and cerebral atrophy [5]. Although rubella infection in adults is typically mild, rare cases of rubella-associated encephalitis and immune-mediated neurological sequelae have been reported, especially in under-immunized populations [8].

Chronic alcohol consumption is increasingly recognized as a state of functional immune suppression. Alcohol disrupts innate and adaptive immune responses, impairs T-cell and natural killer cell function, alters cytokine signaling, and compromises blood–brain barrier integrity [9]. These effects increase susceptibility to infection and facilitate reactivation of latent neurotropic viruses, including CMV and HSV-1. In this context, alcohol-related neurotoxicity and viral-mediated CNS injury may plausibly act synergistically, amplifying neuroinflammation and accelerating cerebral atrophy beyond that attributable to alcohol alone [10].

Despite the biological plausibility of interactions between chronic alcohol use and neurotropic viral infections, the contribution of TORCH-related pathogens to adult cerebral atrophy remains underexplored in clinical literature. This gap is particularly relevant in district hospital settings, where patients often present late in the disease course, diagnostic resources are limited, and viral exposure may be inferred from clinical history and serology rather than advanced molecular testing. Although seropositivity for CMV, HSV-1, and rubella is common in the general population, its interpretation in individuals with chronic alcohol use requires careful consideration of immune dysfunction, cumulative neurological injury, and the potential for viral reactivation rather than assumptions of direct causality.

Accordingly, this article presents a clinical perspective based on observations from a district-level hospital with referral access to tertiary care, where adults with long-standing alcohol use demonstrated cerebral atrophy and ventricular enlargement in association with clinical suspicion or serological evidence of CMV, HSV-1, and rubella exposure. By integrating routine clinical observations with a narrative review of the literature, the paper explores hypothesized mechanisms through which alcohol-related neurotoxicity, immune dysfunction, and prior exposure to neurotropic viruses may interact to influence adult brain structure. These associations are presented explicitly as hypothesis-generating rather than established causal relationships, with the aim of informing diagnostic reasoning and clinical interpretation in resource-limited settings.

Literature Review

Chronic Alcohol Use and Structural Brain Changes

Chronic alcohol consumption is strongly associated with structural brain abnormalities, most notably diffuse cerebral and cerebellar atrophy [11]. Neuroimaging studies consistently demonstrate reductions in total

brain volume, cortical thinning, white matter loss, and ventricular enlargement among individuals with alcohol use disorder [1, 3]. The extent of these changes is closely related to the duration and intensity of alcohol exposure.

The pathophysiology of alcohol-related brain injury is multifactorial and includes direct neurotoxicity of ethanol and its metabolites, oxidative stress, glutamate-mediated excitotoxicity, neuroinflammation, and disruption of neurogenesis [2]. Nutritional deficiencies, particularly thiamine deficiency, further contribute to selective vulnerability of regions such as the mammillary bodies, thalamus, and cerebellum [1].

Ventricular enlargement observed in chronic alcohol use is typically attributable to loss of surrounding brain parenchyma rather than altered cerebrospinal fluid (CSF) dynamics. This phenomenon, known as hydrocephalus ex vacuo, may radiologically resemble true hydrocephalus but is distinguished by normal or reduced intracranial pressure and absence of obstructive pathology [3]. Accurate differentiation is clinically important, as misinterpretation may result in unnecessary neurosurgical referral or intervention.

Longitudinal imaging studies suggest partial reversibility of alcohol-related brain changes with sustained abstinence, particularly within white matter tracts. However, persistent cortical and cerebellar volume loss has been documented in individuals with prolonged or severe exposure [11, 12]. These findings indicate that while some alcohol-induced changes may be dynamic, a substantial proportion of neuronal injury becomes irreversible, increasing susceptibility to additional neurotoxic or inflammatory insults.

Neurotropic Viruses and Adult Central Nervous System Injury

Neurotropic viruses can infect neural tissue and produce both acute and chronic central nervous system (CNS) pathology. In adults, viral CNS disease ranges from fulminant encephalitis to subclinical infection with long-term neurological sequelae, including residual cerebral atrophy [13]. Mechanisms of injury include direct cytopathic effects, immune-mediated inflammation, and interference with neural repair processes [4].

Several viruses associated with CNS injury are included in the TORCH group, a classification traditionally applied to congenital infections. However, many TORCH pathogens remain clinically relevant in adults, particularly in immunocompromised states, where they may contribute to encephalitis, chronic neuroinflammation, and residual cerebral atrophy [6].

Cytomegalovirus (CMV) and Adult Cerebral Atrophy

Cytomegalovirus is a ubiquitous herpesvirus that establishes lifelong latency following primary infection. Although infection is usually asymptomatic in immunocompetent adults, CMV reactivation is well documented in individuals with impaired cell-mediated immunity, including those with HIV infection, organ transplant recipients, and patients with chronic systemic illness [5].

CMV exhibits tropism for glial cells and neurons and can cause CNS pathology through both direct viral replication and immune-mediated mechanisms. Adult CMV encephalitis and ventriculoencephalitis have been associated with neuroimaging findings such as periventricular abnormalities, cortical and subcortical atrophy, and ventricular enlargement [4]. In some cases, chronic or recurrent infection results in progressive neuronal loss and persistent neurocognitive impairment.

Importantly, CMV-related CNS involvement may be clinically subtle. Low-grade neuroinflammation and sustained microglial activation have been proposed as mechanisms by which CMV contributes to cumulative brain injury over time [5]. In immunocompromised populations, this pattern

has been described as a "smouldering encephalopathy," characterized by persistent inflammation, gradual neuronal loss, and progressive cognitive decline without overt encephalitis [14, 15]. While extrapolation to alcohol-exposed but otherwise immunocompetent adults must be cautious, alcohol-induced immune dysfunction may create a permissive environment for similar subclinical processes.

Herpes Simplex Virus Type 1 (HSV-1) and Adult CNS Disease

HSV-1 is among the most prevalent neurotropic viruses globally and remains the leading cause of sporadic viral encephalitis in adults [6]. Following primary infection, HSV-1 establishes lifelong latency in sensory ganglia and may reactivate under conditions of immune suppression or physiological stress.

Acute HSV-1 encephalitis is characterized by focal necrotizing inflammation with a predilection for the medial temporal and inferior frontal lobes—regions essential for memory, behavior, and executive function [7]. Survivors often demonstrate residual neurological deficits, including cognitive impairment and focal temporal lobe atrophy on follow-up imaging.

Beyond acute encephalitis, emerging evidence suggests that recurrent or subclinical HSV-1 reactivation may contribute to progressive brain changes through persistent neuroinflammatory signaling, microglial activation, and synaptic dysfunction [16–18]. Although these mechanisms remain largely hypothesis-driven in humans, they are supported by converging experimental and epidemiological data. In individuals with chronic alcohol use, HSV-1–associated neuroinflammation may exacerbate pre-existing alcohol-related neurotoxicity, particularly within vulnerable cortical regions.

Rubella Virus and Neurological Sequelae in Adults

Rubella virus is best recognized for its role in congenital rubella syndrome, where CNS manifestations include microcephaly, cerebral atrophy, and progressive encephalopathy. Postnatal rubella infection in adults is typically mild; however, rare cases of rubella-associated encephalitis and immune-mediated neurological sequelae have been reported [8].

Adult rubella encephalitis is thought to be primarily immune-mediated rather than the result of direct viral cytotoxicity. Reported sequelae include seizures, cognitive impairment, and residual cerebral atrophy. In settings with incomplete vaccination coverage, adult exposure remains possible, and prior rubella infection may contribute modestly to cumulative neurological injury, particularly when compounded by alcohol-related neurotoxicity or immune dysfunction.

TORCH Pathogens as a Conceptual Framework in Adult Neurology

Although TORCH infections are classically discussed in congenital disease, the pathogens within this group share features relevant to adult neurological pathology, including neurotropism, capacity for latency or persistence, and the potential to induce immune-mediated CNS injury [4]. In adults, TORCH-related pathogens such as CMV and HSV-1 are particularly relevant in immunocompromised states, where reactivation may lead to encephalitis, chronic inflammation, or progressive neuronal loss.

Reframing TORCH pathogens as a conceptual framework rather than a diagnostic category allows clinicians to consider cumulative infectious exposures interacting with host factors—such as chronic alcohol use—when evaluating complex neurological presentations.

Alcohol-Induced Immune Dysfunction and Viral Reactivation

Chronic alcohol consumption exerts profound effects on immune function, including impaired antigen presentation, reduced T-cell proliferation, altered cytokine signaling, and dysfunction of natural killer cells [9]. Alcohol also compromises blood–brain barrier integrity, increasing CNS vulnerability to systemic inflammatory and infectious insults.

These immunological alterations facilitate reactivation of latent viruses, particularly herpesviruses such as CMV and HSV-1. Viral reactivation within the CNS may trigger sustained microglial activation and chronic neuroinflammation, thereby contributing to progressive neuronal injury [10]. Alcohol-related immune suppression has been shown to impair viral clearance and dysregulate inflammatory responses, providing a biologically plausible basis for synergistic interactions between chronic alcohol use and neurotropic viral persistence or reactivation [4, 19, 20].

Methods

Study Design

This study employed a descriptive observational design based on routine clinical observations. It was conducted as a retrospective case series without intervention, hypothesis testing, or inferential statistical analysis. The primary aim was to characterize clinical and neuroimaging patterns in adults with chronic alcohol use and to explore plausible explanatory mechanisms through integration with existing literature.

Study Setting

The study was conducted at a district-level hospital in Namibia with referral access to tertiary care services. The facility serves a mixed urban and peri-urban population and operates with limited on-site diagnostic resources. Non-contrast computed tomography (CT) represents the primary neuroimaging modality available for neurological assessment in this setting.

Study Population and Eligibility Criteria

Eight adult patients aged 42–65 years were included. Patients were identified consecutively through routine clinical care during the observation period, and no formal sampling strategy was employed.

Eligibility criteria included documented long-standing alcohol use, presentation with neurological symptoms warranting neuroimaging, and availability of CT findings. Patients with clinical or radiological evidence of acute central nervous system infection, intracranial mass lesions, or recent head trauma were excluded.

Clinical Assessment and Data Collection

Clinical data were obtained from medical records and supplemented by direct clinical evaluation where applicable. Information collected included demographic characteristics (age and sex), alcohol use history, neurological presentation, relevant medical history, and available laboratory findings.

Assessment of infectious history was based on documented clinical information and serological results obtained as part of routine patient care. Data on prior exposure to neurotropic viral infections were derived from available serology and clinical history. No additional laboratory testing was performed for research purposes.

Neuroimaging Assessment

All patients underwent non-contrast CT of the brain as part of standard clinical management. Imaging findings were reviewed descriptively, with attention to patterns of cerebral atrophy and ventricular enlargement. Ventricular dilatation was interpreted in relation to the degree of parenchymal loss to distinguish hydrocephalus ex vacuo from obstructive or communicating hydrocephalus.

Data Analysis

Data analysis was descriptive. Given the small sample size, no statistical comparisons or modeling were performed. Findings are presented narratively and in aggregate, emphasizing common clinical and radiological patterns.

Ethical Considerations

This study was based exclusively on anonymized clinical data derived from routine patient care. No patient identifiers were collected or retained, and no additional investigations or interventions were undertaken for research purposes.

Results

Patient Characteristics

Eight adult patients were included in the analysis. Ages ranged from 42 to 65 years, and the majority were male. All patients had a documented history of long-standing alcohol use extending over several years.

Clinical Presentation

Patients presented with a range of neurological manifestations, including cognitive impairment, gait disturbance, behavioral changes, seizures, and altered level of consciousness. Several individuals had a history of recurrent hospital admissions related to alcohol use.

Neuroimaging Findings

Non-contrast CT imaging demonstrated diffuse cerebral atrophy in all patients, accompanied by ventricular enlargement. Ventricular dilatation was proportional to parenchymal loss, consistent with hydrocephalus ex vacuo [2, 3], rather than obstructive or communicating hydrocephalus. No focal intracranial mass lesions or imaging features suggestive of acute infection were identified.

Infectious History and Serology

Clinical history and available laboratory data suggested prior exposure to neurotropic viral infections. CMV and HSV-1 seropositivity were documented in several patients, while rubella exposure was inferred from serological findings or historical information in selected cases. No patient exhibited clinical features of acute viral encephalitis at presentation. Serological results were interpreted as evidence of prior exposure rather than active infection.

Discussion

This clinical perspective explores the potential interplay between chronic alcohol use and neurotropic viral exposure—particularly cytomegalovirus (CMV), herpes simplex virus type 1 (HSV-1), and rubella virus—in contributing to adult cerebral atrophy. Although the descriptive nature of the observations does not permit causal inference, the findings raise clinically relevant hypotheses regarding synergistic mechanisms of neuronal injury in alcohol-exposed populations.

Alcohol Use as a Central Modifying Factor

Chronic alcohol consumption is a well-established cause of diffuse cerebral and cerebellar atrophy. Beyond its direct neurotoxic effects, alcohol induces a state of functional immune suppression characterized by impaired cell-mediated immunity, altered cytokine signaling, and disruption of blood–brain barrier integrity [9]. These immunological alterations increase susceptibility to infection and facilitate reactivation of latent neurotropic viruses.

In this context, alcohol may be conceptualized not only as an independent etiological factor but also as a biological amplifier that enhances the neurological impact of prior or concurrent viral exposures. In the present series, all patients had prolonged histories of alcohol use, supporting alcohol-related neurotoxicity as the dominant substrate upon which additional infectious or

inflammatory factors may act. By simultaneously promoting neuronal injury and impairing immune surveillance, chronic alcohol use may lower the threshold at which latent or subclinical viral activity becomes clinically relevant. This multifactorial framework supports a model of cumulative cerebral injury rather than a single-agent disease process.

Neurotropic Viral Reactivation and Chronic Neuroinflammation

Both CMV and HSV-1 establish lifelong latency within neural or immune cells and may reactivate in states of immune dysfunction [5, 6]. Viral reactivation within the central nervous system (CNS), even in the absence of overt encephalitis, can promote neuronal injury through direct cytopathic effects, sustained microglial activation, and chronic neuroinflammatory signaling.

HSV-1 is the most common cause of sporadic viral encephalitis in adults, and survivors frequently demonstrate residual focal or diffuse cerebral atrophy on follow-up imaging [7]. Emerging experimental and epidemiological evidence suggests that recurrent or subclinical HSV-1 reactivation may plausibly contribute to progressive neurodegeneration through persistent inflammatory mechanisms, particularly affecting temporal lobe structures [16–18]. This regional vulnerability is clinically relevant given the overlap between temporal lobe dysfunction and the cognitive, behavioral, and seizure-related manifestations commonly observed in chronic alcohol use. Although regional involvement could not be specifically assessed using computed tomography in this series, the well-described temporal lobe predilection of HSV-1 in the literature provides a plausible explanatory framework.

CMV similarly contributes to CNS injury through immune-mediated pathways. In immunocompromised populations, CMV encephalitis and ventriculoencephalitis have been associated with periventricular injury, ventricular enlargement, and cerebral atrophy [4, 14, 15]. A pattern of low-grade or "smouldering" encephalopathy has been described in transplant recipients and individuals living with HIV, characterized by persistent inflammation and gradual neuronal loss without overt encephalitis. While extrapolation to immunocompetent adults must be cautious, alcohol-induced immune dysfunction may create a permissive environment in which similar subclinical CMV-related neuroinflammatory processes contribute to cumulative brain injury.

Taken together, these observations support a hypothesis in which alcohol-related immune dysregulation permits episodic or persistent viral-driven neuroinflammation, thereby amplifying alcohol-associated neurotoxicity. Importantly, these relationships remain associative and hypothesis-generating rather than proven.

Rubella and Cumulative Neurological Injury

Rubella virus is best recognized for its role in congenital neurological disease; however, rare adult neurological complications, including encephalitis and immune-mediated sequelae, have been reported [8]. In under-immunized populations, prior rubella exposure may contribute subtly to cumulative CNS injury that becomes clinically apparent in the presence of additional neurotoxic or immunosuppressive factors.

In the present context, rubella is unlikely to represent a primary cause of adult cerebral atrophy. Rather, it may function as a minor contributory factor within a broader milieu of alcohol-related neurotoxicity, immune dysregulation, and exposure to other neurotropic viruses. As with CMV and HSV-1, seropositivity alone should not be interpreted as evidence of causation.

TORCH Pathogens as a Conceptual Framework in Adult Neurology

Although the TORCH classification was originally developed for congenital infections, the pathogens included share characteristics—neurotropism, immune-mediated injury, and potential for latency or persistence—that remain relevant in adult neurological disease [4]. Reframing TORCH pathogens as a conceptual framework rather than a diagnostic category allows clinicians to consider cumulative infectious exposures alongside host vulnerability factors such as chronic alcohol use.

Importantly, this perspective does not imply the existence of an adult TORCH syndrome. Instead, it provides a lens through which multiple low-grade or historical infectious insults may be integrated into the clinical assessment of adults presenting with non-specific neurological syndromes, particularly in settings with limited diagnostic resources.

Ventricular Enlargement: Hydrocephalus or Hydrocephalus Ex Vacuo?

A key clinical implication of this analysis relates to the interpretation of ventricular enlargement on neuroimaging. In individuals with chronic alcohol use, ventricular dilatation most commonly reflects hydrocephalus ex vacuo secondary to parenchymal loss rather than disturbed cerebrospinal fluid dynamics. Viral-mediated neuronal injury may further accentuate this process, leading to imaging findings that mimic true hydrocephalus.

Accurate differentiation is critical, especially in district-level settings where CT imaging predominates. Misclassification may result in unnecessary referral or invasive intervention. Comprehensive clinical assessment—integrating alcohol history, neurological findings, and cautious interpretation of serological results—is therefore essential.

Clinical and Public Health Implications

Clinically, these observations highlight the importance of maintaining a broad differential diagnosis when evaluating adults with chronic alcohol use and neurological symptoms. Awareness of potential interactions between alcohol-related neurotoxicity, immune dysfunction, and prior neurotropic viral exposure may improve diagnostic reasoning and prevent misinterpretation of imaging or serological findings.

From a public health perspective, the findings underscore the importance of alcohol use disorder prevention, improved vaccination coverage, and integrated care approaches addressing both infectious and non-communicable contributors to neurological disease. In resource-limited settings, heightened clinical awareness of these interactions may support conservative management, reduce unnecessary interventions, and inform targeted follow-up and preventive strategies.

Limitations

This study is limited by its small sample size, descriptive design, reliance on computed tomography rather than advanced neuroimaging, and incomplete serological data. No inferential statistical analysis was performed. These limitations restrict generalizability and preclude causal inference.

Conclusion

Adults with long-standing alcohol use may exhibit cerebral atrophy and ventricular enlargement consistent with hydrocephalus ex vacuo. While alcohol-related neurotoxicity remains the primary explanatory factor, immune dysfunction and prior exposure to neurotropic viruses such as CMV, HSV-1, and rubella may plausibly contribute to cumulative brain injury. Further prospective studies incorporating advanced imaging and immunovirological assessment are warranted.

Ethical Clearance

This article is based on anonymized clinical observations from routine patient care. No patient identifiers were included, and formal ethical approval was not required under applicable institutional and national guidelines.

Author Contributions

The author conceived the study, collected and analyzed the clinical data, conducted the literature review, and drafted and revised the manuscript.

Data Availability

Data supporting the findings of this study are available from the author upon reasonable request.

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Conflict of Interest

The author declares no conflict of interest.

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