AAMS Dentistry & Oral Sciences
ISSN: 2834-7120 (Print) | eISSN: 2834-7121 (Online)
Volume 07, Issue 05, Pages 1-15
DOI: 10.4103/aams.0498
ORIGINAL ARTICLE

DIFFERENTIAL DIAGNOSIS OF CHRONIC ENCEPHALITIS VS. NEURODEGENERATIVE DISEASES (ALZHEIMER'S DISEASE AND FRONTOTEMPORAL DEMENTIA)

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Received: 2026-03-11 · Accepted: 2026-04-09

Abstract

Chronic encephalitis and neurodegenerative disorders such as Alzheimer's disease and frontotemporal dementia represent complex neurological conditions characterized by progressive cognitive decline, behavioral disturbances, neuropsychiatric manifestations, and impairment of functional activity. Despite similarities in clinical presentation, these disorders differ significantly in etiology, pathophysiology, inflammatory activity, neuroimaging characteristics, cerebrospinal fluid biomarkers, progression patterns, and therapeutic response. Accurate differential diagnosis is critically important because chronic encephalitis may be reversible or partially treatable if identified during early stages, whereas neurodegenerative diseases are usually characterized by progressive neuronal degeneration and irreversible cognitive deterioration. Chronic encephalitis involves persistent inflammatory processes affecting the central nervous system and may result from autoimmune, viral, paraneoplastic, infectious, or immune-mediated mechanisms. Long-standing inflammation contributes to neuronal dysfunction, gliosis, synaptic disruption, and diffuse cerebral injury leading to cognitive impairment and psychiatric symptoms. Alzheimer's disease is primarily associated with accumulation of beta-amyloid plaques and hyperphosphorylated tau protein causing progressive cortical atrophy and memory dysfunction. Frontotemporal dementia is characterized by degeneration of frontal and temporal lobes accompanied by behavioral abnormalities, executive dysfunction, language impairment, and personality changes. Clinical differentiation among these disorders requires comprehensive neurological evaluation including neuropsychological testing, magnetic resonance imaging, electroencephalography, cerebrospinal fluid analysis, autoimmune antibody screening, molecular biomarkers, and assessment of inflammatory activity. Neuroimaging studies play an essential role in identifying inflammatory lesions, cortical atrophy patterns, hippocampal degeneration, white matter abnormalities, and metabolic changes. Cerebrospinal fluid analysis additionally contributes to diagnosis through detection of inflammatory markers, oligoclonal bands, viral antibodies, tau proteins, amyloid alterations, and neuronal injury biomarkers. Early recognition of chronic encephalitis is especially important because immunotherapy, antiviral treatment, corticosteroids, plasmapheresis, and immunomodulatory strategies may significantly improve neurological outcomes. Advances in neuroimmunology, molecular diagnostics, biomarker research, and neuroimaging technologies have substantially improved differentiation between inflammatory encephalitic conditions and primary neurodegenerative disorders. Comprehensive understanding of clinical, radiological, immunological, and pathological differences therefore remains essential for accurate diagnosis, optimization of therapeutic strategies, and improvement of long-term neurological prognosis.

Keywords: Chronic encephalitis, Alzheimer's disease, frontotemporal dementia, neurodegeneration, cognitive impairment, neuroinflammation, differential diagnosis, MRI, cerebrospinal fluid, autoimmune encephalitis, dementia

1. Introduction

Differential diagnosis between chronic encephalitis and neurodegenerative diseases represents a major challenge in modern neurology because these disorders frequently demonstrate overlapping clinical manifestations including memory impairment, behavioral disturbances, executive dysfunction, psychiatric symptoms, and progressive decline of cognitive function. Accurate identification of the underlying pathological process is critically important because inflammatory encephalitic disorders may respond to immunological or antimicrobial treatment, whereas neurodegenerative diseases are generally characterized by irreversible neuronal loss and gradual progression despite symptomatic therapy. Chronic encephalitis refers to persistent inflammatory involvement of the brain parenchyma resulting from autoimmune, viral, infectious, paraneoplastic, or immune-mediated mechanisms. Chronic neuroinflammation contributes to neuronal injury, synaptic dysfunction, gliosis, and disruption of cerebral connectivity leading to progressive neurological and psychiatric manifestations. Autoimmune encephalitis has become increasingly recognized as an important cause of potentially reversible cognitive decline and psychiatric abnormalities. Antibodies directed against neuronal surface antigens, synaptic proteins, or intracellular neuronal structures contribute to inflammatory dysfunction affecting limbic structures, cerebral cortex, basal ganglia, and white matter regions. Viral encephalitis may additionally produce chronic inflammatory consequences associated with persistent infection, immune activation, and secondary neurodegeneration. Alzheimer's disease represents the most common neurodegenerative disorder and is characterized by accumulation of extracellular beta-amyloid plaques and intracellular neurofibrillary tangles composed of hyperphosphorylated tau protein. Progressive cortical atrophy primarily affects hippocampal and temporoparietal regions leading to episodic memory impairment, cognitive decline, language dysfunction, and deterioration of daily activities. Frontotemporal dementia constitutes a heterogeneous group of neurodegenerative disorders involving degeneration of frontal and temporal lobes accompanied by behavioral disinhibition, executive dysfunction, emotional disturbances, language abnormalities, and personality changes. Unlike Alzheimer's disease, frontotemporal dementia often presents at younger age and may initially preserve episodic memory while significantly affecting behavior and social cognition. Clinical overlap between chronic encephalitis and neurodegenerative diseases frequently complicates diagnostic evaluation. Patients with autoimmune or chronic inflammatory encephalitis may demonstrate memory loss, confusion, hallucinations, emotional instability, depression, psychosis, and executive dysfunction resembling primary dementia syndromes. Conversely, neurodegenerative diseases may occasionally exhibit inflammatory responses, psychiatric manifestations, or atypical progression patterns leading to diagnostic uncertainty. Neuroimaging techniques including magnetic resonance imaging, functional imaging, and positron emission tomography provide important diagnostic information regarding cortical atrophy, inflammatory lesions, hippocampal abnormalities, white matter changes, and metabolic dysfunction. Cerebrospinal fluid analysis additionally contributes to differential diagnosis through detection of inflammatory cells, oligoclonal bands, neuronal antibodies, viral markers, tau proteins, beta-amyloid alterations, and biomarkers of neuronal degeneration. Electroencephalography may reveal epileptiform activity or diffuse slowing more commonly associated with encephalitic disorders. Advances in neuroimmunology, molecular pathology, biomarker analysis, and neuroimaging have substantially improved recognition of chronic inflammatory encephalitic syndromes previously misdiagnosed as primary neurodegenerative conditions. Early diagnosis remains critically important because prompt immunotherapy, corticosteroids, plasmapheresis, intravenous immunoglobulins, and targeted immunomodulatory treatment may prevent irreversible neuronal damage and significantly improve neurological outcomes in patients with chronic encephalitis. Comprehensive understanding of clinical features, inflammatory mechanisms, neurodegenerative processes, imaging patterns, and biomarker profiles therefore remains essential for accurate differentiation between chronic encephalitic disorders and neurodegenerative dementias.

2. Materials and Methods

The study was conducted through comparative clinical and diagnostic evaluation of patients presenting with chronic cognitive decline, behavioral disturbances, psychiatric manifestations, and progressive neurological dysfunction suggestive of chronic encephalitis, Alzheimer's disease, or frontotemporal dementia. Clinical neurological examination included assessment of cognitive function, memory impairment, executive performance, behavioral abnormalities, speech disturbances, emotional changes, and motor symptoms. Neuropsychological testing was performed using standardized cognitive assessment scales evaluating attention, language, orientation, executive function, and memory capacity. Magnetic resonance imaging was used to identify cortical atrophy, inflammatory lesions, hippocampal degeneration, white matter abnormalities, and temporal or frontal lobe involvement. Cerebrospinal fluid analysis included evaluation of inflammatory markers, oligoclonal bands, neuronal antibodies, viral antibodies, tau proteins, beta-amyloid levels, and biomarkers of neuronal injury. Electroencephalography was additionally performed to detect diffuse cerebral dysfunction or epileptiform activity. Laboratory investigations included autoimmune screening, infectious disease markers, inflammatory parameters, and metabolic assessment. Comparative analysis was conducted between inflammatory encephalitic conditions and neurodegenerative dementias according to clinical progression, neuroimaging characteristics, biomarker profiles, and treatment response.

3. Results

Clinical evaluation demonstrated that patients with chronic encephalitis frequently exhibited subacute onset of cognitive decline accompanied by psychiatric symptoms, seizures, fluctuating confusion, sleep disturbances, emotional instability, and rapid progression of neurological dysfunction. Autoimmune encephalitis patients commonly demonstrated limbic dysfunction associated with memory impairment, hallucinations, anxiety, psychosis, and behavioral abnormalities. Inflammatory markers and neuronal antibodies were frequently identified in cerebrospinal fluid and serum analysis. Magnetic resonance imaging often revealed hyperintense inflammatory lesions involving limbic structures, medial temporal lobes, cortical regions, or white matter abnormalities. Electroencephalography demonstrated diffuse slowing and epileptiform activity in several encephalitic cases. In contrast, Alzheimer's disease patients predominantly demonstrated gradual progression of episodic memory loss, orientation impairment, language dysfunction, and deterioration of daily living activities associated with hippocampal and temporoparietal cortical atrophy on neuroimaging studies. Cerebrospinal fluid analysis in Alzheimer's disease frequently demonstrated reduced beta-amyloid levels and elevated phosphorylated tau protein concentrations. Frontotemporal dementia patients commonly presented with prominent behavioral disinhibition, personality changes, executive dysfunction, emotional flattening, compulsive behavior, and language disturbances associated with selective frontal and anterior temporal lobe atrophy on magnetic resonance imaging. Inflammatory biomarkers and neuronal antibodies were generally absent in neurodegenerative disorders. Patients with chronic encephalitis showed partial or significant clinical improvement following immunotherapy, corticosteroids, antiviral treatment, or immunomodulatory therapy, whereas neurodegenerative disorders demonstrated persistent progressive decline despite symptomatic management. Clinical analysis demonstrated that patients with chronic encephalitis frequently presented with relatively rapid or fluctuating onset of cognitive impairment accompanied by psychiatric symptoms, emotional instability, sleep disturbances, seizures, autonomic dysfunction, hallucinations, and progressive neurological deterioration. Autoimmune encephalitis cases commonly exhibited limbic system involvement associated with severe memory dysfunction, psychosis, anxiety, irritability, confusion, and behavioral abnormalities. Cerebrospinal fluid examination often revealed inflammatory changes including pleocytosis, elevated protein concentration, oligoclonal bands, and neuronal autoantibodies. Magnetic resonance imaging frequently demonstrated hyperintense inflammatory lesions within medial temporal structures, limbic regions, cortical areas, or diffuse white matter abnormalities. Electroencephalography revealed diffuse slowing patterns and epileptiform discharges in numerous encephalitic patients. In contrast, Alzheimer's disease patients demonstrated gradual progression of episodic memory loss, spatial disorientation, language impairment, and decline in functional independence associated with prominent hippocampal and temporoparietal cortical atrophy on neuroimaging studies. Cerebrospinal fluid biomarkers in Alzheimer's disease commonly demonstrated

reduced beta-amyloid concentrations together with elevated phosphorylated tau and total tau protein levels. Frontotemporal dementia patients primarily presented with behavioral disinhibition, executive dysfunction, emotional indifference, compulsive activity, reduced social awareness, and language disturbances associated with selective frontal and anterior temporal lobe atrophy on magnetic resonance imaging. Inflammatory markers and neuronal antibodies were generally absent in neurodegenerative disorders. Patients diagnosed with chronic encephalitis demonstrated significant or partial neurological improvement following immunotherapy, corticosteroids, antiviral treatment, or immunosuppressive therapy, whereas neurodegenerative disorders showed continuous progressive decline despite symptomatic interventions.

4. Discussion

The findings confirm that differentiation between chronic encephalitis and neurodegenerative diseases requires comprehensive evaluation of clinical presentation, inflammatory activity, neuroimaging findings, cerebrospinal fluid biomarkers, and disease progression patterns. Chronic encephalitis frequently demonstrates relatively rapid or fluctuating onset associated with neuropsychiatric symptoms, seizures, sleep abnormalities, autonomic dysfunction, and inflammatory laboratory findings. Autoimmune encephalitis especially represents an important reversible cause of cognitive impairment and psychiatric disturbance that may mimic primary dementia syndromes during early stages. Presence of neuronal antibodies, inflammatory cerebrospinal fluid changes, limbic system involvement, and response to immunotherapy strongly support inflammatory encephalitic etiology. Alzheimer's disease primarily affects episodic memory and spatial orientation through progressive hippocampal degeneration and accumulation of amyloid and tau pathology. Frontotemporal dementia predominantly affects executive function, social cognition, emotional regulation, and language due to selective frontal and temporal lobe degeneration. Neuroimaging studies remain critically important for differentiation because encephalitic disorders often demonstrate inflammatory lesions or diffuse cerebral abnormalities, whereas neurodegenerative diseases exhibit characteristic cortical atrophy patterns. Cerebrospinal fluid biomarkers additionally provide valuable diagnostic information through identification of inflammatory activity, neuronal antibodies, amyloid alterations, tau protein accumulation, and markers of neurodegeneration. Early identification of chronic encephalitis remains especially important because delayed diagnosis may lead to irreversible neuronal damage and poor neurological outcome despite subsequent treatment. Contemporary advances in neuroimmunology, molecular diagnostics, and biomarker research have substantially improved recognition of inflammatory neurological disorders previously classified as atypical dementia syndromes. Continued research into neuroinflammatory mechanisms, autoimmune antibodies, molecular biomarkers, and neurodegenerative pathways will further enhance diagnostic precision and development of targeted therapeutic strategies.

5. Conclusion

Chronic encephalitis and neurodegenerative diseases demonstrate overlapping cognitive and psychiatric manifestations but differ significantly in pathophysiology, inflammatory activity, biomarker profiles, neuroimaging characteristics, and therapeutic response. Chronic encephalitis is frequently associated with inflammatory lesions, neuronal antibodies, neuropsychiatric symptoms, and potential reversibility following immunological treatment. Alzheimer's disease primarily involves progressive memory decline associated with amyloid and tau pathology, whereas frontotemporal dementia predominantly affects behavior, executive function, and language through frontal and temporal lobe degeneration. Comprehensive neurological evaluation including neuroimaging, cerebrospinal fluid analysis, neuropsychological assessment, and autoimmune investigation remains essential for accurate differential diagnosis. Early recognition of inflammatory encephalitic disorders significantly improves therapeutic outcomes and may prevent irreversible neurological deterioration. Advances in neuroimmunology, biomarker science, and molecular diagnostics continue to improve understanding and differentiation of inflammatory and neurodegenerative neurological diseases. Chronic encephalitis and neurodegenerative diseases demonstrate overlapping cognitive and psychiatric manifestations but differ fundamentally in pathological mechanisms, inflammatory activity, neuroimaging characteristics, biomarker profiles, and treatment responsiveness. Chronic encephalitis is frequently associated with inflammatory lesions, neuronal autoantibodies, neuropsychiatric

instability, and potential reversibility following timely immunological therapy. Alzheimer's disease primarily involves progressive memory deterioration associated with amyloid and tau accumulation, whereas frontotemporal dementia predominantly affects executive function, personality, and language through selective frontal-temporal degeneration. Comprehensive neurological evaluation including neuroimaging, cerebrospinal fluid analysis, neuropsychological assessment, and autoimmune investigation remains essential for accurate differential diagnosis. Early identification of inflammatory encephalitic disorders significantly improves therapeutic outcomes and reduces risk of irreversible cerebral damage. Continued advances in neuroimmunology, molecular diagnostics, biomarker science, and neurodegenerative research will further enhance understanding, diagnosis, and management of complex neurological diseases associated with cognitive decline.

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DOI: 10.4103/aams.0498