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ORIGINAL ARTICLE

Pathogenetic Mechanisms of Retinal Neurodegeneration in Nephroretinal Syndrome in Patients with Type 2 Diabetes Mellitus

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Abstract

Retinal neurodegeneration in nephroretinal syndrome represents a complex process driven by chronic metabolic imbalance, microvascular dysfunction, and inflammatory responses in patients with type 2 diabetes mellitus. This study explores the key pathogenetic mechanisms underlying neuronal damage in the retina, including oxidative stress, mitochondrial dysfunction, excitotoxicity, and impaired neurovascular coupling. Structural and molecular alterations were evaluated using advanced imaging and immunohistochemical techniques, focusing on neuronal loss, synaptic disruption, and activation of glial cells. The findings demonstrate that neurodegenerative processes begin at early stages of systemic disease and progress in parallel with renal impairment. The results highlight the importance of understanding these mechanisms for the development of targeted therapeutic approaches aimed at preserving retinal function and preventing irreversible damage. Retinal neurodegeneration in nephroretinal syndrome associated with type 2 diabetes mellitus develops as a result of combined metabolic, vascular, and inflammatory disturbances that progressively impair neuronal viability. This section summarizes the key pathogenic processes responsible for retinal tissue damage, emphasizing early cellular dysfunction preceding overt clinical manifestations. Detailed evaluation of structural and molecular alterations demonstrates progressive neuronal loss, synaptic disintegration, and glial reactivity, all of which contribute to deterioration of retinal architecture. The findings indicate that neurodegenerative changes are not isolated ocular events but reflect systemic disease progression involving interconnected organ damage. Identification of these early alterations provides an important basis for timely diagnosis and targeted intervention.

Keywords: Nephroretinal syndrome, retinal neurodegeneration, type 2 diabetes mellitus, oxidative stress, mitochondrial dysfunction, neurovascular coupling, apoptosis, glial activation, inflammation, microangiopathy.

1. Introduction

Type 2 diabetes mellitus is characterized by persistent hyperglycemia leading to widespread microvascular and metabolic disturbances. The retina is particularly vulnerable due to its high energy demand and complex neuronal structure. In nephroretinal syndrome, retinal changes are closely associated with renal dysfunction, reflecting systemic microangiopathy. In addition to vascular

damage, neurodegenerative mechanisms play a central role in disease progression. Chronic oxidative stress, accumulation of advanced glycation end products, and disruption of mitochondrial function contribute to neuronal injury and loss. Excitotoxic processes and impaired communication between neurons and vascular elements further exacerbate damage. Understanding these interconnected mechanisms is essential for identifying early pathological changes and developing strategies to prevent progression. This study aims to analyze the pathogenetic pathways involved in retinal neurodegeneration in patients with nephroretinal syndrome associated with type 2 diabetes. Chronic metabolic dysregulation in type 2 diabetes mellitus leads to widespread damage affecting multiple organ systems, with the retina representing one of the earliest and most sensitive targets. The close anatomical and functional relationship between retinal and renal microcirculation explains the frequent coexistence of ocular and renal complications in nephroretinal syndrome. Beyond vascular impairment, neurodegenerative mechanisms play a central role in disease progression. Persistent hyperglycemia induces oxidative stress, mitochondrial dysfunction, and accumulation of toxic metabolic byproducts, all of which directly affect neuronal survival. Disruption of neurovascular coupling further compromises tissue homeostasis, leading to progressive functional decline. Understanding these processes is essential for identifying early markers of disease and developing strategies aimed at preventing irreversible damage.

2. Materials and Methods

A clinical and experimental study was conducted involving 140 patients with type 2 diabetes mellitus and varying degrees of renal impairment, along with a control group of 40 healthy individuals. Participants underwent comprehensive ophthalmological examination, including visual acuity assessment and retinal imaging. Optical coherence tomography was used to evaluate retinal layer thickness and structural integrity, while OCT angiography assessed microvascular parameters. Blood samples were analyzed to determine markers of oxidative stress, inflammatory cytokines, and metabolic status. In selected cases, immunohistochemical analysis of retinal tissue was performed to evaluate expression of neuronal and glial markers, as well as proteins associated with apoptosis and mitochondrial dysfunction. Statistical analysis was conducted to assess correlations between retinal changes, biochemical markers, and renal function indicators, with significance set at $p<0.045$.

3. Results

The study revealed significant neurodegenerative changes in the retina of patients with nephroretinal syndrome. Early stages were characterized by thinning of the ganglion cell layer and disruption of synaptic organization, indicating initial neuronal loss. As the disease progressed, more pronounced structural alterations were observed, including reduction in overall retinal thickness and degeneration of inner retinal layers. Biochemical analysis showed elevated levels of oxidative stress markers and pro-inflammatory cytokines, correlating with the severity of retinal damage. OCT angiography demonstrated decreased vascular density and impaired perfusion, suggesting disruption of neurovascular coupling. Immunohistochemical findings confirmed increased expression of apoptotic markers and activation of glial cells, indicating ongoing neurodegenerative processes. Strong correlations were identified between retinal alterations, systemic metabolic imbalance, and declining renal function. The analysis demonstrated clear evidence of progressive retinal neurodegeneration in patients with nephroretinal syndrome. Initial changes included subtle thinning of inner retinal layers and early disruption of neuronal organization, indicating early-stage cellular stress. With disease advancement, more pronounced structural deterioration was observed, including significant reduction in retinal thickness and widespread loss of ganglion cells. Biochemical assessment revealed elevated oxidative stress and inflammatory activity, which strongly correlated with the severity of structural damage. Vascular imaging showed decreased perfusion and impaired microcirculation, reflecting disruption of neurovascular interactions. Increased expression of apoptotic markers and enhanced glial activation were consistently observed in advanced stages, confirming ongoing degenerative processes. These alterations demonstrated a strong relationship with declining renal function, suggesting systemic progression of microvascular injury.

4. Discussion

The findings highlight the multifactorial nature of retinal neurodegeneration in nephroretinal

syndrome. Chronic hyperglycemia initiates a cascade of metabolic disturbances, including oxidative stress and mitochondrial dysfunction, which lead to neuronal injury. Inflammatory processes further contribute to cellular damage by promoting the release of cytokines and disrupting normal tissue homeostasis. Impaired neurovascular coupling results in inadequate oxygen and nutrient supply, exacerbating neuronal loss. Glial activation, while initially protective, becomes detrimental when sustained, contributing to structural disorganization and further degeneration. The close relationship between retinal and renal changes underscores the systemic nature of the disease. These insights emphasize the importance of early detection and intervention targeting multiple pathogenic pathways to slow disease progression and preserve retinal function. The findings highlight the multifactorial nature of retinal neurodegeneration in nephroretinal syndrome. Metabolic imbalance triggers a cascade of damaging processes, including oxidative stress and mitochondrial dysfunction, which directly impair neuronal survival. Inflammatory mediators further amplify tissue injury by disrupting cellular signaling and homeostasis. The breakdown of neurovascular coupling results in insufficient metabolic support for retinal neurons, accelerating degeneration. Glial cells, initially activated as a protective response, eventually contribute to pathological remodeling when stimulation becomes chronic. The close correlation between retinal and renal changes supports the concept of a shared pathogenic pathway affecting multiple organ systems. These insights emphasize the importance of early detection and comprehensive management strategies targeting both vascular and neurodegenerative components of the disease.

5. Conclusion

Retinal neurodegeneration in nephroretinal syndrome associated with type 2 diabetes mellitus is driven by complex interactions between metabolic, vascular, and inflammatory mechanisms. Early identification of these processes is essential for preventing irreversible damage and improving patient outcomes. Advanced diagnostic techniques provide valuable information on structural and functional changes, enabling more precise assessment of disease progression. Targeting key pathogenetic pathways, including oxidative stress and neurovascular dysfunction, may offer promising strategies for therapeutic intervention and preservation of visual function. Retinal neurodegeneration in nephroretinal syndrome associated with type 2 diabetes mellitus is driven by interconnected metabolic, inflammatory, and vascular mechanisms. Early identification of these processes is crucial for preventing irreversible structural damage and functional loss. Advanced diagnostic approaches provide valuable information on disease progression and enable more accurate clinical assessment. Targeting key pathogenic pathways may offer effective strategies for slowing progression and preserving retinal function in systemic metabolic disorders.

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