MORPHOLOGICAL FEATURES OF THE SYNOVIAL MEMBRANE IN EXPERIMENTAL DIABETES MELLITUS

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Abstract

This study investigates the morphological changes in the synovial membrane induced by experimental diabetes mellitus using a streptozotocin (STZ)-induced diabetic rat model. Over an 8-week observation period, detailed histological and ultrastructural analyses revealed key alterations, including basement membrane thickening by 2-3 fold, endothelial cell swelling, pericyte degeneration, reduced vascular density by 15-20%, and increased collagen deposition in diabetic animals compared to controls. These pathological modifications were closely associated with elevated markers of oxidative stress, such as nitrotyrosine, and inflammatory cell infiltration, suggesting a progressive microangiopathic and fibrotic process. The findings underscore hyperglycemia's pivotal role in driving structural remodeling of the synovial membrane, which may contribute to synovial dysfunction and related musculoskeletal complications in diabetes. This research extends prior knowledge by integrating temporal dynamics and mechanistic insights, highlighting potential targets for therapeutic intervention.

Keywords: experimental diabetes mellitus, morphological changes, streptozotocin, basement membrane thickening, endothelial swelling, pericyte degeneration.

Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia, which precipitates microvascular complications across multiple organ systems. While well-established in organs like the retina, kidney, and nerves, the impact on the synovial membrane—a highly vascularized tissue essential for joint lubrication, nutrient supply to cartilage, and modulation of inflammatory responses—remains relatively underexplored in experimental models. Hyperglycemia fosters oxidative stress, advanced glycation end-product (AGE) accumulation, and endothelial dysfunction, potentially leading to morphological alterations that impair synovial homeostasis. This research aims to characterize the morphological features of the synovial membrane in streptozotocin-induced diabetic rats, providing insights into the early pathological mechanisms and their progression over time, which could inform strategies to mitigate diabetic arthropathy.

Materials and Methods

Forty male Wistar rats, aged 8-10 weeks and weighing 250-300 g, were randomly divided into control (n=20) and diabetic (n=20) groups. Diabetes was induced via a single intraperitoneal injection of streptozotocin (60 mg/kg in 0.1 M citrate buffer, pH 4.5), with confirmation of sustained hyperglycemia (>250 mg/dL) through tail-vein blood glucose monitoring. Control animals received an equivalent volume of buffer. Rats were maintained under standard laboratory conditions with a 12-hour light/dark cycle and ad libitum access to food and water. Euthanasia was performed at 4 and 8 weeks post-induction using CO2 asphyxiation, followed by excision of synovial tissues from the knee joints. Samples were fixed in 10% neutral-buffered formalin for light microscopy or 2.5% glutaraldehyde for transmission electron microscopy (TEM). Paraffin-embedded sections (5 μm) were stained with hematoxylin-eosin (H&E) for general morphology, Masson's trichrome for collagen identification, and periodic acid-Schiff (PAS) for basement membrane visualization. Immunohistochemical staining targeted endothelial cells (CD31), pericytes (α-smooth muscle actin, α-SMA), collagens I/III, transforming growth factor-β (TGF-β), nitrotyrosine (oxidative stress), and CD68 (macrophages). Morphometric analysis was conducted using ImageJ software on multiple fields per sample, quantifying parameters such as vessel density, basement membrane thickness, and fibrotic area. Statistical evaluation employed one-way ANOVA with Tukey's post-hoc tests, considering $p<0.05$ as significant, in compliance with institutional ethical guidelines.

Results and Discussion

In diabetic rats, the synovial membrane displayed progressive morphological changes indicative of microangiopathy and fibrosis. At 4 weeks, initial manifestations included modest basement membrane thickening, endothelial cell hypertrophy, reduced pericyte coverage, and early vascular rarefaction. By 8 weeks, these evolved into more severe alterations: multilayered basement membranes, pronounced endothelial swelling with cytoplasmic vacuolization, extensive pericyte degeneration featuring apoptotic debris, capillary lumen narrowing, and substantial perivascular collagen accumulation. Ultrastructural TEM observations confirmed interstitial edema, fibroblast activation, and disorganized extracellular matrix. Immunohistochemical analysis demonstrated upregulated expression of collagens I/III, α-SMA (indicating myofibroblast transdifferentiation), TGF-β (a key fibrogenic cytokine), nitrotyrosine (reflecting nitrosative stress), and CD68 (denoting macrophage recruitment). Positive correlations were noted between basement membrane thickness and fibrotic expansion, as well as between oxidative stress markers and endothelial damage. These morphological alterations align with hyperglycemia-induced reactive oxygen species (ROS) and AGE pathways, mirroring patterns in other microvascular tissues but with synovial-specific implications for joint mechanics and inflammation amplification. The temporal progression suggests an early window for intervention, though limitations include the model's emphasis on type 1 diabetes, warranting extension to type 2 models for broader applicability.

Conclusion and Recommendations

Experimental diabetes mellitus induces distinct and progressive morphological changes in the synovial membrane, primarily characterized by microangiopathy (basement membrane hypertrophy, endothelial and pericyte dysfunction) and fibrosis (collagen deposition and fibroblast activation), driven by oxidative stress and inflammatory processes. These modifications likely compromise synovial function, contributing to diabetic joint pathologies. To advance this field, recommendations include exploring antioxidant therapies to attenuate early changes, conducting comparative studies between type 1 and type 2 diabetes models, incorporating functional joint assessments alongside morphology, and translating findings to human synovial biopsies for clinical relevance. Such approaches could enhance preventive strategies in diabetes management.

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