Dysregulation of the Reproductive Axis: Crosstalk Between Peritesticular Adipose Tissue and Testicular Arteriolar Endothelial Cells in Obesity-Induced Inflammation

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Abstract :

Statement of the Problem:

Obesity-induced inflammation arises from chronic low-grade immune activation in adipose tissue (AT), driven by adipocyte hypertrophy, hypoxia, and mechanical stress. In this study, we investigated the effects of low-grade inflammation induced by a hypercaloric diet ' formulated to sustain lactation in female rabbits' on male rabbits physiologically unadapted to this diet (nutritional stress). The focus centered on reproductive axis dysfunction and structural alterations in adipose, testicular, and vascular tissues

Methodology and Theoretical Orientation :

Two groups of local adult male rabbits (n = 16) were fed a high-calorie diet (HCD: 4538 Kcal/kg DM) and a finishing diet (FD: 3964 Kcal/kg DM). After fifteen weeks, the animals were sacrificed according to Algerian legislation. Blood levels of glucose, total cholesterol, high-densitylipoprotein (HDL), low-densitylipoprotein (LDL), and triglycerides were measured. Testosterone, estradiol, LH, FSH, and insulin levels were determined using RIA Kit protocols (Immunotech SAS, Marseille, France), while leptin and adiponectin were measured by ELISA method (DRG Diagnostics GmbH, Germany). Visceral adipose tissue (VAT), liver, and testicles were dissected and fixed in 4% formalin. These organs were analyzed histologically and immunohistochemically for CD45 expression. Total body weight and relative weights for VAT, testicles, were estimated. Quantitative and statistical analyses were conducted using the ImageJ program and the R programming language.

Findings:

The diet administered to rabbits induces nutritional stress by disrupting the adrenal axis (Mokrani et al., 2021). This stress drives low-grade inflammation, which manifests as endocrine disorders of the reproductive axis in experimental rabbits, characterized by elevated plasma FSH and testosterone levels, as well as increased testicular estradiol. Plasma LH and testicular testosterone exhibited moderate increases. Local low-grade testicular inflammation was observed, marked by enlarged intertubular spaces due to lipid deposition. Concurrently, seminiferous tubule diameter, lumen size, and spermatozoa proportion were reduced.

Immunohistochemical (IHC) analysis using the CD45 antibody on the liver of obese rabbits revealed structural alterations, including microvesicular steatosis and infiltration of the hepatic parenchyma by immune cells, indicating the onset of inflammation. Additionally, CD45 IHC

expression demonstrated fibrosis in visceral adipose tissue and immune cell infiltration, characterizing a state of chronic low-grade inflammation.

The most significant finding of this study is the expansion of peritesticular adipose tissue and the development of varicocele in obese male rabbits, indicating a crosstalk between these fascial tissues in driving adipogenesis (new adipocyte formation) in response to low-grade inflammation.

Conclusion

This study demonstrates the impact of low-grade inflammation on the reproductive axis by examining glandular interactions between gonadal, vascular, and adipose tissues. The exploration of these interactions aims to provide a better understanding of the molecular mechanisms underlying this crosstalk, with the goal of developing novel therapeutic strategies to address adipose tissue dysfunction.