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The kidney in an animal model of metabolic syndrome: A morpho-functional study

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Metabolic syndrome (MetS) is characterized by obesity, insulin resistance, dyslipidemia, hyperglycemia, and hypertension. Obesity is a chronic pathological condition characterized by an accumulation of adipose tissue associated with an increase in morbidity and mortality. Adipose tissue is a primary source for the production and secretion of leptin. Plasma concentrations of leptin increase parallel to fat mass augmentation. This regulates food intake and energy expenditure to maintain body fat deposits. In this work, the obese Zucker rat (OZR, fa/fa) which show several metabolic dysfunctions were investigated. The mutation (fa/fa) of the gene that codifies for the leptin receptor causes hyperphagia and leads to a marked obesity. In our experiments, OZRs developed simultaneously with hyperphagia, obesity, insulin resistance and arterial hypertension. This highlights the influence of MetS on the kidney and the correlations with degenerative phenomena linked to obesity. OZRs and age-matched lean Zucker controls (LZR) were studied at the age of 12, 16 and 20 weeks. The kidneys were removed and processed for morphological analysis. Furthermore, several inflammatory parameters such as IL-1β and IL-6 and some endothelial markers namely ICAM-1 and PECAM-1 were investigated by immunochemical and immunohistochemical techniques. Morphological changes involving primarily the glomerulus and convoluted tubules were observed in OZR rats of all ages. In the glomeruli, an increase in the glomerular and capsular volume, as well as a more pronounced glomerulosclerosis in older obese rats, were observed. To evaluate oxidative stress, levels of malondialdehyde (MDA) and the oxidation status of plasma proteins were assessed. This analysis revealed an oxidative stress status characterized by an increasing level of oxidated proteins and no changes in the concentration of MDA. An increase of IL-6 expression was noticeable in the proximal and distal convoluted tubules. In summary, the above findings suggest that in the OZRs nephropathy is an extremely complex phenomenon, related both to inflammatory phenomena typical of MetS and to increased oxidative injury. These results can contribute to better characterize end-organ damage in Mets, the relationships of it with chronic kidney disease and to identify therapeutic approaches avoiding renal failure that could result in dialysis or organ transplantation.