535

Mizoguchi S[1], Mori K[1], Yamanaka N[1], Sato F[1], Mimata H[1]
1. *Oita University*

PROSTATIC ENLARGEMENT ASSOCIATED WITH INFLAMMATION IN HIGH FAT DIET INDUCED OBESITY RAT MODEL

Hypothesis / aims of study

Central obesity is known to be an important risk factor of benign prostatic hyperplasia (BPH). Altough chronic Intraprostatic inflammation and alteration in androgen to estrogen conversion process associated with increased fat tissue are assumed as the factors which contribute to the development of BPH in obesity (1), the underlyning pathophysiological mechanism is unclear. Therefore, to findout the effect of obesity on the prostate, we investigated alternations in the histopathology and expression of inflammatory related cytokines and estrogen receptors (ERs) in the prostate using a high-fat diet-induced obesity rat model.

Study design, materials and methods

Male wistar rats (190-210g, n=8) were randomly assigned to either a normal diet (ND, n = 4) or a high fat diet (HFD, n = 4). The ND formula consisted of standard rodent chow containing 5 % fat. In contrast, HFD consisted of rodent chow containing 32 % fat. After the animals were maintained on these diets for 16 weeks, visceral fat and the lateral prostate were excized for analysis of weigt gain, histopathology and protein level of IL1α, IL1β, IL6, IL10, and monocyte chemotactic protein-1 (MCP-1) by multiple beads suspension array system as well as mRNA level of ERα and G protein-coupled estrogen receptor (GPER) by RT-qPCR. Statistical analysis was performed using Mann-Whitney U test. P values less than 0.05 were considered statistically significant

Results

After 16 weeks, HFD showed increased weight of body, visceral fat and lateral prostate compared to ND($P < 0.05$). In hematoxyline eosin stain, lymphcyte and macrophage infiltration into glandular and stromal area were shown in the lateral prostatic tissue section from HFD while ND did not demostate inflammatory cell infiltration. Additionally, masson's trichrome stain demonstrated increased collagen fiber in the stroma of the lateral prostate of HFD compared to ND. Protein levels of IL1α, IL1β, IL6 and MCP-1 were significantly increased compared to ND ($P < 0.05$). In contrast, protein levels of IL10 was significantly decreased in HFD compared to ND ($P < 0.05$) (Figure1). Furthermore, RT-qPCR revealed significantly increased mRNA level of ERα and GPER in HFD compared to ND (Figure2).

Interpretation of results

In this study, HFD-induced obesity rats demonstrated lateral prostatic inflammation in association with alterd immunobalance evidenced by increased protein level of IL1α, IL1β, IL6 and MCP-1 and decreased level of IL10, an anti-inflammatory cytokine which is known to be decreased in metabolic syndrome (2), correlated with central obesity in rats evidenced by increased weight body and visceral fat. Furthermore, lateral prostatic enlargement was shown in HFD associated with upregulation of ERα and GPER which are reported to play an important role in prostatic abberant proliferation and inflammation leading to prostatic hyperplasia(3). These results suggest that high fat diet intake might caused prostatic inflammation and enlargement via metabolic inflammation and hormonal change followed by ERs activation.

Concluding message

We demonstrated that high fat diet intake induces prostatic enlargement and inflammation in association with alterd immunobalance and expression of estrogen receptors. Therefore, anti –inflammatory agents or estrogen receptor modulater could be therapeutic alternatives for the treatment of BPH in patients with obesity.

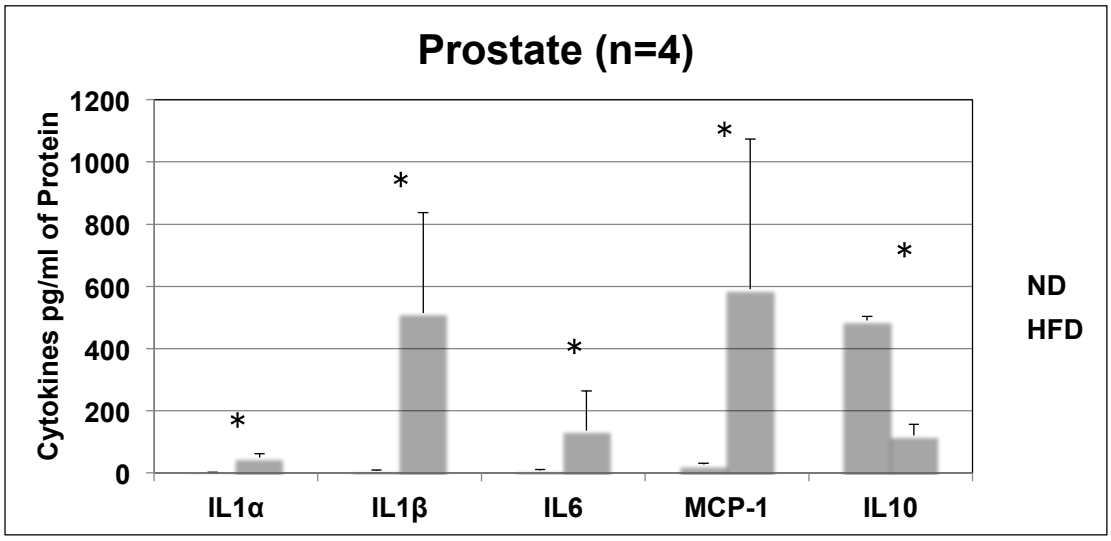

Figure1 Cytokines expression analysis in the lateral prostate

*p < 0.05, Mann–Whitney U test

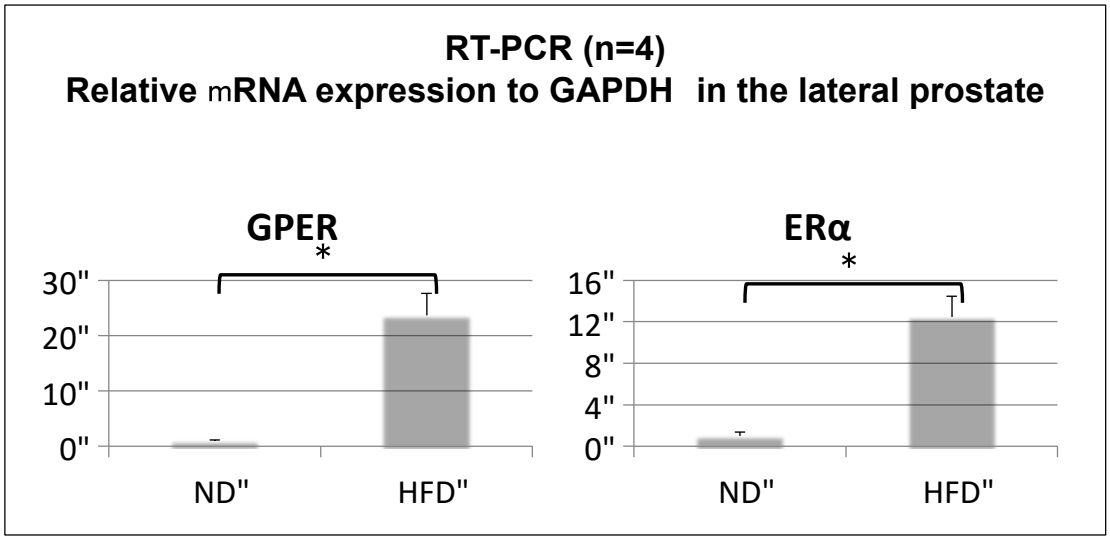

Figure 2. Relative mRNA expression to GAPDH in the lateral prostate

* $p < 0.05$ Mann–Whitney U test

References

1. Parikesit D, Mochtar CA, Umbas R, Hamid AR. The impact of obesity towards prostate diseases. Prostate Int. 2016;4(1):1-6.
2. Nishimura S, Manabe I, Takaki S, Nagasaki M, Otsu M, Yamashita H, et al. Adipose Natural Regulatory B Cells Negatively Control Adipose Tissue Inflammation. Cell Metab. 2013.
3. Williams G. Aromatase up-regulation, insulin and raised intracellular oestrogens in men, induce adiposity, metabolic syndrome and prostate disease, via aberrant ER-alpha and GPER signalling. Mol Cell Endocrinol. 2012;351(2):269-78.

Disclosures

Funding: none **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Oita University Institutional Animal Care and Use Committee