Parasitic nematode *Trichinella* infection improves obesity-induced diabetes

H. Okada, K. Kajita, M. Yamauchi, T. Ikeda, Y. Uno, H. Morita, T. Ishizuka; Department of General Internal Medicine, Gifu University Graduate School of Medicine, Japan.

**Background and aims:** Insulin resistance associated with obesity, particularly visceral obesity, is involved in the pathogenesis of lifestyle-related diseases such as type 2 diabetes. In addition, inflammation caused by chronic bacterial infection such as periodontal disease is known to deteriorate glucose tolerance and insulin sensitivity. However, the effects of parasite infection on glucose tolerance have remained unknown. In addition, that chronic low grade inflammation in adipose tissue is currently considered as a main cause of insulin resistance associated with obesity. Interestingly, a parasitic helminth is known to secrete an immunosuppressive agent and anti-inflammatory materials to suppress an attack from a host. We investigated the effects of nematode parasite, *Trichinella spiralis*, infection on glucose tolerance and macrophage status in adipose tissue.

**Materials and methods:** Ob/ob mice and C57/BL mice fed with normal or high fat diet (HF) were divided into two groups (10 mice each), and then infected orally with (infected group) or without (un-infected group) *Trichinella*. Four weeks later, body weight, fat weight, fasting plasma glucose and insulin levels were measured. To evaluate glucose tolerance, intraperitoneal glucose tolerance test (ipGTT, glucose: 2g/kg) was performed. To determine the expression levels of adipocyte specific genes (PPARγ and adiponectin) in adipocytes isolated from epididymal fat, M1 macrophage markers (CD11c Nos and IL6) and M2 macrophage marker (CD206, arginase 1 and IL10) in stromal vascular fraction (SVF) and peritoneal lavage (PT), real time PCR was performed. Immunostaining of paraffin sections of the fat tissues was performed using anti-CD11c antibody and anti-CD206 antibody.

**Results:** Although *Trichinella* infection for four weeks reduced fasting plasma glucose level, it had no influence on the plasma insulin level in C57 /BL and ob /ob mice. These results implied that *Trichinella* infection improves insulin sensitivity. *Trichinella* infection did not affect body weight and fat weight. *Trichinella* infection suppressed plasma glucose levels during GTT in ob/ob mice and HF fed mice, but not lean C57 /BL mice. The expression of M1 markers were suppressed in PT and SVF isolated from infected mice. In contrast, M2 marker, mRNA levels were elevated in SVF and PT isolated from infected mice. These results indicated that *Trichinella* infection shifted macrophage polarization from M1 to M2 in SVF and PT. On the other hand, *Trichinella* infection did not influence mRNA levels of PPARγ, adiponectin, IL-6, IL-10 and MCP-1 in adipocytes. Double immunostaining for CD11c, and for CD206 revealed that more abundant expression of CD206 in the infected group was detected.

**Conclusion:** *Trichinella* infection increased the ratio of M2/M1 macrophage, which results in a pro-inflammatory state in adipose tissue and amelioration of glucose tolerance in obese mice.