Obesity And The Spleen

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Abstract

This review describes the relationship of splenomegaly, or "splenic obesity", with metabolic syndrome, obesity and metabolic – associated steatohepatic disease (MAFLD), based on animal and human studies. The spleen is enlarged in obesity. It may play a protective role against obesity-associated inflammation and complications. This protection may be lost after splenomegaly. Persons with splenic disease must be evaluated for obesity, and vice versa and counselled to avoid injury to the organ.

Keywords: MASLD, NAFLD, obesity, overweight, portal hypertension, spleen, splenectomy, weight.

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Introduction

Weighing 70-200 g, and measuring up to 12 cm in cranio caudal diameter, the healthy spleen is an important storage organ, and a 'sink' or sanitizer for various haematopoietic cells, immune peptides and immunoglobulins.[1]

The spleen plays a major role in haematopoiesis and immunosurveillance. Splenomegaly, or enlargement of the spleen, may occur due to infiltrative, immunogenic, invasive and vascular diseases.[2] While the relationship between obesity and immunity is a major focus of research, not much discussion has taken place regarding obesity and the spleen.

Is there an entity such as 'the obese spleen'? Does splenic health impact weight homoeostasis, and vice-versa? Does splenectomy impact weight? In this narrative review, we explore the various facets of the obese spleen.

Animal Studies

A study on mice fed on a high-fat, high-sugar diet shows that this leads not only to obesity, hyperglycaemia, elevated interleukin-6, but also to splenomegaly. The spleen weight in obese mice is 50% larger than in normal weight mice. The spleen weight is reversed by a combination of exercise and genistein. This reduction in splenomegaly is associated with an improvement in red-to-white pulp area, as well as glucose and interleukin-6 levels.[3]

An animal study assessed the role of the spleen in pathogenesis of obesity. This was done by performing splenectomy in rats with monosodium glutamate-induced obesity and lean controls, and comparing the results with non-operated subjects. Splenectomy decreased insulin resistance, normalized nitric oxide response in pancreatic islets, and reduced adipocyte and islet hypertrophy in obese rats.[4] If splenectomy has a role in management of obesity and insulin resistance, it stands to reason that the spleen may have a role in pathogenesis of obesity.

Obesity has been shown to increase the splenic oxidation and inflammation in mice. However. It also enhances antioxidant activity, and reduce proinflammatory cytokines, so as to fight splenic injury induced by exposure to infection.[5] (intranasal drip of E coli)

In another study on high-fat diet fed obese mice, obesity was found to reduce serum levels of interleukin-10. Splenectomy aggravated renal inflammation as well as hypertension, but these effects were inhibited by systemically administered interleukin-10. These results imply that the obese spleen is functionally compromised, with low interleukin-10, and this may lead to development of obesity related chronic kidney disease.[6] Splenectomy has also been shown to enhance the progression of hepatic steatosis to steatohepatitis in obese rats.[7]

The spleen has been shown to have a beneficial effect on the inflammatory profile, of the mesenteric perivascular adipose tissue in obese mice on high fat diet. Splenectomized mice demonstrated hypertrophy of adipocytes, infiltration of mesenteric perivascular adipose tissue by immune cells, and increase in proinflammatory cytokines. This suggest that the spleen has a protective effect against obesity.[8]

The spleen may supply and support innate-like B lymphocytes of white adipose tissue. This has been postulated by an animal study on mice with diet induced

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obesity. These B lymphocytes, capable of producing the anti-inflammatory interleukin-10, are impaired in obese models. This suggests that the spleen protects against obesity- associated insulin resistance.[9] It is possible that splenic sympathetic nervous system efferents are activated by high fat diet induced obesity in mice. This implies that there is an autonomic component to obesity as well.[10]

An autonomic facet of the spleen has been suggested by animal studies, in which vagotomy has been shown to reduce weight gain, serum triglycerides and adipocyte size in rats with MSG-induced obesity. Concomitant splenectomy, however prevented this effect from occurring in non-obese rats. The autonomic- spleen axis, therefore, seems to work in non-obese healthy animals, but not in hypothalamic obese animals.[11]

Human Studies

A cross-sectional study of 1095 adults, aged 30 to 90 years, assessed the correlation of splenic volume with body composition. The spleen volume, as measured by magnetic resonance imaging (MRI), demonstrated a positive correlation with body mass index (BMI), body weight, waist circumference, hip circumference, waist-to-hip ratio, absolute fat mass, absolute fat free mass, visceral adipose tissue, and subcutaneous adipose tissue. Thus, the concept of the 'obese spleen' seems tenable. A fat free mass that is 8.12kg greater is associated with a 38.4(26.7-50.1) ml higher splenic volume in men. In women, a 5.21kg higher fat free mass is linked to a 42.6 (26.2-59.0) ml higher splenic volume.[12]

In a study based on UK Biobank data (37066 participants, spleen volume (measured by magnetic resonance) was compared with various factors. Splenic volume was found to correlate with body size, and was higher in younger people, in men, and in people with nonalcoholic fatty liver disease. Positive associations of splenic volume were noted with liver fat fraction, liver volume and fibrosis- 4 score. This association, probably due to a rise in portal vein pressure, suggests that splenomegaly may be reviewed as a part of obesity as well as metabolic-associated steatohepatic disease (MASLD).[13]

The obese spleen, or splenomegaly, in obese persons is an indicator of the presence of metabolic-associated steatohepatic disease (MASLD). This may be associated with increase in hepatic growth factors (HGF). Based upon data of 80 obese persons with nonalcoholic fatty liver disease, the relationship of splenic length with HGF and basal metabolic rate (BMR) was assessed. BMR was predicted by spleen length, which in turn was predicted by interleukin-16 and HGF. Splenic length was also able to predict hepatic steatosis in men. The author postulates that the spleen which represents the immune system, is a sensor of, and the metabolic status of the body.[14]

Another study, of 60 cases with metabolic syndrome, compared with 30 healthy controls, explored spleen size and the factors influencing it. Splenic longitudinal diameter was higher in persons with metabolic syndrome, and correlated positively with waist circumference, liver enzymes (aminotransferases and alkaline phosphatase). No correlation with interleukin-10 was found, however.[15]

A study of 48 overweight/obese adult women has reported a correlation of splenic longitudinal diameter with metabolic syndrome, and with lower insulin like growth factor-1/insulin like growth factor binding protein-3 (IGF-1/IGFBP-3) ratio. This suggests that splenomegaly is associated with the 'maladaptive anabolism' of metabolic syndrome.[16]

The spleen may be a target of obesity, too. Emphysematous splenitis has been reported in a morbidly obese lady.[17] These findings raise an important question as well: should altered immunity be considered a cause or a consequence of metabolic syndrome?

Clinical Implications

Put together, these findings suggest a distinct 'obese spleen' with anatomic and physiologic abnormalities. The heavier than normal spleen is associated with altered immune health and autonomic function. However, the spleen also acts as a bulwark against the worsening of steatotic liver disease, insulin resistance, and obesity. The obese spleen, therefore needs to be studied in greater detail. Research in this field may reveal novel means of improving immune health in obesity, and of managing obesity and its related complications as well.

In summary, it is clear that spleen volume is increased in persons living with obesity. It is also raised in persons with MASLD, and other facets of metabolic syndrome. The spleen acts as protection against immune dysregulation noticed in obesity, which is a chronic low grade inflammatory disorder. This protection is lost with splenectomy.

Persons living with obesity must be screened for splenomegaly. If required, other causes of splenomegaly must be ruled out. Pragmatic advice to avoid splenic injury, such as avoidance of contact sports, must be shared. Patients diagnosed to have splenomegaly must be evaluated for obesity, and appropriate anti-obesity measures instituted if needed. Immunosurveillance must be put in place for all patients with splenomegaly and/or obesity, and adequate immunization insured. It must be

noted that persons with a history of splenectomy are a high –risk group for immunization.

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