

Importance of controlling obesity and associated immune response changes in prevention and treatment of cancer—with plant therapies of help

Opinion

Obesity has reached epidemic proportions. WHO cites that >1.9 billion people are overweight of which 600 million are obese of which 10.8% are males and 14.9% females. Obesity is associated with numerous complications like insulin resistance (IR), Type 2 Diabetes Mellitus (T2DM), along with increased numbers of cancers, cardiovascular and autoimmune diseases among others. Chronic low grade inflammation accompanies obesity.¹⁻³ More and more data points to the involvement of intestinal immune system with inflammation of other metabolic tissues like liver and visceral Adipose tissue (VAT) also getting involved. Obesity leads to Altered intestinal immunity, which correlates with gut microbiota changes, changes in intestinal barrier function, innate and adaptive immunity residing in the gut along with oral tolerance to luminal antigens.^{4,5} Now obesity has overtaken undernourishment for the first time and is increasing by leaps and bounds. Hence marked efforts are being done to understand the aetiopathogenesis. In our earlier reviews we have tried to understand the aetiopathogenesis involving different aspects like inflammation in general in obesity, hypothalamic inflammation, GIT inflammation, and others which have influenced development of medical treatments having edge over bariatric surgery but have not been successful in getting any stable medical therapy that can be used for long.⁶⁻¹⁰ Natural Killer (NK) cells represent one of the populations of the lymphocytes belonging to the innate immune system. By definition they are the cells that have the capacity to kill infected or transformed cells without needing any previous activation. Besides their cytotoxic capacity, they can also produce inflammatory cytokines like interferon gamma (IFN γ) and thus are a key part of early immune responses. In view of these abilities which make them stand out, these NK cells are very important part for host protection, mainly antitumor and antiviral immunity. In the last 10 years, a lot of work has been done to study the effect of obesity on NK cell biology, giving a full briefing of systemic dysregulation of NK cell functions. Recently various publications have examined the role of NK cells in the homeostasis of adipose tissue (AT) and the aetiopathogenesis of obesity. Worldwide, cancer has become a leading cause of mortality, with 7.6 million deaths occurring yearly.¹¹ A report from centre of diseases control (CDC) in United States have pointed to obesity being responsible for 40% of cases of cancer, that accounts for 630,000 diagnosis in 2014 alone.¹² This study is similar to what has been found all over the world.¹³ Multifactorial changes like hormones, cytokines and immunity observed in cancers related to obesity. Obesity is related to increased insulin levels that further promote the development of some obesity related cancers like colorectal, pancreatic, liver and endometrial.¹⁴⁻¹⁶ Various studies have also picked up links with leptin, an adipokine levels that are raised in obese children and adults and cancer. Most researchers trying to study leptin in relation to obesity

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have mainly concentrated on breast cancer, in which case leptin has the ability to directly stimulate breast cancer cells proliferation.¹⁷ Also the other part common to obesity related cancer occurring is the chronic inflammation present in obesity.¹⁸ Various studies have emphasized on the interaction between inflammation and cancer developing as exemplified by colonic carcinogenesis in patients suffering from inflammatory bowel disease.¹⁹ Thus we have reviewed the role of NK cells in how the Alteration in Natural Killer (NK) cell Function in Obesity, correlates with the development of comorbidities like cancer and type 2 diabetes.²⁰

With the alteration in metabolism in the cells, variety of immune subsets gets activated. The fuel provided for these changes comes from nutrients like glucose, amino acids, and fatty acids, which are normally associated in a big way with the immune cell fate and function. The newer hypothesis that is being proposed, point that the control of nutrient utilisation via competitive uptake and use is essential for regulating immune responses. We discussed various immune microenvironments in which limitation of nutrients occurs, and how important availability of nutrients is in the control of immune responses.²¹

Earlier we have reviewed the role of natural products like flavonoids, monoterpenes, lentils like chickpeas and soybeans and walnuts for treating diabetes mellitus and insulin resistance besides importance of treating the 2 closely associated conditions that is obesity and diabetes mellitus (DM) together in view of which the term diabetes got coined.⁶⁻⁹ Further we have further tried to explain the mechanism of some of the natural Chinese products in Diabetic nephropathy, cardiomyopathy and obesity besides taste problems.²²

Resveratrol (trans 3,4,5-trihydroxy stilbene) is a natural polyphenol found in red wine, rhubarb, along with fruits like blueberries, many red grape varieties and peanuts, etc, which play an important role in a large variety of biological activities.²³ Resveratrol has anti-oxidative, anti-inflammatory, anticancer, antimicrobial, anti-neurodegenerative, and estrogenic properties. By interacting with several molecular targets, Resveratrol regulates innate and adaptive immunity.²⁴ Thus Malagauatnera L 2019 reviewed the Influence of Resveratrol on the Immune Response.²⁵

Over centuries, plants have been exploited by mankind as sources of numerous cancer chemotherapeutic agents. Good examples of anticancer compounds of clinical significance today include the taxanes (like paclitaxel; taxol), vincristine, vinblastine and the podophylline analogues which all trace their origin to higher plants. Although all these drugs along with different other options, gave some relief in cancer management, real breakthrough or cure has not been achieved. With the research on the iridoid glycoside geniposide and its aglycone genipin, are being used right now as gold standard reference compounds in cancer studies. We further highlight subtle points regarding effects on tumor development, cancer cell survival and death and mechanism of action.²⁶

Conclusions

Thus obesity is a state which alters the normal immune response by which the body fights against infections and protects from cancer by converting any mutant cell to normal (benign) or kill the abnormal cells, is altered, which explains why the incidence of cancers is so high in obesity. In earlier centuries when we did not have knowledge about how to fight these cancers we neither had such a high incidence of obesity nor cancer, when diet eaten was in pure form with plants and vegetables having the right amount of nutrients to keep the body healthy to be able to fight any infection. Now a day's once any obese patient undergoes any intervention in the form of any surgical procedures with lot of interference in natural gut flora with antibiotics intake. Thus the requirements of the immune system for nutrients increase so much that to fight any infection the immune cells have to work hard and at the rate of these immunometabolism reactions occur, a lot of enzymes and coenzymes get used leading to deficiencies of many vitamins etc which are the ones acting as coenzymes, enzymes and thus immunity goes haywire and ultimately ending up in cancerous state, unless proper replacement of those nutrients are done. Moreover earlier it was these plants which provided the ways by which natural remedies prevented these cancers and today it is big pharma dictating chemotherapies to be developed which might not be helping in the cure rate or 5 year survival rates and thus going back to products from these natural plants seems to be the correct answer for the natural tackling up of these abnormal cells formed. Further the state of mind has a big role in controlling immune response with the psycho-immunoneurotherapy being developed as a field which explains how miracles occur in the field of cancer.

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Conflicts of interests

There is no conflict of interest present in the realization of this clinical case.

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