Obesity and Cancer: How Understanding the Connection Early Can Have an Impact on Prevention

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Abstract

There is a common understanding that obesity is associated with increased incidence of heart disease and diabetes. Recent synthesis of literature links obesity with several cancers including cancers of colon, esophagus, breast, endometrium, and kidney. Increased risk of developing several other cancers has also been associated with high fat diet and low physical activity. The risk of developing type II diabetes is high in obese patients due to Insulin resistance. Insulin's ability to induce cellular proliferation has been linked to progression of cancers.

There is an immense need to implement health education to adolescent populations by training teachers to promote awareness of the role of obesity in cancer and benefits of not being obese. Education and research in this area is critical to prevention of obesity and cancer. Psychologically, obesity does not cause an immediate alarm as compared to being diagnosed with cancer. Promoting outreach programs by universities and other health professionals can enhance knowledge and understanding at an early age. Implementing a required science course in schools to focus on biology and progression of cancer and the importance of healthy habits may have impact in the future of the health of coming generations.

Introduction

When cells proliferate without restraints, there is development of cancer. Increased risk of cancer is observed in overweight children. However, the underlying cause and mechanism are unclear [1]. Thus, there is urgent need to investigate the cause-and-effect relationship between overweight children and their increased risk to developing cancer, with a long-term desirable goal of cancer prevention.

Cancer in Adolescent Years

Leukemia and brain cancers top the list of cancers in ages 0-16. There has been noticeable improvement in the survival of children with cancer. However, whether or not dietary habits and obesity in early years of life influence and predispose this segment of the population

to developing cancer in future when they are older have not been systematically investigated. Nevertheless, obesity is linked to development of several types of cancers.

Role of obesity in cancer

Obesity is often linked to diabetes and heart diseases: on the other hand, there is considerable recent evidence linking obesity to cancer. Furthermore, diabetes itself increases the risk to developing cancer. For example, increase in carbohydrate intake and obesity parallels the increase in esophageal cancer. It has also been shown that 14% of deaths in men and 20% of deaths in women resulting from cancer at age 50 or older are due to obesity [5].

Association of obesity with prostate cancer has been reported by Quin and Babb (2002) [2]. Moreover, obesity may be a predictor of poor diagnosis at higher tumor grade and stage [3]. In the same studies, high waist to thigh circumference rather than body mass index (BMI) was associated with increased prostate cancer risk [2]. Adipokines that correlate with BMI enhance angiogenesis process which is critical in the progression of cancer [4].

Higher BMI also has been shown to increase the risk of breast cancer in post-menopausal women [6]. Mechanism underlying this risk is not well understood but has been suggested to be the consequence of increased secretion of estrogens. Increased risk of developing colon and rectal cancer is associated with increasing waist circumference whereas higher BMI only increased risk in men for rectal cancer [7, 8]. Several other studies link increased risk of cancer to obesity, BMI or waist-to-hip ratio (WHR) [9, 10, 12, 13, and 14]. Consequently, an improved understanding of the mechanisms underlying the biological linkage of obesity to cancer development and progression will throw new light the linkage.

Warburg Hypothesis and Cell Signaling: Systems Biological Approach

Within the context of our studies, it is relevant to note that the Kech School of Medicine, University of Southern California has been funded for 5 years to study relationships between obesity and cancer. The goal of their studies is to examine metabolic risk factors in obesity.

Considerable progress has been made in the area of understanding of differences between normal and cancer cells. Biological differences have led us to delineate mechanisms involved in progression of cancer. The multi-step mechanisms include mutations, clonal expansion of mutated cells, changes in gene expression, alteration in cell signaling, invasion, angiogenesis, and metastasis. These mechanisms involve carefully orchestrated biochemical pathways that are tuned by energy from cellular intermediary metabolism. The coordination of these pathways in a normal cell is disrupted by the environmental stress and in some cases genetic predispositions (e.g, obesity and diabetes). The ensemble adapts itself by favoring cellular milieu that leads to activation of pathways that favor progression of cancer.

The influence of the energetics in tumor genesis and progression was hypothesized by Warburg [11] who showed increase in aerobic glycolysis and dependence of the glycolytic pathway for production of ATP. This phenomenon is known as the Warburg effect. Several cell signaling pathways involve phosphorylation of signaling proteins for driving tumor progression. Blocking these pathways will have major significance in the treatment of cancer. Regulation of the pathways early may have a profound effect on retarding or even blocking the progression of cancer, ultimately leading to cancer prevention. Several studies, including ours, indicate a crosstalk between metabolism and mitogenic signal pathways critical in invasion, angiogenesis and metastasis.

Treating the body to an overwhelming increased influence of metastatic pathways may tune cells to be ready for an opportunity for a mutated cell in a favorable environment to progress to cancer. Several epidemiological studies indicate this association with cancer formation [16, 17]. Obesity, lack of exercises, sedentary lifestyle, and decreased consumption of fruits and vegetables are some of the factors that increase the risk of developing cancer [18, 19, and 20]. A systematic approach that focuses on the interactions between components of biological systems as discussed above will greatly facilitate our understanding of the progression of cancer. Interactions of key metabolic pathways and cell signaling may indeed be critical in determining how obesity may increase the risk of developing cancer. The understanding of the mechanisms underlying these metabolic and signaling interactions may provide new approaches to the area of anticancer drug discovery.

We studied in our laboratories the effects of inhibitors of glycolytic enzymes on influencing cell signaling that leads to the progression of cancer. 4-bromopyruvate and iodoacetate that specifically block two glytolytic enzymes resulting in alteration of the mTOR pathway that is important for progression of cancer. These studies show the crosstalk of metabolic pathways with mitogenic pathways and possible linkage between cellular metabolism and cancer development [21].

Even now we have to cope with finding the right anti-cancer drugs to treat and improve the survival and quality of life of patients with cancer. It would be more ideal and beneficial to the population at large to prevent the occurrences of cancer and have a strategy that would minimize the incidence and deaths due to cancer. In broad terms the Warburg hypothesis argues that it is imperative to revisit metabolic characteristics that favors development of obesity which ample epidemiological data suggest ultimately favor development and progression of cancer.

Having established a strong argument that obesity and associated metabolic syndrome(s) will precipitate cancer and cancer progression, we now need to finally focus on how to prevent it.

Outreach on Cancer prevention in grade schools onward and upward

We have promoted Mr. Yuk to keep children avoiding dangerous materials for the fear of food poisoning. However, a devastating disease such as cancer that in majority of cases, is due to environmental factors, is not something we often discuss with school children. Cartoon figures like Shrek have increased influence on children but do we also tell children their susceptibility to diseases? A health course focusing on the influence of obesity in making individuals more prone to diseases is necessary during the early years of childhood education. This approach will help in cautioning students to develop more healthy habits for a better future.

Dr. Colin Waine has shown that obese boys have a fourteen percent increased risk and obese girls have a twenty percent risk of developing cancer in their adult life [22]. A decrease in energy expenditure and dietary changes in children have contributed to the obesity in children [23]. Studies carried out by Gascon et al. have shown that childhood obesity and hormonal abnormalities associated with cancer risk [24]. For all ages, WHO suggests that after omitting tobacco use, obesity is the second most important form of preventing cancer [25].

Conclusion

In developing the argument that obesity could lead to development of cancer, we have argued that it is imperative to educate children at as early a stage possible about such a devastating health linage. Clearly, as other presenters in our forum have also shown or will have also demonstrated, education makes a difference. We advocate that this is a golden opportunity

for faculty, nurses, pharmacist, physician's assistants, and other health professionals to visit grade schools and older children about the dire importance of weight control. We have already a system in place to undertake such important health education outreach in Idaho and Utah. We give seminars in high schools to educate students about cancer and emphasize the importance of maintaining good health for a healthy life into adulthood. Implementation of these outreach programs by health professionals, science academicians, graduate and undergraduate students can create a network in communities and schools that will have impact on reducing obesity in children by educating and bringing awareness about potential impact of obesity.

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