Cancer cachexia as a model for treatment of obesity

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Received: 30 July 2011 / Accepted: 9 December 2011 / Published online: 4 January 2012

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Dear Sir,

Cancer cachexia describes a syndrome of progressive weight loss, anorexia and persistent erosion of host body cell mass in response to malignant growth. Cachexia is a complex metabolic state with progressive weight loss and depletion of host reserves of adipose tissue and skeletal muscle mass. Cachexia seen in cancer patients is not only due to the persistence of anorexia, but is mainly due to both proteolysis and lipolysis constantly occurring in the body. This leads to both muscle as well as fat loss [1]. Factors implicated in cancer cachexia are eicosanoids, decreased nutrient intake, increased catabolism due to surgery and chemotherapy.

The cancer cells produce various factors like Lipid Mobilizing Factor (LMF) and Proteolysis Inducing Factor (PIF). Host cell and tumour cell interaction leads to pro-inflammatory cytokine production like TNF- α , Interleukin-1 (IL-1), Interleukin-6 (IL-6) [2, 3]. Tumour-host immune interaction also leads to neuroimmune activation, especially by IL-1 and TNF- α . These cytokines mediate “hypothalamic resistance” by hyper-activating anorexigenic neurones and suppressing prophagic neurones [4]. Neuro hormones and pro-inflammatory cytokines contribute to an imbalance in anabolic and catabolic pathways.

Leptin (released by adipocytes) helps in regulating food intake and energy expenditure by stimulating neuropeptide Y (orexigenic neuropeptide) in a negative feedback mechanism. In cancer, the hypothalamic actions of cytokines like IL-1, IL-6 and TNF- α stimulate and/or mimic the release of leptin alongwith other anorexigenic neuropeptides like Corticotropin releasing factor (CRF) thus inhibiting the negative release of NPY leading to

its dysregulation, therefore producing anorexia and unopposed weight loss [5].

A small number of studies indicate the role of certain tumour-derived factors like Proteolysis-inducing factor (PIF) and Lipid mobilizing factor (LMF) which are closely related to weight loss in cachexia. PIF induces protein degradation in skeletal muscles while LMF induces lipolysis in murine adipocytes [6]. However, their definitive role in the mechanism of cachexia has yet not been established.

We know that both cachexia and anorexia coexist as an anorexia-cachexia syndrome in cancer patients. They act synergistically causing loss of muscle mass, reduction in total fat and reduction in bone mineral density. Although the cause of cancer cachexia is undoubtedly multi-factorial, cytokines play a pivotal role in the mechanism of weight loss in such patients. If we can identify those factors which only aggravate lipolysis without affecting muscle mass and bone density and use it in the management of obesity, one can hope to achieve positive results. Thus research could also be directed towards this cachexia model for further insights.

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