Chapter

87

AIDS Wasting Syndrome: Current Concepts in Management

SANJEEV SINHA, MOHAMMAD TAHIR

INTRODUCTION

Since its first recognition in homosexual population in USA, human immunodeficiency virus (HIV) infection has taken the form of a pandemic. Clinical manifestations of HIV infection are varied. HIV infection leads to changes in the body composition[1]. Variable degree of malnutrition has been found in HIV infected patients[2]. During the course of HIV infection patients develop AIDS-related cachexia also known as 'wasting syndrome' (WS) which is a chronically debilitating and potentially life threatening metabolic disorder. WS is one of the AIDS defining illnesses listed in Center for Disease Control (CDC), Atlanta guidelines[3]. In this article we present the clinical characteristics and current concepts in the management of WS.

DEFINITION

WS is a term employed for AIDS-related cachexia. Cachexia has been described since ancient times as:

"….the shoulders, clavicles, chest and thighs melt away. This illness is fatal….."

—*Hippocrates* (*460-370 BC*)

CDC defined WS in 1987 as loss of >10% of baseline body weight plus chronic diarrhea (at least 2 stools per day for ≥ 30 d) or chronic weakness and documented fever (for ≥ 30 d, intermittent or constant) in the absence of a concurrent condition illness or conditions other than HIV infection that could explain the findings (e.g. tuberculosis, cancer, isosporiosis, cryptosporidiosis, or other specific enteritis)[3,4].

PATHOPHYSIOLOGY

Pathophysiology and development of WS is multifactorial. Dysregulation in the levels of various molecules including cytokines, myostatin, insulin like growth factors, testosterone and adrenal hormones have been implicated. Various co-morbid medical conditions affect its development[5]. Flow diagram (Fig. 1) depicts the mechanism of development of WS and its manifestation.

CLINICAL MANIFESTATIONS

Ongoing reduction in lean body mass is the result of body cell mass as well as the extra-cellular matrix. This leads to extreme weakness, an inability to perform simple tasks, reduced health related quality of life (HR-QOL), secondary immune dysfunction, organ failure and death[6,7].

WASTING SYNDROME IN THE ERA OF HAART

Introduction of HAART has led to significant reduction in morbidity and mortality. WS continues to occur, though the incidence of WS has reduced by approximate 50%[8]. The percentage of persons with WS at the time of their AIDS diagnosis has increased during 1992 through 1997, with the highest percentage in 1997[9]. One study showed that > 50% of HIV infected patients with WS were receiving HAART[10]. Though, the characteristic and predictor of WS has changed. WS seen in the HAART era represent gradual loss of lean body mass without severe weight loss as compared to catastrophic weight loss seen in pre-HAART era[11]. One study has shown that predictors of WS in the pre-HAART era (1988-1995) such as fatigue, anemia, and lower than expected CD4 cell count no longer predict WS in the HAART era (1996-1999)[8].

Various mechanism including the disturbances of cytokine milieu by HIV has been proposed. Shikuma

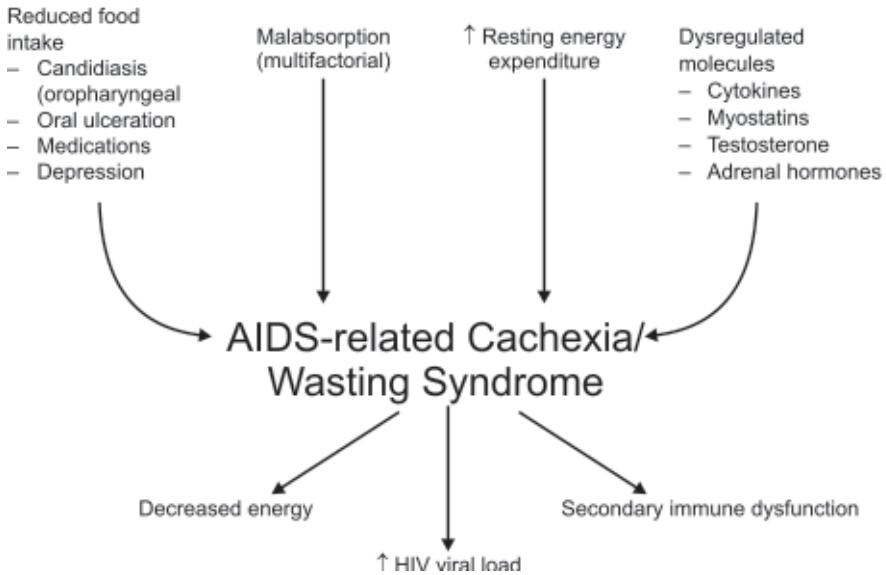

Fig. 1: Pathophysiology and manifestations of wasting syndrome

CM, et al have shown that HIV infection in peripheral blood macrophages may be responsible for the development of WS in the HAART era. They found that level of HIV proviral DNA was significantly higher in subjects with > 5% weight loss 1 year after initiation of HAART as compared to those who had stable weight or gained weight after HAART[12].

MANAGEMENT

Management of WS should be an integral part of comprehensive AIDS care. WS has become a major problem in the HAART era. Management primarily involves attention to medical, psychological and nutritional aspects of the illness. Opportunistic infections management, ensuring adequate caloric intake and proper food absorption are the cornerstone of management[13]. Other considerations include optimum antiretroviral therapy, appetite stimulation and progressive resistance exercise training.

No therapy is fully effective to revert back the lost weight but many drugs are being used. In USA, megestrol has approval for treatment of anorexia, cachexia or an unexplained, significant weight loss in an AIDS patient[14]. For appetite stimulation, dronabinol is used[15]. However, both dronabinol as well as megestrol primarily increase body fat but not the lean body mass and physical function[16,17]. Though not approved, testosterone therapy in patients with hypogonadism (seen in about 20% men with wasting)[18] has shown to increase lean body mass in small, well controlled studies in men[19] but may not be as effective in woman[20].

FUTURE TRENDS

Recently, somatotropin has been advocated for management of WS. At a dosage of 0.1 mg/kg/day subcutaneous administration for 12 weeks, it has been shown to increase work output, body weight, lean body mass and improved HR-QOL, as compared to placebo. Its tolerability profile is manageable. However, long term efficacy and tolerability, cost effectiveness, optimum dosage, management of patient after 12 weeks therapy, maintaining the gained lean body mass and possibility of a maintenance dose remains to be determined[21].

REFERENCES

1. Ott M, Lembcke B, Fischer H, et al. Early changes of body composition in human immunodeficiency virus-infected patients: Tetrapolar body impedance analysis indicates significant malnutrition. Am J Clin Nutr 1993;57:15-9.
2. Dannhauser A, van Staden AM, van der Ryst E, et al. Nutritional status of HIV-1 seropositive patients in the Free State Province of South Africa: Anthropometric and dietary profile. Eur J Clin Nutr 1999;53:165-73.
3. Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. Council of State and Territorial Epidemiologists; AIDS Program, Center for Infectious Diseases. MMWR Morb Mortal Wkly Rep 1987;36 Suppl 1:1S-15S.
4. Faintuch J, Soeters PB, Osmo HG. Nutritional and metabolic abnormalities in pre-AIDS HIV infection. Nutrition 2006;22:683-90.
5. Morley JE, Thomas DR, Wilson MM. Cachexia: Pathophysiology and clinical relevance. Am J Clin Nutr 2006;83:735-43.
6. Nemechek PM, Polsky B, Gottlieb MS. Treatment guidelines for HIV-associated wasting. Mayo Clin Proc 2000;75: 386-94.

7. Perry CM, Wagstaff AJ. Recombinant mammalian cell-derived somatropin: A review of its pharmacological properties and potential in the management of wasting associated with HIV infection. Biodrugs 1997;8: 394-414.
8. Smit E, Skolasky RL, Dobs AS, et al. Changes in the incidence and predictors of wasting syndrome related to human immunodeficiency virus infection, 1987-1999. Am J Epidemiol 2002;156: 211-8.
9. Jones JL, Hanson DL, Dworkin MS, et al. Surveillance for AIDS-defining opportunistic illnesses, 1992-1997. MMWR CDC Surveill Summ 1999;48: 1-22.
10. Wanke CA, Silva M, Knox TA, Forrester J, Speigelman D, Gorbach SL. Weight loss and wasting remain common complications in individuals infected with human immunodeficiency virus in the era of highly active antiretroviral therapy. Clin Infect Dis 2000;31: 803-5.
11. Roubenoff R, Grinspoon S, Skolnik PR, et al. Role of cytokines and testosterone in regulating lean body mass and resting energy expenditure in HIV-infected men. Am J Physiol Endocrinol Metab 2002;283: E138-45.
12. Shikuma CM, Valcour VG, Ratto-Kim S, et al. HIV-associated wasting in the era of highly active antiretroviral therapy: A syndrome of residual HIV infection in monocytes and macrophages? Clin Infect Dis 2005;40:1846-8.
13. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. Clin Infect Dis 2003;36: S69-78.
14. Par Pharmaceutical Companies Inc. Megace ES prescribing information (online). Available from URL: http://www.parpharm.com/pdf/megace/megace es pi final.pdf. [Accessed November 6, 2006].
15. Solvay Pharmaceuticals Inc. Marinol prescribing information (online). Available from URL: http://www.solvay-pharmaceuticals-us.com/static/wma/pdf/1/3/1/9/Insert%20Text%20500012%20Rev%20Jul%202006.pdf [Accessed November 6, 2006].
16. Oster MH, Enders SR, Samuels SJ, et al. Megestrol acetate in patients with AIDS and cachexia. Ann Intern Med 1994;121: 400-8.
17. Von Roenn JH, Armstrong D, Kotler DP, et al. Megestrol acetate in patients with AIDS-related cachexia. Ann Intern Med 1994; 121:393-9.
18. Rietschel P, Corcoran C, Stanley T, Basgoz N, Klibanski A, Grinspoon S. Prevalence of hypogonadism among men with weight loss related to human immunodeficiency virus infection who were receiving highly active antiretroviral therapy. Clin Infect Dis 2000;31:1240-4.
19. Grinspoon S, Corcoran C, Askari H, et al. Effects of androgen administration in men with the AIDS wasting syndrome. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 1998;129: 18-26.
20. Miller K, Corcoran C, Armstrong C, et al. Transdermal testosterone administration in women with acquired immunodeficiency syndrome wasting: A pilot study. J Clin Endocrinol Metab 1998;83:2717-25.
21. Goldsmith DR, Wagstaff AJ. Mammalian cell-derived somatropin: A review of its use in the management of HIV-associated wasting. Drugs 2006; 66:387-401.