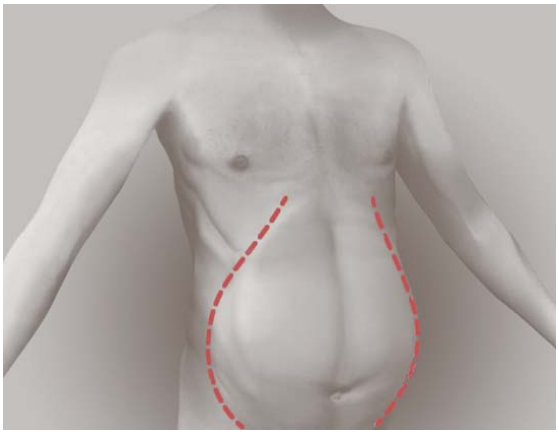
HIV-Associated Lipodystrophy

OVERVIEW

Antiretroviral therapy (ART) has revolutionized treatment of human immunodeficiency virus (HIV), markedly suppressing HIV replication and dramatically improving the daily life, prognosis and survival of HIV-infected patients.[1,2] However, patients living with HIV are at risk for other complications. For example, in a recently published study, HIV patients experienced acute myocardial infarctions (heart attacks) at nearly twice the rate of non-HIV patients and the incidence of diabetes was similarly nearly twice that of non-HIV patients.[3]

HIV-associated lipodystrophy affects many HIV patients who take ART, but the medications are not the only drivers of the condition. Characterized by metabolic abnormalities that may be associated with body composition changes and increased risk of cardiovascular disease and diabetes, HIV-associated lipodystrophy is a serious condition with long-term health implications and there is currently no approved treatment for these patients.

DESCRIPTION AND CLINICAL IMPACT



- The primary metabolic abnormalities associated with HIV-associated lipodystrophy are dyslipidemia (high levels of LDL-cholesterol and triglycerides, as well as low levels of HDL-cholesterol) and insulin resistance.
- The body composition changes include accumulation of excess fat (lipohypertrophy) in the abdomen (primarily as visceral fat), breast, and over the dorsocervical spine. Some patients may experience loss of extremity and subcutaneous fat (lipoatrophy), most noticeably in the face, limbs, and buttocks.

- All these conditions place patients at increased risk for cardiovascular disease and type 2 diabetes.
- In addition, the body composition changes and particularly excess abdominal fat may stigmatize HIV-infected patients and discourage their compliance with antiretroviral treatment.

PREVALENCE

- In 2008, it was estimated that among the 2 million HIV-positive patients (both diagnosed and undiagnosed) in North America and Europe, approximately 285,000 suffer from HIV-associated lipodystrophy.

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- Based on proprietary market research with payors, patients and physicians, Theratechnologies estimates that by 2012 approximately 380,000 patients treated with antiretrovirals will have lipohypertrophy in North America and Europe.
- A recent study showed that one in five HIV-infected patients worldwide has the metabolic complications associated with HIV-associated lipodystrophy.[4]
    - 39 percent of HIV-infected patients had high cholesterol and 56 percent had high triglyceride levels.[4]
    - Patients had a five-to-eightfold increased prevalence of diabetes.[4]

POTENTIAL THERAPEUTIC OPTIONS

- There are currently no approved treatments for excess abdominal fat accumulation associated with HIV-associated lipodystrophy and more specifically with lipohypertrophy.
- Growth hormone (GH) has been shown to play an important role in regulating fat metabolism, body composition (e.g., muscle mass), and lipid formation. In clinical studies, GH reduced trunk fat and visceral adipose (fat) tissue (VAT) and increased lean body mass. However, a significant number of GH-treated patients experience problematic side effects, such as fluid retention (swelling), significant joint pain and high blood sugar.
- A potential therapeutic approach involves the use of human Growth Hormone Releasing Factor (GRF), which induces an increase in endogenous GH generally within the physiological range. One therapy under development is a synthetic form of GRF. Clinical studies have shown that it reduces abdominal fat (in particular, visceral fat), without compromising glycemic control (the regulation of blood sugar levels); increases muscle mass; and is associated with fewer side effects than administration of pharmacological doses of GH used to treat HIV-associated lipodystrophy.

[1,2] Marschner IC et al. Use of changes in plasma levels of human immunodeficiency virus type 1 RNA to assess the clinical benefit of antiretroviral therapy. *J Infect Dis* 1998;177(1):40-47.

Sterne JA et al. Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study. *Lancet* 2005;366(9483):378-84.

[3] Triant VA, et al. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab. 2007;92:2506-2512.

[4] Milinkovic Ana et al. Current perspectives on HIV-associated lipodystrophy syndrome. *Journal of Antimicrobial Chemotherapy*. 2005. doi:10.1093/jac/dki165.