Treatment of Human Immunodeficiency Virus–Associated Facial Lipodystrophy Syndrome With Dermafat Graft Transfer to the Nasolabial Fold Areas: A Case Report and Review of the Literature

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Human immunodeficiency virus (HIV) infection affects millions of people worldwide. At the end of 2005, an estimated 40.3 million people were living with HIV globally. In North America, approximately 1.2 million adults and children are reportedly living with HIV, with an additional 43,000 newly infected individuals diagnosed in the past year.¹ Until recently, HIV-positive patients had a bleak prognosis, but now HIV infection has been transformed into a chronic disease with an extended life expectancy due to treatment options with the multiple antiviral medications now available. Oral and maxillofacial surgeons are routinely providing cosmetic corrections of facial deformities and should be familiar with the pathogenesis and treatment options available for HIV-associated facial lipodystrophy.

Currently, a combination of protease inhibitors (PIs), reverse-transcriptase inhibitors, and nucleoside analogs are being used to control the progression of this disease. The prolonged course of medical therapy has led to a group of secondary side effects manifested as body fat dystrophy and other metabolic disorders. HIV-associated lipodystrophy has been reported in up to 83% of individuals treated with current antiviral treatments, specifically protease and nucleoside reverse-transcriptase inhibitors (NRTIs).²⁻⁶

The physical findings associated with the lipodystrophy syndrome include fat wasting of the facial areas (specifically in the nasolabial folds) and the extremities. Adipose tissue hypertrophy is noted in the cervicodorsal area (ie, “buffalo hump”) and the abdomen. Numerous treatment options have been reported in the surgical literature for treatment of HIV-associated lipodystrophy, including augmentation of fat-atriphied areas with alloplastic and autogenous graft material, and liposuction or surgical excision of fat from the hypertrophied dorsocervical areas.

Report of a Case

A 54-year-old HIV-positive man was referred to our Oral and Maxillofacial Surgery service for cosmetic correction of
FIGURE 1. A-D Note the severe subcutaneous fat wasting in the areas of nasolabial fold. E, Dorsocervical fat accumulation. “Buffalo Hump” appearance (arrow).


facial fat wasting. The patient was first diagnosed with HIV in 1997. He has been under the care of his infectious disease physician and has been treated with multiple antiviral medications, including stavudine, atazanavir, and lamivudine, in different regimens and combinations since 1998. Currently the patient is receiving emtricitabine and tenofovir disoproxil fumarate for management of his HIV infection. The patient’s medical history included recent onset of hyperglycemia and a history of shingles in the upper extremities. Laboratory findings included the following: white blood cell count, 11.8; hemoglobin, 13.6; hematocrit, 39.3; platelets, 241; lymphocyte %, 23; monophil %, 9.3; neutrophil %, 7.8; glucose, 135; hemoglobin A1C, 6.3; blood urea nitrogen, 10; creatinine, 1.2; CD4 + CD3, 574; total cholesterol, 167; triglycerides, 381; and low-density lipoprotein, 66. Vital signs and anthropometric measurements on the date of examination were blood pressure, 135/72 mmHg; heart rate, 78 beats/minute; height, 5’7’’; and weight, 156 lb.

The patient presented with severe subcutaneous fat wasting in the nasolabial fold areas bilaterally (Fig 1). He was completely edentulous, and on removal of his upper and lower dentures, the buccal defects were even more accentuated. The remainder of the examination revealed mild fat deposition in the dorsocervical area (“buffalo hump”) (Fig 1), but no evidence of hyperadiposity in the abdominal area. Cranial nerves II to XII were grossly intact.

The patient was offered autogenous and/or allogeneic grafting material to enhance and normalize the contours of the nasolabial folds. The patient was taken to the operating room and was given general anesthesia with orotracheal intubation. The periumbilical area was chosen as the donor site. The proposed outline of the dermagraft was outlined in
the nasolabial regions bilaterally, and the drawing was transferred to the donor site using a sterile aluminum foil template (Fig. 2). The epidermis was excised in situ, and the graft was elevated with the fat and dermis as a single unit to a depth of about 1 to 1.5 cm. The medial ends of the grafts were vertical, and the lateral ends were narrowed to a U-shape. Excessive fat was trimmed to ensure a uniform thickness of 1 to 1.5 cm, with the edges of the graft thinner...
FIGURE 2 (cont’d.)

than the center to create a beveled effect. The volume of the harvested fat was oversized, anticipating a loss of volume of approximately 30% to 50% over an approximate 3-month period, as demonstrated by other surgical cases in the literature.6 Dermfat grafts were stored in cool normal saline solution. The abdominal donor site was closed in layers. Attention was turned to the nasolabial folds. The incision was outlined in the nasolabial folds and injected with approximately 72 mg of 2% lidocaine with 36 μg of epinephrine. The incision was created following the contour of the nasolabial folds. Dissection was carried out in a lateral fashion, creating a subcutaneous pocket in the nasolabial area, taking care to maintain a plane between the subcutaneous layer and the underlying muscles of facial expression and to avoid damage to the facial nerve (Fig 2). Hemostasis was achieved with minimal electrocautery of the area. The dermafat grafts were further trimmed to fit the created pockets. The main rationale for including the dermis was in its vasoinductive quality embedded within its capillary architecture (Fig 2).10 To maintain the graft as a single unit within the recipient pockets, a 1-mm-thick piece of allograft (life cell) material was attached to the underlying fat layer by suturing it to the fat graft before inserting it into the recipient site. The dermaf composite unit was placed and secured into the pockets using 2 sterile buttons and transcutaneous silk sutures by passing a Keith needle through the skin and the graft in place and tying the knot over the buttons, to prevent movement of the graft and eliminate dead space within the recipient sites. The incision was closed in layers using 4-0 Vicryl and 5-0 Prolene running sutures (Fig 2). The patient was allergic to penicillin and thus was given intravenous clindamycin preoperatively and every 8 hours during the hospital course. The patient was discharged on the second postoperative day. Discharge medications included topical bacitracin and oral gatifloxacin 200 mg twice daily for a total of 7 days. Postoperatively, sensory and motor functions of cranial nerves V and VII were intact and the patient had good perioral range of motion. He was instructed to maintain a soft diet for 1 week and to not wear his upper and lower prostheses for 5 days. On the fifth postoperative day, there were no signs or symptoms of infection, and all wounds were closed primarily. Subsequently, sutures were removed, and the patient was advanced to a soft diet as tolerated. Percutaneous buttons were maintained and removed on the tenth postoperative day. The patient was followed up for a period of 12 months with good contour and esthetic results in the nasolabial region (Fig 3).

Discussion

Lipodystrophy in HIV-1–infected individuals is considered a side effect of antiviral therapy. The pharmacokinetics of such drugs alters body fat metabolism, resulting in dyslipidemia, insulin resistance, and generalized loss of subcutaneous fat with or without fat deposition in the dorsocervical and abdominal areas. Although lipodystrophy is not considered life-threatening, such body fat changes may be perceived as social stigmata, leading to poorer compliance with antiviral therapy.11 Furthermore, metabolic abnormalities may result in adverse cardiovascular disease. Currently multiple antiviral agents have been approved by the FDA for managing HIV infection (Table 1). These antivirals are divided into 4 categories based on their pharmacologic site of action: PIs, NRTIs, non-nucleoside reverse-transcriptase inhibitors (NNRTIs), and fusion inhibitors. These drugs are routinely administered as a combination of 2 or more pharmacologic categories to maximize antiviral therapy. This combination of potent antiviral combination is referred to as highly active antiretroviral therapy (HAART). Most HIV patients are taking a regimen of 2 NRTIs plus 1 PI or 2 NRTIs plus 1 NNRTI.

The HAART regimen has revolutionized the management of HIV-infected patients by significantly reducing the viral load, increasing CD4 count, and decreasing morbidity and mortality. But these medications are not free of side effects, however. The use of multiple antiviral drugs to control the progression of
HIV infection has increased the rate of such effects as lipodystrophy.

The etiology and pathogenesis of lipodystrophy associated with HIV treatment have not been clearly determined; however, PI and NRTI use have been associated with the development of such lipodystrophy. Molecular pathophysiologic mechanisms proposed to explain the development of lipodystrophy by Nolan et al. demonstrated an interaction between PIs and NRTIs. PIs induce insulin resistance, dyslipidemia, and visceral and dorsocervical fat accumulation, whereas NRTIs promote mitochondrial toxicity, adipose tissue loss, and subcutaneous fat wasting (Fig 4).

Patients who develop metabolic side effects of lipodystrophy syndrome are at significantly greater risk for development of cardiovascular disease. Elevated blood lipids, compounded with insulin resistance, predispose these patients to developing diabetes mellitus. Cardiovascular disease and diabetes can result in serious systemic complications, including myocardial infarction, nephropathy, neuropathy, stroke, and blindness. 

Currently, there is no proven cure for the treatment of lipodystrophy syndrome associated with HIV HAART therapy. Alterations in the HAART medication regimen to minimize or reverse the pattern of lipodystrophy have been attempted, with minimal positive outcomes. The medical goals of treatment for the syndrome focus on minimizing the metabolic consequences of HAART treatment by managing hyperlipidemia.

Table 1. ANTIVIRAL MEDICATIONS

<table>
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<tr>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>PIs</th>
<th>Fusion inhibitors</th>
<th>Combination NRTI products</th>
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<tr>
<td>Abacavir</td>
<td>Delavirdine</td>
<td>Amprenavir</td>
<td>Enfuvirtide</td>
<td>Abacavir + lamivudine + zidovudine</td>
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<td>Zidovudine</td>
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<td>Saquinavir</td>
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HAART associated Lipodystrophy

NRTIs

Mitochondria toxicity

Adipocyte Loss/or loss Of function

Subcutaneous Fat Wasting

PIs

Insulin Resistance

Dyslipidemia

Visceral Fat Accumulation

Increase Risk of Cardiovascular Disease


Idiopathy, insulin resistance to prevent diabetes, and, most importantly, continuing with an antiviral regimen to control the progression of HIV infection. In addition, it has been noted that HIV patients with lipodystrophy have lower levels of growth hormone than patients without lipodystrophy. Therefore, recombinant human growth hormone (rhGH) has been investigated in the management of lipodystrophy. The results reveal a reduction in the hyperadiposity associated with lipodystrophy, but the use of rhGH further exacerbates the loss of subcutaneous fat from the facial areas. Studies continue to explore the medical management of HIV HAART-associated lipodystrophy.

Surgical management of HIV-associated lipodystrophy has been described in the literature with good success. Augmentation of subcutaneous facial areas with allogeneic and autogenous grafts and liposuction of the hyperadipose tissues of the dorsocervical areas are the most common surgical therapies. James et al classified the severity of facial lipoatrophy into 4 grades: 1, mild localized facial lipoatrophy, appearance almost normal; 2, deeper and longer central check atrophy, with facial muscles (especially zygomaticus major) beginning to show through; 3, deeper and wider atrophic area with muscles clearly showing; 4, atrophy covering a wide area and extending up toward the orbit. Most patients seeking surgical correction are in the grade 3 or 4. Our patient had grade 3 facial lipoatrophy.

Among autogenous graft materials for correction of contour defects in the head and neck area resulting from trauma, congenital defects, and neoplasm, the use of dermal fat graft has remained as a well-known and time-honored choice. Dermal grafts have been classified into 3 main categories.

- Camouflage grafts: Small dermal fat grafts harvested from the head and neck area near the recipient site, such as the periauricular region to camouflage small defects in the malar and cheek areas, particularly after facial rhytidectomy or midface lift procedures.
- Transition grafts: Large dermal fat grafts harvested from outside of the head and neck areas, usually removed from the suprapubic or periumbilical areas. These grafts are used to augment and reconstruct major volumetric soft tissue defects, such as in the case of HIV-associated facial lipodystrophy.
- Secondary grafts: Obtained from outside of head and neck area for soft tissue replacement resulting from imperfect previous facial cosmetic surgery or significant trauma.

Technical principles recommended in the surgical literature have some variability. Dermafat grafts are sculptured to a maximum thickness of about 1 to 1.5 cm to minimize resorption and necrosis. The concept of overcorrection is followed by many practitioners to obtain a more esthetic final result. The dermal layer is the vasoinductive layer for the underlying adipose graft and is usually placed facing against the subadjacent subcutaneous layer for optimal blood supply. Grafts are placed in tension-free subcutaneous pockets and are immobilized in place using bolsters as
described in this case report. Intravenous antibiotics and immersion of dermafat grafts into an antibiotic solution have also been described. Excess fat harvested can also be frozen and stored for future augmentations.16

Alloplastic materials including silicone, collagen, polyactic acid, and expanded polytetrafluoroethylene implants also have been used to augment HIV-associated facial lipoatrophy. Such materials have been used for a number of years for esthetic augmentation of facial skeleton and soft tissues. However, documented complications, such as granuloma formation, infection, implant migration, and unnatural “lumpiness” felt by the patient, may occur.

Finally, surgeons must address the dorsocervical fat deposition, which has been reported to create difficulty in dressing, reaching for items, turning, or lying supine. The dorsocervical hump also may further exacerbate a preexisting sleep disorder, such as obstructive sleep apnea. In addition, the “buffalo hump” may have a negative psychological impact on the HIV-infected patient. Ultrasonic tumescent liposuction and surgical lipoectomy have proven successful in correcting dorsocervical hyperadiposity.17

Performing surgical procedures for immunocompromised patients may be considered risky in terms of postoperative surgical infections; however, documented cases in the literature have not been associated with a higher risk of surgical infection in this group of patients. Consultation with infectious disease physicians can optimize the timing of surgery due to the variable immune status of such patients. Intraoperative and postoperative antibiotic therapy is also recommended.

Facial lipoatrophy adds to the enormous challenges that HIV disease has always presented for patients and healthcare providers. Metabolic and morphological complications of HAART are probably caused by several interrelated and complex physiological pathways currently under investigation. Whereas medical treatment focuses on prevention and pharmacologic treatment of this disease, surgeons must be able to provide reconstructive procedures to alleviate the disfiguring result of the syndrome. The objective of this article has been to familiarize the oral and maxillofacial surgeons with the evaluation and management of HIV-associated facial lipoatrophy.

References