

Antiretroviral Treatment-Associated Labia Majora Lipohypertrophy: A Rare Case and Plastic Surgical Treatment Options

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ABSTRACT

The emergence of highly active antiretroviral therapy (HAART) has revolutionized the prognosis of HIV-infected patients. However, the extended use of HAART is associated with a disfiguring complication termed lipodystrophy, a disorder of body fat maldistribution causing peripheral fat loss (lipoatrophy) and central fat accumulation (lipohypertrophy). Lipoatrophy commonly affects the face, legs, buttocks and arm, whilst lipohypertrophy frequently favours the abdomen, breast and dorsocervical region. To our knowledge, we present only the second documented case in the literature of a labia majora lipohypertrophy in a HIV-positive patient receiving long-term HAART. The severity of labial abnormality caused significant physical and functional morbidities. Labiaplasty with dermolipectomy of the labia majora and excisional lipectomy of the mons pubis was successfully performed. At a 6-month follow-up, patient had no recurrence with resolution of symptoms and resumption of normal activities of daily living (ADL).

KEYWORDS: HIV-associated lipodystrophy, lipohypertrophy, lipoatrophy, labia majora

INTRODUCTION

The introduction of highly activated antiretroviral therapy (HAART) circa mid-1996 has revolutionized the prognosis of HIV-infected patients. Unfortunately, prolonged HAART is associated with a disfiguring side effect that causes abnormal body fat distribution termed 'lipodystrophy' [1]. Its prevalence has been reported to range widely between 11-83% [2].

HIV-associated lipodystrophy is a syndrome of morphological changes consisting of peripheral lipoatrophy (fat loss) and central lipohypertrophy (fat accumulation), presents separately or in combination in the same individuals. Lipoatrophy commonly affects the face, legs, buttocks and arm, whilst central fat accumulation frequently favors the abdomen, breast and dorsocervical region [1, 2]. It is usually, but not invariably, associated with metabolic changes such as

hyperlipidaemia, hypercholesterolaemia, insulin resistance and type II diabetes mellitus [2].

The aetiology of HIV-associated lipodystrophy is multifactorial and differs between lipoatrophy and lipohypertrophy [3], but many studies attributed to HAART, especially protease inhibitors (PIs) and nucleotide reverse-transcriptase inhibitors (NRTIs) [2, 4]. PIs have been shown to inhibit zinc metalloprotease, the key enzyme involved in correct maturation and processing of prelamin A, leading to accumulation of toxic farnesylated prelamin A and subsequently causing dysregulation of transcription factors involved in adipogenesis [4]. NRTIs (especially stavudine) inhibit mitochondrial polymerase- γ and has been postulated to induce lipodystrophy by causing mitochondrial toxicity [4].

It should be mentioned that stavudine, which is a thymidine analogue NRTI is one of the first line

antiretroviral therapy available in Malaysia. Although it is cheap, stavudine is greatly associated with lipodystrophy. Hence, the use of stavudine is no longer recommended as the first line therapy internationally [5].

Standardized clinical assessment of lipodystrophy has been described in a Multicenter AIDS Cohort Study (MACS). This study defines mild, moderate and severe lipodystrophy as fat changes “only noted after close inspection” (mild), fat changes “noticed by the clinician without specifically looking for them” (moderate), and fat changes “easily noted by a casual observer” (severe) [6].

Whilst reports and procedures concerning lipohypertrophy of the aforementioned areas are common, reports of lipohypertrophy in the labio vulvar region are extremely scarce. Our literature search, to the best of our knowledge, yielded only one similar reported case. Lapalorcía et al. [7] described a labioplasty technique in a patient with HIV-associated labia majora lipohypertrophy. They performed liposuction and dermolipectomy of the longitudinal aspect of the labia majora.

We present a rare case of labia majora lipohypertrophy in a HIV-infected patient which was successfully treated with excisional lipectomy. The aims of our surgical treatment were: (1) to remove the areas of adiposity hence providing symptomatic relief and restoration of functional impairment, (2) to achieve aesthetically acceptable appearance in an intimate and sensitive part of the patient, and (3) to minimize the risk of recurrence.

CASE PRESENTATION

A 42-years-old woman was diagnosed with HIV in 1996 at the age of 23. She developed bilateral progressive labia majora swelling over 6 years. The swelling caused a number of restrictions in her ADL, namely; difficulty in selecting appropriate clothing, avoidance of sexual activity and disruption of her urinary, bowel and menstrual outflow.

She started HAART in 2001 consisting of Didanosine 300mg OD, Stavudine 30mg BD and Efavirenz 600mg ON. The didanosine and stavudine were discontinued and replaced with Combivir 1 tablet OD (Zidovudine 300mg/lamivudine 150 mg) and

Efavirenz 600mg ON in 2010. Her other medical history includes pulmonary tuberculosis in 2001.

On examination, she has a severe hypertrophy of bilateral labia majora extending up to the mons pubis (Figure 1). She also exhibits other lipodystrophic features including mild dystrophic fat accumulation in the dorsocervical and abdominal region, with peripheral fat wasting of the bilateral thighs. Her BMI is at 23 kg/m² (weight = 59kg, height = 1.60 m). Her pre-operative HIV RNA viral load was undetectable (less than 20 copies/ml) and the pre-operative and nadir CD4 lymphocyte counts was high at 613 and 561 cells/uL, respectively. Her baseline CD4 was at 977 cells/uL.

Plasma levels of triglyceride (1.14 mmol/L), cholesterol (4.90 mmol/L) and fasting blood glucose (5.9 mmol/L) were within normal ranges, excluding the presence of metabolic abnormalities.



Figure 1 Pre-operative view of the labia majora lipohypertrophy

Treatment & Outcome

She underwent a labioplasty with the excisional lipectomy technique similar to that performed by Lapalorcía et al. [7] without performing liposuction and fat grafting. Patient was placed in supine position with slight legs abduction, the crural creases and the vulvar mucosa were first marked to avoid violation of these anatomical landmarks. Then the incision markings over the longitudinal aspect of the labia majora were made. This marks were drawn at least 1 cm from the previously identified crural creases and the vulvar mucosa. Next the inguinal creases were identified bilaterally. Then the incision marking over the mons

pubis were drawn, 2 cm medial and parallel to the inguinal creases to avoid any surgery in the creases and to hide the scar within the hair-bearing area of the mons.

The resection of the excess skin and fat (dermolipectomy) over the labia majora was performed. At the mons pubis, the skin flap over the outlined area was elevated and followed by the resection of the excess fat (lipectomy) in this region. Main neurovascular structures supplying the genitovulvar area, which include the pudendal artery and vein, pudendal nerve and perineal nerve are located deep to the subcutaneous tissue [8]. However, careful resection was performed to avoid injury to these important structures.

Suction drains were left in place to monitor for bleeding and to reduce dead spaces. Postoperative period was uneventful and she was discharged on postoperative day 3.

Histopathology examination confirmed the lipodystrophic changes of the subcutaneous fat tissue. She was reviewed at 2 weeks showing a well-healed wound (Figure 2). At 6 months, the external genitalia had resembled a normal appearance, and sensitivity of the labia majora was restored. The patient had an uneventful recovery with no recurrence and resolution of symptoms within a 6-month follow-up (Figure 3).



Figure 2 Post-operative view of the labia majora at 2 weeks



Figure 3 Post-operative view of the labia majora at 6 months

DISCUSSION

Labia majora lipohypertrophy is a rare manifestation of HIV-associated lipodystrophy. Although it is less evident compared to facial or truncal changes, it can be severely disfiguring and lead to considerable functional morbidities as demonstrated in this present case. In addition to the obvious physical limitations, she experienced difficulties in urinating, defaecating and menstruation. She was successfully treated with an excisional lipectomy as described above. Although the long-term follow up is not available, she had a resolution of symptoms and no hypertrophic recurrence at a 6-month follow-up.

HIV-associated lipodystrophy can manifest in various anatomical distributions. Dorsocervical fat accumulation or facial lipoatrophy for example, are disfiguring and carries the risk of social stigmatization. Consequently, lipodystrophy could hinder adherence to treatment, affects patient self-esteem and quality of life [9]. Additionally, the presence of metabolic changes is associated with an increased risk of cardiovascular disease [2, 4, 10].

Therefore, it is pertinent for clinicians to be aware of the role of plastic surgery and the surgical treatment options for this unique condition. Davidson et al. stated three problems that can be addressed with reconstructive surgery: (1) lipohypertrophy, especially in the cervicodorsal fat pad, (2) facial lipoatrophy and (3) gynaecomastia [11]. The treatment of gynaecomastia is subcutaneous mastectomy with or without liposuction, but this is not the focus of this article [12].

Treatment options to remove the excess fat accumulation in lipohypertrophy include (1) liposuction or lipoplasty and (2) excisional lipectomy or surgical resection of the excess fat and skin [11, 13]. In our patient, we opted for the latter technique in view of the severity of her labial hypertrophy and her symptomatology. The use of liposuction in this case will likely result in recurrence or inadequate reduction, such as the case reported by Lapalorcía et al. [7].

Although liposuction is appealing given its relative non-invasive approach, minimal scarring and low rate of complication, the hypertrophied fat in these patients are very fibrous, making passage of the lipoplasty cannulas into the region quite difficult. High rates of recurrence are seen with lipoplasty alone due to inadequate removal. This leads to hyperplasia and subsequent hypertrophy of remaining adipocytes. Furthermore, liposuction carries risk of paresthesia, hyperesthesia, ecchymosis, increased seroma formation and infection [17].

Liposuction can be performed either using the traditional suction-assisted liposuction (SAL) technique or the ultrasound-assisted liposuction (UAL) [11, 13]. Combination of both methods can be performed using a superwet technique of tumescent to prepare the site and performed in three stages which are adipocyte cavitations, emulsification, and extraction [17].

SAL procedure uses an external source of suction to facilitate the removal of subcutaneous fatty tissue [14]. Prior to this procedure, tumescent solution prepared with mixture of Lignocaine, Adrenaline, and added into 1-litre Ringer Lactate fluid. This solution is infiltrated through 4mm access site for each treated area at 300mmHg pressure with hydro-dissection pump. Cannulas are used for feathering and refinement with attachment to vacuum curettage. Access site incisions are closed with simple interrupted nylon sutures and elastic compression garment applied [18].

Ultrasound assisted liposuction uses a cannula or probe to deliver fat-liquefying ultrasound vibration subcutaneously, allowing the removal of fat from dense and fibrous fatty tissue with greater ease [14, 15]. UAL setting of 5-6/10 for duration is expected to yield 50-100ml of cavitation per minute. End points of UAL include loss of resistance within the area of lipohypertrophy, reaching the pre-calculated duration of

cavitation, and/or appearance of blood tinged lipos aspirate [18].

Newer liposuction techniques such as laser-assisted liposuction and radiofrequency-assisted liposuction are available but its usage in HIV-associated lipodystrophy has not been described [15].

For facial lipoatrophy, the aim of the treatment is facial volume restoration. Currently, the mainstays of treatment are injectable dermal fillers and autologous fat transfer [12, 16].

Many type of dermal filler products are available and they are generally divided into temporary and permanent fillers. Temporary fillers can last from 3 months to 24 months and require multiple injections to maintain adequate aesthetic results. Examples include poly-L-lactic acid (Sculptra®), calcium hydroxylapatite (Radiesse®) and hyaluronic acid [9, 12]. Permanent fillers are synthetic materials, not resorbable and induce fibroplasia around the injection sites. Available products include polymethylmethacrylate, (PMMA; ArteFill®, Artecoll®), polyalkamide (Bio-Alcamid®) and silicone oil [9, 12, 13, 16].

Autologous fat transfer is another increasingly popular option for soft tissue augmentation [16]. This procedure involves fat harvesting from the abdomen, thighs or lipohypertrophic areas of the patient by liposuction or syringe aspiration, followed by injection of the fat into the volume-deficient areas of the face [13, 14]. A recent review by Shuck et al. demonstrate that both of these interventions resulted in high rates of facial volume restoration and patient satisfaction, with autologous fat transfer appearing to be a cheaper option compared to injectable fillers [16].

Other modalities such as dermis-fat-graft, rhytidectomy or facelift, implants insertion and parotid flaps have been described. However, these procedures are less commonly employed, more invasive, associated with lengthy operation time and a higher rate of complication. A comprehensive review of these modalities has been described elsewhere and is outside the scope of this report [11, 13].

In conclusion, HIV-associated lipodystrophy is a well-known complication of HAART, but manifestation with severe labia majora hypertrophy is extremely rare and carries considerable morbidities. Surgical correction with excisional lipectomy has

provided a satisfactory outcome in our patient with no recurrence noted. Several modalities of plastic surgical treatment are available and thus, treatment should be considered for cases of severe HIV-associated lipodystrophy.

Conflict of Interest

Authors declare none.

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