

Lipoatrophy as a manifestation of different clinical scenarios: Corticosteroid injection, lupus profundus and morphea induced lipoatrophy

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Abstract *Objective* To report the frequency of different types of acquired dermolipoatrophy in relation to different etiological factors.

Methods In this observational case series descriptive study, twenty nine patients with different clinical forms of acquired lipoatrophy were enrolled during the period from 2006-2020. For every patient, a full history and complete systemic and cutaneous examination were performed. Laboratory investigations were done, when needed.

Results Twenty nine patients with localized lipoatrophy, 16 (55.2%) females, 13 (44.8%) males, with ages ranged from 3-55 years (mean 16.7 years) were evaluated and analyzed. The current work showed that intralesional and intramuscular triamcinolone injection was the most frequent cause responsible for development of localized lipoatrophy in 27 (93.1%) patients followed by morphea and lupus profundus in only 1 (3.45%) patient for each. With regard to corticosteroid induced lipoatrophy, the buttock was the most commonly affected site in 14 (51.9%) patients and all the affected patients were children while the scalp was involved in 12 (44.4%) patients and forearm in 1 (3.7%) patient.

Conclusion Lipoatrophy following intramuscular and intralesional corticosteroid preparation particularly triamcinolone acetonide is an important and common cause for acquired lipoatrophy with significant psychological sequelae for the affected patients and/ or their parents. Also lupus profundus and linear morphea are important diseases to be considered while evaluating patients with acquired lipoatrophy.

Key words

Lipoatrophy, corticosteroids, triamcinolone, lupus profundus, morphea.

Introduction

Lipodystrophies are a defect of lipid metabolism resulting in adipose tissue atrophy or altered fat deposition.¹ On the bases of etiology, lipodystrophies are categorized into congenital or acquired and also, it can be classified according to the pattern and bulk of fat loss into either generalized or partial.² Patients with

localized lipodystrophies encounter only cosmetic issues, while insulin resistance, hypertriglyceridemia and fatty liver diseases can occur earlier in patient with generalized lipodystrophies.³

Congenital lipodystrophies are rare disorders and the two commonest types are congenital generalized lipodystrophy and familial partial

lipodystrophy.⁴

Patients with acquired types can be classified into acquired generalized lipodystrophy, acquired partial lipodystrophy, lipodystrophy in patients infected with the human immunodeficiency virus (HIV) receiving HIV-1 protease inhibitors, and localized lipodystrophies.³

Acquired generalized lipodystrophy usually presents with progressive fat loss from the face and extremities beginning in childhood and adolescent period. It can be idiopathic or develops in association with autoimmune disorders or panniculitis.⁵ Approximately 25% of cases are caused by panniculitis, 25% by autoimmune disease and 50% are of idiopathic origin.⁶ The autoimmune disorders include juvenile onset dermatomyositis, Sjögren syndrome, rheumatoid arthritis and systemic lupus erythematosus.⁷

Acquired partial lipodystrophy is a very rare type presented with fat loss initially affecting the face then proceeding to the shoulder, upper extremities, and trunk. The prevalence of autoimmune diseases is proposed to be approximately 40%, in particular systemic lupus erythematosus and dermatomyositis, and less frequently autoimmune thyroiditis, localized scleroderma, Sjogren's syndrome, and rheumatoid arthritis.⁸

HIV-associated lipodystrophy syndrome

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presented with fat loss affecting the buttocks, limbs, and face resulting in marked hollowing and wrinkling of the skin of the buttocks and face.⁹ It typically appears after receiving protease inhibitors-containing HAART for 2 years or more.¹⁰

Localized lipodystrophies are characterized by focal loss of adipose tissue, thus these disorders will not result in metabolic dearrangement that occur in extensive lipoatrophy. Localized lipodystrophies could be drug induced, pressure induced, panniculitis associated, or idiopathic in origin. Many drugs implicated as a cause for development of localized lipodystrophy such as insulin, glucocorticoids, antibiotics, and methotrexate.¹¹ Lipoatrophy was a common adverse immunological side effect of insulin therapy before development of recombinant human insulin which lead to dramatic decrease in development of lipodystrophic complication.¹²

Intralesional corticosteroid injections, particularly triamcinolone acetonide, are common treatment for many cutaneous disorders such as keloids, alopecia areata and others.¹³ The treatment is generally safe but complications including local lipoatrophy and hypo pigmentation which are largely cosmetic in concern, are known to occur.¹⁴

Corticosteroids induced lipoatrophy generally begins within 1 to 3 months after an intralesional injection with an estimated incidence of 0.5–40%. The exact pathogenesis is not well understood but crystal formation and corticosteroids induced vasoconstriction lead to tissue hypoxia, decreased glycosaminoglycans and collagen synthesis, and ultimately involution of subcutaneous fat. Corticosteroid-induced lipoatrophy may resolve spontaneously over period of 1-2 years, but it may persist longer in many patients.¹⁵

Lupus profundus is a variant of cutaneous lupus erythematosus manifested by subcutaneous nodular lesions affecting the face, arms, legs, trunk, and abdomen followed by lipoatrophy after resolution of the nodular lesions. Lipoatrophy is psychologically distressing problem in this patient particularly when the face involved.¹⁶ Serologic analyses are often normal. Variable positivity for antinuclear antibody and less frequently, anti-double-stranded DNA antibodies have been observed in many published studies.¹⁷

Morphea as localized scleroderma is a rare fibrosing disorder with indefinite etiology affecting the skin and underlying structures including subcutaneous tissue, bone and rarely central nervous system. But morphea is a common skin problem encountered among Iraqi population and linear morphea including encoope de sabre is a common presentation especially among children and often in association with atrophy of the skin, lipoatrophy of fatty layer and the underlying structures like muscles and even bones.¹⁸ While the most common type in adults is plaque morphea.^{18,19} Hence localized lipoatrophy has been described in many patients with morphea especially in linear variant.^{8,20}

So the aim of this study is to report the frequency of different factors involved in the etiopathogenesis of acquired lipodystrophies in pediatric and adult population.

Patients and methods

This is observational case series descriptive study, where twenty-nine patients with different clinical forms of acquired lipoatrophy were enrolled during the period from 2006-2020. The study followed the Declaration of Helsinki Principles and informed consent was obtained from each patient after explanation of the nature

of the study. Close-up photographs were taken at the same place with constant distance and illumination. For every patient, a full history including the duration and progression of disease or lesion was gathered. Precipitating factors and the associated cutaneous and/or systemic diseases were obtained. Precipitating factors were carefully searched for, in almost all patients either the parents or the patients themselves gave a history of either intramuscular or intralesional corticosteroid injection by expert dermatologist and also by non-trained medical staff. In addition, personal and family history of autoimmune diseases was also reviewed with every patient. In each patient, the skin was carefully inspected and examined for any atrophy and/ or pigment alteration. Woods light examination was done in selected hypo pigmented lesions to rule out or to confirm the total pigment loss. In addition, careful generalized skin examination was done in every patient for any possible associated skin disease particularly in patient with leukodermic patches. When needed, laboratory investigation such as screening for suspected autoimmune connective tissue diseases with anti-nuclear antibodies and complement testing were done in selected cases. Statistical package for social science (SPSS) version 23 was used for data input and analysis. Data were statistically described in terms of mean, frequencies (no. of cases), standard deviation (SD), male to female ratio and percentage (%).

Results

Twenty-nine patients, 16 (55.2%) females and 13 (44.8%) males, suffering from localized lipoatrophy during fourteen years' time period were included in the present study. Their ages at presentation was ranged from 3-55 years with mean 16.7 ± 13.8 years. The sites affected by lipoatrophy linked with its etiology were shown in **Table 1**.

Table 1 The causes and sites linked with number of patients affected by lipoatrophy.

Cause	Sites affected	Patient no. (%)	Sex		Total no. (%)
			Male	Female	
Triamcinolone injection					
Intramuscular					
Intradermal	Buttock	14 (51.9%)	6	8	27 (93.1%)
	Scalp	12 (44.4%)	5	7	
	Forearm	1 (3.7%)	1		
Lupus profundus	Face and upper extremities	1		1	1 (3.45%)
Morphea (linear variant)	Buttock and upper thigh	1	1		1 (3.45%)



Figure 1 Seven years old female patient showing right and left lipoatrophy of the buttock and with associated focal hypopigmented area on the right buttock.

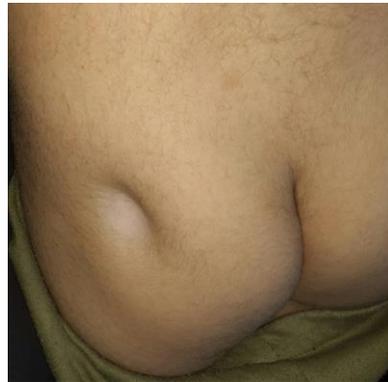


Figure 2 Six years old female patient showing lipoatrophy of the left buttock presenting as depressed hypopigmented lesion.



Figure 3 Eleven years old male patient showing scalp dermolipoatrophy following intradermal triamcinolone injection for alopecia areata of scalp.

According to precipitating events or diseases, intralesional and intramuscular triamcinolone was the most frequent cause responsible for development of localized lipoatrophy in 27 (93.1%) patients, followed by morphea and lupus profundus in only 1 (3.45%) patient for each disease. With regard to corticosteroid induced lipoatrophy, 27 patients, 15 (55.6%) females, 12 (44.4%) males with median 10 years were observed with sixteen (59.3%) patients were children. The mean duration of lipoatrophic lesions was 15.9 weeks. The buttock was the most commonly affected site affecting 14 (51.9%) patients followed by scalp in 12 (44.4%) patients and forearm in 1 (3.7%) patient. All patients with buttock lipoatrophy were children, 8 (57.1%) females and 6 (42.9%) males, with age ranging from 3–11 years old with median 6.5 years. They presented with

marked depressed lesions or hollowing of gluteal region and completely normal overlying skin apart from focal hypopigmented lesions limited to injection sites that were seen in 7 children making the parents worried about the possibility of vitiligo and all gave history of intramuscular triamcinolone injection for treatment of different skin problems including vitiligo (5 patients), atopic dermatitis (4 patients), chronic urticaria (3 patients) and alopecia areata (2 patients) which provides a path for diagnosis of corticosteroid induced lipoatrophy. In 3 patients both buttocks were affected (**Figure 1**) while in the remaining 11 patients only one side was involved (**Figure 2**).

Twelve patients, 7 (58.3%) females, 5(41.7%) males with age range from 10-37 years with a median age 28.5 years developed scalp



Figure 4 Fifty-five years old female patient showing prominent facial lipoatrophy manifested by volume loss in the temple and malar fat pad (A, B) and localized lipoatrophic lesions of the upper extremities (C).

Figure 5 Nine years old male patient with morphea showing marked atrophy of the right buttock and thigh.

dermolipoatrophy after intradermal triamcinolone as part of their treatment protocol for their scalp alopecia. Ten (83.3%) patients were adult and two were children and all the affected patients, had single or multiple severely atrophic and hypopigmented scalp patches in corresponding to previously injected alopecic sites (**Figure 3**).

In one patient with hair loss from forearm, lipoatrophy at triamcinolone injection sites developed after injection by non-trained nurse presented with focal atrophic lesions with marked hypopigmentation that worried the patient about the possible development of vitiligo.

Face and upper limb lipoatrophy was observed in 1 (3.45%) female patients with lupus profundus complaining of recurrent panniculitic lesions as part of their disease progress (**Figure 4**). Severe hollowing of both cheeks and upper limbs given her cachexic look. Screening for antinuclear antibodies and complement were negative and a diagnosis of autoimmune disease associated acquired partial lipodystrophy was made. In another one (3.45%) child with linear morphea, the skin was sclerotic and atrophic

with buttock lipoatrophy affecting unilateral right buttock and upper thigh and the course of the disease developed over months (**Figure 5**).

Discussion

Lipodystrophy is an umbrella term always used to define diversified groups of inherited or acquired disorders manifested by partial or complete loss of fatty tissue (lipoatrophy) that may occur in association with abnormal accumulation of fat in other regions of the body. The severity of associated metabolic disorders correlates with the degree of fat loss. Inherited lipodystrophies are extremely rare while the acquired lipodystrophy is much commoner and further could be subdivided into generalized, partial and localized types.²

In the current work, no congenital nor generalized lipodystrophy was observed but the acquired localized lipoatrophy was the common type.

Intramuscular corticosteroid injections are commonly used treatment option in dermatology practice. Many adverse reactions are associated with systemic and local use of corticosteroids.

Dermal and/ or subcutaneous atrophy, dyspigmentation and alopecia had been reported as cutaneous adverse effects after intramuscular corticosteroid injection.²¹ Lipoatrophy usually appears within 2-3 months after corticosteroid injection and resolves in about 1-2 years, but it may persist longer up to 5 years. The appearance of cutaneous atrophy and dyspigmentation can result in cosmetic issues and significant distress, particularly in colored skin patients as hypopigmentation can be more apparent. The severity, duration and clinical appearance of cutaneous atrophy and dyspigmentation depend on corticosteroid solubility, dose, concentration, injection depth and injected site.²² The commonest injectable steroids are triamcinolone, methylprednisolone, betamethasone, and dexamethasone. Betamethasone and dexamethasone are more soluble preparation with lower risk of cutaneous atrophy and hypopigmentation when injected locally but with higher chance of systemic side effect including adrenal suppression nullifying the goal of local injection. Corticosteroid preparations used for intralesional administration should be long acting glucocorticoid preparation, such as triamcinolone acetonide. The mechanism of corticosteroids induced lipoatrophy is not completely understood but in addition to corticosteroid induced vasoconstriction, ester compounds particularly in triamcinolone make it highly insoluble in water leading to formation of microcrystals in already constricted vessels and the ultimate higher risk of cutaneous atrophy due to tissue hypoxia, decreased production of glycosaminoglycans and collagen synthesis but with much lower risk of adrenal suppression. On the other hand, the hypopigmentation induced by corticosteroid result from inhibition of prostaglandin production in the epidermal cells that leads to impaired melanocytes function without affecting the number of melanocytes.¹⁵ The exact prevalence of corticosteroid-induced lipoatrophy is not well known although in one

study approximately 62% of patients with lipoatrophy have preceding history of an injection.²³

In the present study, with regard to corticosteroid induced lipoatrophy the mean age of the presenting patients was 15.6 years that is lower than the reported by Sharma *et al.*¹⁵ which can be explained by slightly higher percentage of children (59.3% child versus 40.7% adult) involved in the present study as many parents were very worried and distressed about this observation in their children particularly in those receiving intramuscular triamcinolone for indications other than vitiligo, in addition, corticosteroid induced lipoatrophy are largely disease of cosmetic issues with younger adult population were mainly concerned about this complication which always neglected by older adult as its symptomless. The females were affected more than males in agreement with another study¹⁵ which also can be explained by cosmetic impact of this problem even on female child aesthetic future.

The mean duration of lesions was 15.9 weeks which is in line with many other studies where corticosteroid induced lipoatrophy begin within 1-3 month of local administration.^{15,22-24}

In the present work, the buttock was the most commonly affected site in 14 (51.9%) children patients and this finding is in correspondence with another study.¹⁵ This could be explained by small muscle of the buttock and hence the injection could be mostly located in the fatty layer of the skin rather than intramuscular. Also this higher incidence can be also interpreted by wider applications for intramuscular corticosteroid than intralesional one. The scalp which is the main site for intradermal injection of triamcinolone was also a commonly affected site and this observation is in line with previous study.¹⁵

Lupus profundus is an uncommon variant of lupus erythematosus usually affects females presented with subcutaneous nodules affecting the face and proximal extremities followed by significant scarring and lipoatrophy upon healing with significant cosmetic issues.²⁵

In the present work, lupus profundus was a cause of acquired partial lipodystrophy in one female patient (3.45%) presented with significant lipoatrophy typically involving the face and proximal upper extremities and this finding in accordance with another study.²⁵

Morphea is common skin problem seen in Iraqi population and the linear type and the en coup de sabre variant are commonly associated with lipoatrophy.¹⁸ The patient in the present study had localized lipoatrophy of the buttock as a part of linear morphea. This finding is also approved by other studies.^{26,27}

The present work provides insight into the possible etiological factors involved in pathogenesis of localized lipoatrophy where corticosteroid induced lipoatrophy was the most straightforward diagnosis while the other disorders like lupus profundus, morphea and other autoimmune diseases are challenging cases but should be kept in mind upon evaluation of suspected cases with lipoatrophy.

Conclusion

Lipoatrophy following intramuscular and intralesional corticosteroid preparation particularly triamcinolone acetonide is the important and common cause for acquired lipoatrophy with significant psychological sequelae for the affected patients and/ or their parents. Lupus profundus and morphea are also important diseases to be considered while evaluating patients with acquired lipoatrophy especially patients with linear morphea.

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