5. Case record- A Rare Case Report of Acquired Partial Lipodystrophy Associated with "Connective tissue Panniculitis" in a 59-Year-Old Woman with Diabetes Mellitus.

Name of hospital	- National Hospital of Sri Lanka
Name of the consultant	- Dr.Janaka Akarawita
Case no	- 05
Ward	- 6A
Name of the patient	- Mrs. Fathima Fousiya
Age	-59 years
Address	- Dehiwela. Colombo
Date of Admission	- 13/06/2023
Date of Discharge	-16/06/2023
BHT no	-26877

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A Rare Case Report of Acquired Partial Lipodystrophy Associated with "Connective tissue Panniculitis" in a 59-Year-Old Woman with Diabetes Mellitus.

Abstract

ANA positive connective tissue panniculitis refers to a type of panniculitis that is associated with a positive antinuclear antibody (ANA) test. It is characterized by inflammation in the connective tissue of the subcutaneous fat, often without a specific underlying autoimmune disease, making it a distinct clinical entity. This case report describes a 59-year-old woman with insulin-dependent diabetes mellitus who presented with scalp psoriasis and partial lipoatrophy. Laboratory tests revealed elevated HbA1c levels and a positive ANA test. A skin biopsy confirmed panniculitis, and treatment involved disease-modifying antirheumatic drugs (DMARDs) and repeated fat transfusions. The complex nature of connective tissue panniculitides poses challenges in their treatment. Early diagnosis and prompt management are essential to address the potential cosmetic, functional, and psychological consequences associated with these conditions.

Case presentation

A 59-year-old housewife, known to have diabetes mellitus, ischemic heart disease, and dyslipidemia, presented to the dermatology clinic with a persistent scaly rash on her scalp and worsening facial asymmetry in the bilateral cheeks. Physical examination revealed erythematous scaly lesions on the scalp, indicative of scalp psoriasis, and grooving of the cheeks without tenderness. Laboratory investigations showed elevated HbA1c levels, suggesting poor glycemic control, and a positive antinuclear antibody (ANA) test with a nuclear pattern. A skin biopsy confirmed the presence of panniculitis. Other investigations, including imaging and blood tests, were within normal limits. Based on the clinical findings and the patient's background history, a diagnosis of partial lipoatrophy was made.

The patient's management included addressing scalp psoriasis and lipoatrophy through the use of methotrexate and repeated fat transfusions. Referral to the endocrinology team was made for insulin titration and screening for potential complications. While the presence of a positive ANA test suggested a possible underlying autoimmune component, other specific tests ruled out major autoimmune conditions associated with lipoatrophy.

Conclusion

In conclusion, the case underscores the importance of prompt diagnosis and management of connective tissue panniculitides to address their potential impact on appearance, function, and psychological well-being. Despite the challenges in treating these conditions, further research is necessary to develop effective therapeutic approaches. The findings emphasize the need for a comprehensive evaluation considering both dermatological and systemic factors to provide tailored care for patients with complex presentations of connective tissue panniculitides.

Keyword

Connective tissue panniculitides, Partial lipoatrophy, ANA positive, Scalp psoriasis, Prompt investigation

Introduction

Connective tissue panniculitis is a rare inflammatory condition that affects the layer of fat beneath the skin. It is characterized by inflammation and damage to the connective tissue that separates the fat lobules. While the exact cause is often unknown, it can be triggered by various factors such as trauma, infections, autoimmune disorders, or certain medications. The condition presents with tender, painful nodules on the legs, buttocks, and arms. Diagnosis involves a physical examination and sometimes a biopsy of the affected tissue.

The inflammatory processes can disrupt blood flow, promote the development of fibrous tissue, and cause the deterioration of fat cells. Additionally, systemic effects may lead to a more widespread wasting away of adipose tissue across the body. Early recognition and appropriate management are crucial to prevent significant tissue damage and atrophy. Seeking timely evaluation and treatment from a healthcare professional is vital if panniculitis or related symptoms are suspected.

Case report

A 59-year-old housewife from Colombo, who is a mother of three children, has a past history of diabetes mellitus, ischemic heart disease, and dyslipidemia. Seven years ago, she was put on medical clinic follow-up and prescribed Mixtard insulin due to poor glycemic control. Recently, she presented to the dermatology clinic with a pruritic scaly rash on her scalp, which has been persisting for one year.

She had been experiencing facial asymmetry in bilateral cheeks for the past 15 years, which was not accompanied by pain, but it has worsened for last one year leading to her current presentation. She denied having similar lesions in other parts of her body. There were no associated symptoms such as fever, joint pain, muscle pain, stiffness, photosensitivity rashes, oral ulcers, red eyes, dry mouth, weight loss, loss of appetite, shortness of breath, cough, or palpitations. Her bowel habits and urine output were normal, without any signs of hematuria, frothy urine, or dysuria. She denied having any significant family history of similar lesions or any malignancy.

On examination, she appeared to be a thin-built woman who was afebrile and showed no signs of pallor or icterus. There were erythematous scaly lesions on her scalp, indicative of scalp psoriasis. No oral ulcers or malar rash were observed. There was grooving of the bilateral cheeks without tenderness, there was no other similar lesion in her body and no skin nodules, cervical lymphadenopathy, or ankle edema were present. Her nails appeared healthy, and there were no thickened superficial nerves. The insulin injection site also found

to be healthy. The cardiovascular, respiratory, and neurological system examinations were normal, except for the presence of mild cataracts in her eyes.

Based on the clinical findings and the patient's background history of psoriasis and diabetes mellitus, a diagnosis of partial lipoatrophy was made. Laboratory investigations were initiated to identify the cause of her presentation. The following investigations were performed:

Investigation	Reference range	Patient Results
WBC	4-10 X 10 3/ mm3	9.43 X 10 3/mm3
Hb	11-16 g/dL	13.3 g/dL
Platelet	100-300 X 10^9/L	239 X 10^9/L
Serum sodium	136-145mmol/L	140mmol/L
Serum potassium	3.5-5.1mmol/L	3.7mmol/L
Serum creatinine	0.57-1.11 mg/dl	0.86 mg/dL
UFR	No RBC	Normal (No RBC or protein or cast)
AST	0-45 U/L	43U/L
ALT	5-45U/L	34U/L
ALP	40-150 U/L	63 U/L
Total bilirubin	0.2-1.2 mg/dL	0.4 mg/dL
Total protein	6.6-8.3 g/dL	7.04 g/dL
Albumin	3.5-5.5 g/dL	4.07 g/dL
Globulin	2.2-3.4 g/dL	2.97 g/dL
Fasting glucose	<100 mg/dL	126 mg/dL
Hb A1C	<5.6%	10.9%
ESR	14 mm/hour	13 mm/hour

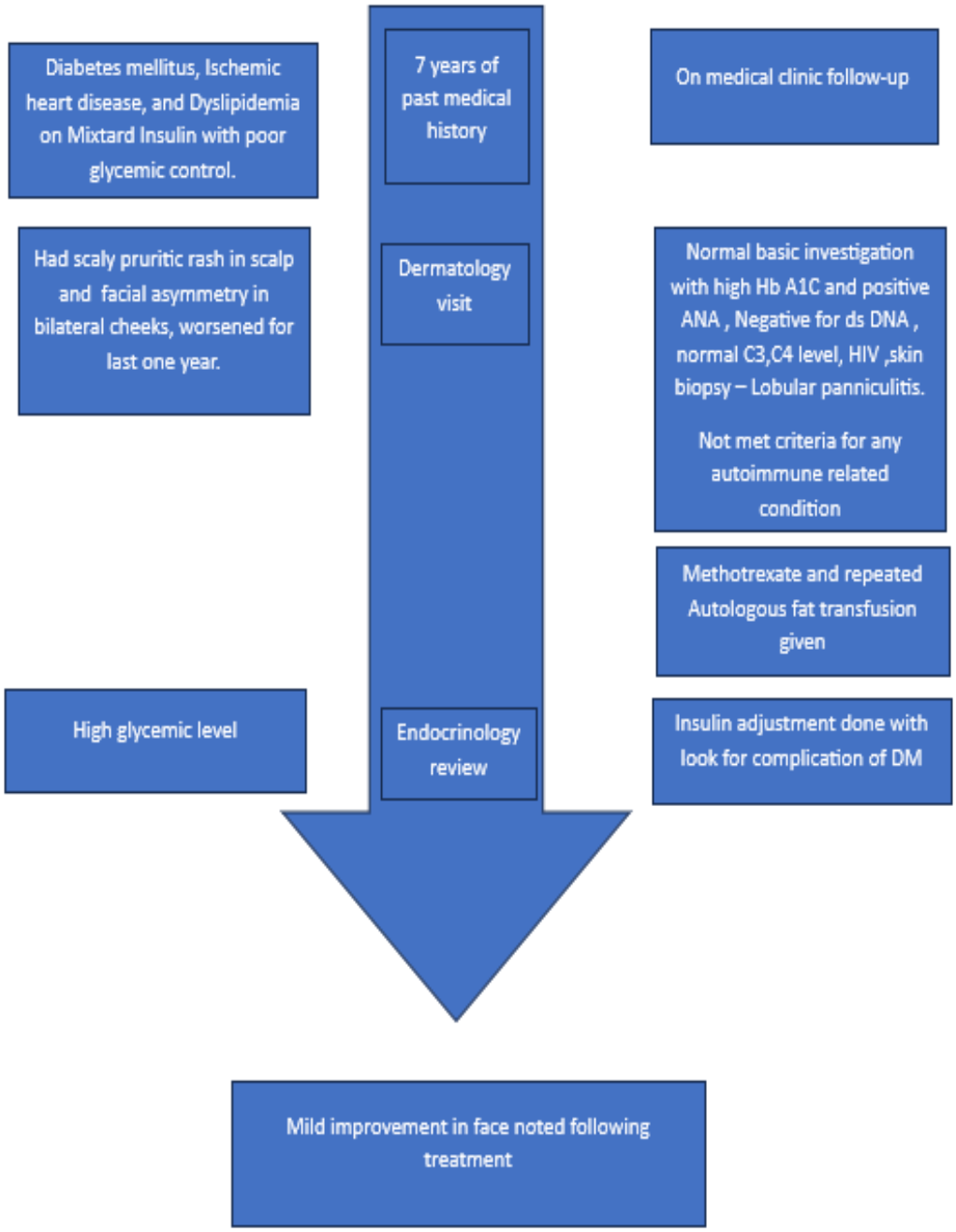
CRP	<5 mg/dL	<5 mg/dL
Total cholesterol	<200 mg/dL	151 mg/dL
Triglyceride	<150 mg/dL	130 mg/dL
HDL	<40 mg/dL	46 mg/dL
LDL	<100 mg/dL	79 mg/dL
Rheumatoid factor	<8 IU/mL	Negative
ANA	<1:80	1:80 positive for nuclear pattern
ds DNA	Negative	Negative
C3 level	97 mg/dL	90-180 mg/dL
C4 level	10-40 mg/dL	29 mg/dL
TSH	0.3-4.2 microIU/mL	2.8 microIU/mL
HIV and VDRL	Negative	Negative

Further Investigation	Results
ECG	Normal
2DECHO	EF: 55% with good systolic and diastolic function
USS Abdomen	No hepatosplenomegaly or lymph nodes detected
USS Face	Lipoatrophy over bilateral cheeks noted
Skin Biopsy	Subcutaneous tissue shows features of lobular Panniculitis. Infiltrate consist of mature lymphocytes, no vasculitis or atypical lymphocytes.

Figure 15 Partial atrophy of face

The patient's management plan involves addressing two conditions: scalp psoriasis and lipoatrophy. Methotrexate was commenced to address both by reducing inflammation and symptoms. Repeated fat transfusions are utilized to manage lipoatrophy, restoring a balanced fat distribution. The endocrinology team is involved in insulin titration and screening for diabetes-related complications. Close monitoring of liver function and blood tests were arranged during methotrexate treatment. Our ultimate aim is to provide comprehensive care, alleviate symptoms, manage underlying conditions, and enhance the patient's overall quality of life by addressing both dermatological and endocrine aspects of their health.

Time line of events



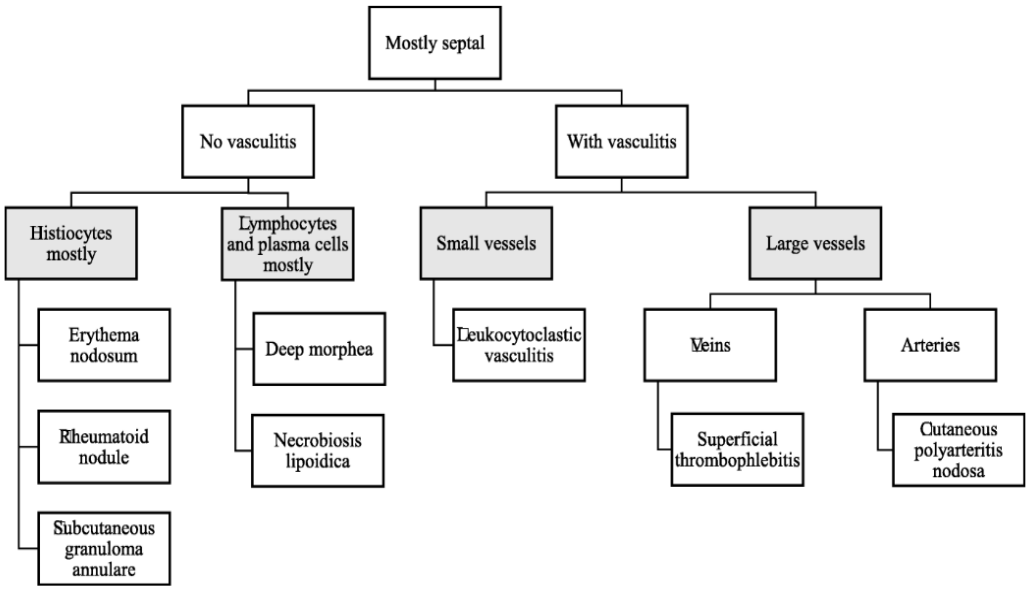
Discussion

Lipodystrophy can either be hereditary or more frequently acquired. Additionally, lipodystrophy can manifest as either partial or generalized (1).Hereditary lipodystrophy arises from genetic mutations impacting fat distribution. Specific genes like LMNA (Lamin A/C), AGPAT2(1-Acylglycerol-3-Phosphate O-Acyltransferase 2), and CAV1(Caveolin-1) are involved (2) . Patients with acquired generalized lipodystrophy (AGL), also known as Lawrence syndrome, experience a gradual loss of fat affecting almost all fat depots, while some areas may retain fat(1). Acquired partial lipodystrophy (APL) or Barraquer Simons syndrome is characterized by fat loss starting in the face and extending to other upper body regions. It typically begins in childhood or adolescence, more prevalent in females. In our case, the patient with acquired partial lipodystrophy (APL) did not have any other parts of the body involved, and her C3 and C4 levels were normal. Unlike some instances of APL that are associated with autoimmune conditions like membranoproliferative glomerulonephritis, low serum C3, and the presence of C3 nephritic factor, her condition did not exhibit these features.

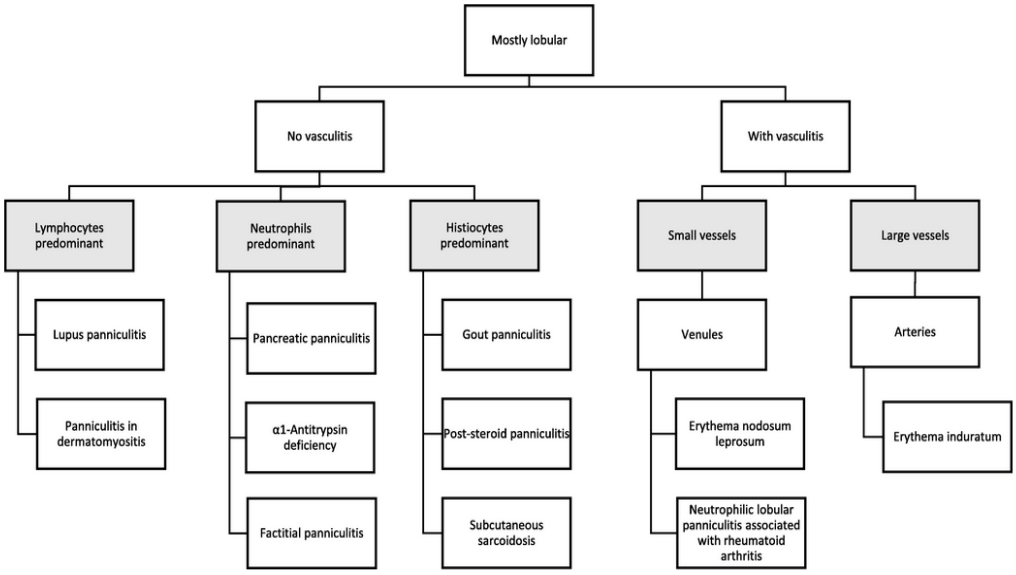
The comorbidities linked to lipodystrophy arise from metabolic disturbances, uncontrolled diabetes, pancreatitis, cirrhosis, proteinuria, premature cardiovascular disease, and renal failure. APL displayed metabolic complications, possibly due to preserved lower body fat (1). Our patient has had diabetes mellitus for 7 years, is on regular clinic follow-up with Mixtard insulin, has high HbA1c levels, normal renal function, no polyneuropathy, and hasn't been screened for diabetic retinopathy. Localized lipodystrophy involves small indentations due to drug injections or immune mediated processes. The most prevalent acquired lipodystrophy is observed in HIV-infected patients, with severe facial lipoatrophy (3), (4). Fascial partial lipoatrophy can be graded as follows (5).

Grade	Description
0	No facial lipoatrophy.
1	Mild flattening or shadowing on one or more facial regions; No prominent bony landmarks and no visibility of the underlying musculature.
2	Intermediate point between Grade 1 and Grade 3.
3	Moderate concavity of one or more facial regions, prominence of bony landmarks, and possible visibility of the underlying musculature.
4	Intermediate point between Grade 3 and Grade 5.
5	Severe depression of one or more facial regions, severe prominence of bony landmarks, and clear visibility of the underlying musculature.

Panniculitis involves inflammation of the subcutaneous fat tissue, resulting in the development of tender nodules or lumps in the affected regions. With prolonged inflammation, the fat cells can be damaged and destroyed, potentially leading to the progression of lipodystrophy over time. Panniculitis can either be the primary and sole manifestation of the disease or coexist with other symptoms and findings related to the underlying disease process (6). It can be classified into two main types based on the histological examination of the affected tissue: lobular panniculitis and septal panniculitis (7).



Primarily-septal panniculitides



Primarily-lobular panniculitides

The best-described types of panniculitis linked to connective tissue diseases include lupus erythematosus and lupus profundus, dermatomyositis, morphea and scleroderma. These panniculitis forms serve as significant cutaneous markers for their respective connective tissue diseases, aiding in diagnosis and treatment (8).

"Connective tissue panniculitides" is separate entity described by Peters and Winkelmann in 1980 linked to autoimmune phenomena but not clearly associated with a specific connective tissue disease (8) (9). Advancements in panniculitis classification have reclassified cases like Weber-Christian disease. Some connective tissue panniculitides lack specific features but associate with other autoimmune diseases. These complexities challenge definitive diagnoses and necessitate further research in understanding the diverse spectrum of connective tissue panniculitides.

Connective tissue panniculitides show a histologic appearance of predominantly lobular lymphocytic infiltrate in adipose tissue, occasionally with mixed pattern (6). In our case, the histology also displays the lobular form of panniculitis. In our case, the patient had positive ANA with negative dsDNA and normal C3 and C4 levels, and she did not fulfill the criteria for SLE or any other connective tissue disease. A rare case of lupus panniculitis was reported in 1993, describing a patient with positive antinuclear antibodies but lacking antibodies to double-stranded DNA. This highlights the variability and complexity of lupus

panniculitis presentations and the need for careful evaluation and diagnosis (10). Histopathologic features aid diagnosis. Connective tissue disease patients may be at increased risk for other panniculitis forms (infection, lymphoproliferative) (11).The response to therapies like methotrexate, prednisolone, hydroxychloroquine, azathioprine and dapsone supports the potential relationship between panniculitis and underlying connective tissue diseases (12).Limited research exists on using autologous fat grafting for lipoatrophy treatment in lupus panniculitis. Fat grafts contain stem cells that aid in volume restoration, angiogenesis, apoptosis, and immune modulation (13). Our patient received methotrexate (DMARD) and multiple fat transfusions, resulting in mild improvement of the condition. Connective tissue panniculitis prognosis varies based on the underlying cause. It can resolve with treatment or become chronic and recurrent. Complications include lipodystrophy, lipoatrophy, scarring, and fibrosis. Early recognition and appropriate management are crucial for better outcomes. Regular follow-up is important for monitoring progress and adjusting treatment as needed (6).

Conclusion

In conclusion, connective tissue panniculitides present a diverse and challenging spectrum of inflammatory conditions associated with the subcutaneous fat tissue. Prompt diagnosis and management are crucial to address potential cosmetic, functional, and psychological consequences. While research on treatment options, such as autologous fat grafting, remains limited, understanding the complex nature of these conditions is essential for tailored care. Multidisciplinary approaches and regular follow-up are necessary to optimize outcomes for patients with connective tissue panniculitides.

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