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Case Report

Anti-phospholipid antibody syndrome with skin as a primary involved organ: an interesting case report

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ABSTRACT

Anti-phospholipid antibody (APLA) syndrome is a multisystem vascular thrombopathy characterized by presence of antibodies against phospholipid antigens. Resulting thrombosis due to these antibodies leads to hallmark obstetric complications, cutaneous and cerebral vascular involvement, pulmonary embolism and thrombosis which can occur in vasculature of any organ system of body. Though APLA syndrome is characterized by pregnancy loss and foetal morbidity, isolated cutaneous or other system presentation has been reported especially in male patients. Here we present an interesting case report of an old aged male patient presenting with cutaneous ulcers and skin involvement as presenting feature.

Keywords: APLA syndrome, Anti-phospholipid antibody, Severe cutaneous necrosis

INTRODUCTION

Anti-phospholipid antibody (APLA) syndrome is characterized by vascular thrombosis in veins and arteries presenting as recurrent pregnancy loss, foetal morbidity, and thrombotic events occurring due to vascular thrombi in cerebral, cutaneous and other systems.[1-3] Thrombosis in APLA syndrome occurs due to antibodies against phospholipids. Most common presentation of APLA syndrome is recurrent child loss but isolated cutaneous involvement although reported is rare. Here we present a rare and interesting case of APLA which presented with skin involvement as primary presentation.

CASE REPORT

A 68-year-old male patient presented to outpatient department with complaints of swelling and redness of skin over left lower limbs. It started gradually on left limb involving lower parts of ankle and foot initially and gradually increased to involve areas up to the knee within 10 days. Right leg also started developing oedema and redness up to midleg level. He later on developed frank livedo reticularis like lesions with ulceration and superficial crusting on bilateral hands dorsal aspect. There was no history of pain, intermittent claudication, fever, loss of sensation or other systemic involvement. He was a known case of systemic hypertension well controlled on oral telmisartan. There was no history of diabetes or any other systemic disease. Patient was having habit of tobacco chewing since last 35 years but there was no history of smoking or alcohol consumption. There was no history of any drug intake. Family history was insignificant. Later on oedema became intense with development of punched out necrotic ulcers on feet. On examination, intense erythema and oedema was there with mild tenderness on palpation. The pulsations of bilateral femoral, popliteal and dorsalis pedis artery was normal. On other systemic examinations his blood pressure was 134/76 mm of mercury, pulse was 80/minute, temperature was normal and oxygen saturation was 97% at room air. No cardiovascular system (CVS), central nervous system (CNS), respiratory or

gastrointestinal (GI) abnormalities found on examination. Patient initially took treatment from general practitioner for 2-3 days but increasing oedema compelled him to visit specialist doctor. Patient was admitted under care of a surgeon initially and investigations were performed to rule out cellulitis and peripheral vascular diseases.

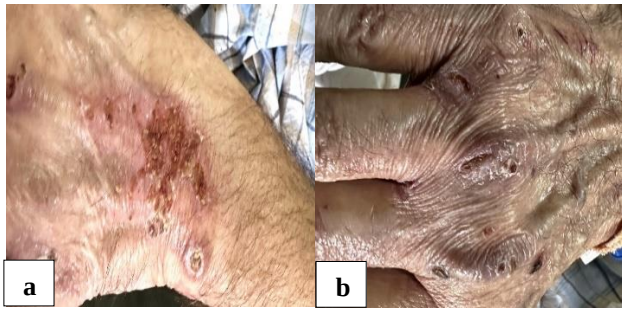

Figure 1 (a and b): Punched out ulcers with superficial necrosis and livedo reticularis like lesions on dorsum of hands.

On investigations his haemoglobin was 11.2 gm%, total counts were 6800/ml and differential counts were also within normal limits. Renal and hepatic functions were normal, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were raised. Serology for hepatitis B human immune-deficiency virus (HIV) and syphilis were negative, and doppler studies didn't revealed any superficial or deep venous thrombi, arterial constrictions or flow abnormalities. Ultrasonography of local part revealed cutaneous oedema. Local part X-ray was performed which ruled out bony involvement. Pus culture and sensitivity was sent which didn't yield any bacterial or fungal growth. A dermatologist opinion was sought to consider for alternate pathology. On examination, he was advised serum ANA titre, p-ANCA and c-ANCA antibody levels, and Antiphospholipid antibody levels (anticardiolipin). Out of all, patient was positive for lupus anticoagulant antibody with high titres. A skin biopsy was performed from margin of ulcer for histopathological examination and other from erythematous skin to be sent for direct immunofluorescence. Computed tomography (CT) angiography of chest was done to see for pulmonary involvement which didn't show any significant finding.

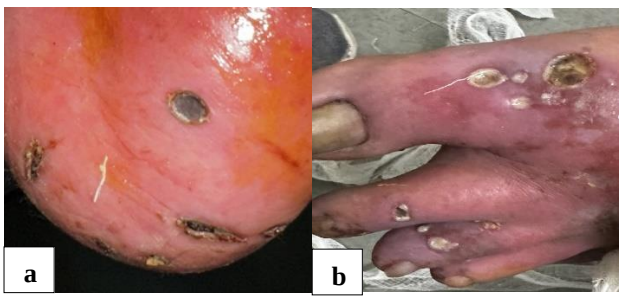

Figure 2 (a and b): Punched out ulcers with cutyaneous oedema and erythema on dorsum of foot and heel.

The skin biopsy revealed segmental ulcerations covered by acute inflammatory exudates and replaced by inflammatory granulation tissue. Viable epidermis showed basketweave hyperkeratosis, preserved granular layer and slight irregular acanthosis. Upper dermis showed oedema, and blood vessels walls with hyalinisation, fibrin deposition, luminal occlusion with fibrin thrombi without associated leukocytoclasia and vessel wall inflammation suggestive of occlusive vasculopathy, while DIF was negative.

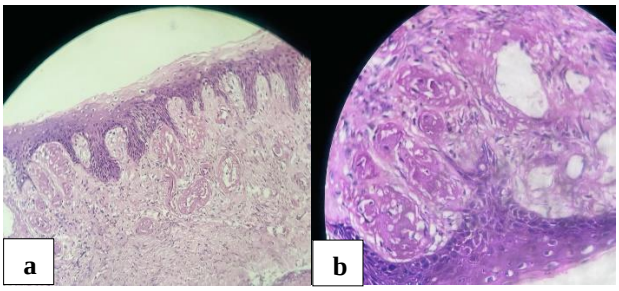

Figure 3 (a and b): Histopathology of skin showing multiple dermal vessels having thrombosis with minimal vessel wall inflammation. DIF from lesional skins was negative.

Table 1: Investigations.

Name of investigation	Findings
Complete blood count	Hb – 11.6%, TC-6800/ml, DC-66/22/4/8/0 (N/L//E/M/B), PLT-312000/ml
Liver function test	SGPT-28 U/l, S. bilirubin: total-0.4 mg/dl, direct-0.3 mg/dl, indirect-0.1 mg/dl
Renal function test	S. creatinine: 0.6 mg/dl, blood urea: 16 mg/dl
ESR	After 1 hour – 26, after 1 hour - 70
CRP	13 mg/dl
S. ANA TITRE	1:80 (negative)
c-ANCA	2.76 AU/ml (negative)
p-ANCA	3.99 AU/ml (negative)
APLA antibody	IgM – 2.80 U/ml, IgG – 60.5 U/ml
Repeat titre of APLA antibody after 12 weeks	IgM – 1.70 U/ml, IgG – 23 U/ml
Serology	HIV- negative, HBSAg-negative, VDRL-negative

Based on these findings a diagnosis of primary antiphospholipid antibody syndrome was made and patient was started on injection dexamethasone 8 mg once a day in morning along with injection low molecular weight heparin 0.6 ml subcutaneous once a day. Also debridement was done to remove necrotic tissues and to lessen oedema. Patient started showing improvement from the 3rd day with

regression of lesions over dorsum of hands first followed by decrease in oedema and erythema on both lower limbs. The dose of dexamethasone was titrated slowly and patient was discharged later on with oral prednisolone and aspirin. We repeated the titre of APLA antibody after 12 weeks which again showed raised antibody levels confirming our clinical diagnosis.

DISCUSSION

APLA syndrome, apart from its hallmark obstetric complications can also present with cutaneous signs and symptoms and utmost care should be taken to consider it as a differential diagnosis while dealing with such cases. Thrombosis in APLA syndrome apart from systemic vasculature, can also involve dermal vasculature.[4] Varied cutaneous presentation in this syndrome includes most commonly livedo reticularis, cutaneous ulcers, necrosis of digits, psedovasculitis like presentation extensive cutaneous involvement with skin necrosis, gangrene and in nails subungual splinter haemorrhages.[5] Though many a times cutaneous features are mostly associated with systemic findings, but isolated involvement of skin has also been reported even in female patients.[6] APLA syndrome is divided into primary and secondary APLA syndrome the former one is isolated while later one is associated with systemic diseases the most common among it is SLE.[7]

Our present clinically presented with rapidly developing cutaneous oedema with ulcers which later on developed to involve dorsum of hand also and though these kind of rapid evolution of disease is seen in catastrophic APLA syndrome commonly our patient didn't show multiorgan involvement or systemic thrombosis with thrombocytopenia may be due to early intervention.[4] Diagnosis of APS depends upon fulfilment of criteria which states presence of at least one clinical finding from these.[5]

Clinical criteria

Clinical criteria included vascular thrombosis comprising of confirmation of thrombosis in arteries, veins or small vessels which has to be objectively confirmed either by imaging or histopathology which should show thrombosis without significant vessel wall inflammation. Or pregnancy morbidity which is defined by: one or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation, with normal foetal morphology documented by ultrasound or direct examination of the foetus; or one or more premature births of a morphologically normal neonate before the 34th week of gestation because of eclampsia or pre-eclampsia diagnosed by standard definitions, or recognized features of placental insufficiency; or three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal or hormonal abnormalities, and maternal and paternal chromosomal causes excluded.

Laboratory criteria

Lupus anticoagulant (LA) present in plasma, on two or more occasions at least 12 weeks apart, detected according to the guidelines of the International Society of thrombosis and haemostasis.

Anticardiolipin antibody (aCL) of IgG and/or IgM isotype in serum or plasma, present in medium or high titre (>40 GPL or MPL, or > the 99th percentile), on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA.

Anti-β2 glycoprotein-I antibody (anti-β2GPI) of IgG and/or IgM isotype in serum or plasma with a titre > the 99th percentile, on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA.

Our patient showed histological confirmation of small vessel thrombosis without significant vasculitis and on two different occasion elevated titres of aCL antibodies hence fulfilling the diagnostic criteria. The treatment of choice for APLA syndrome includes corticosteroids, heparin, oral warfarin and aspirin.[6] As our patient also has widespread cutaneous oedema with ulcers, surgical intervention was done to remove necrotic tissue and release oedema was done.[7] Also had it not been treated on time, there were chances of widespread cutaneous necrosis which is a very rare phenomena reported in very few case reports.[8]

CONCLUSION

As cutaneous involvement in APLA syndrome can be an early indicator of the disease and failing to recognise and treat it could lead to high chances of morbidity and mortality, a high index of suspicion and vigilance is needed while dealing with such cases. This case is presented for its uniqueness and to understand the grievance associated with late diagnosis.

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