Annals of Medicine and Medical Sciences (AMMS)
Volume 04, 2025, *Page No.: 38 to 40*
Available at: *http://ammspub.com*

Case Series

OPEN ACCESS

Digital Gangrene as Initial Manifestation of Anti-Phospholipid Antibody Syndrome: A Case Series

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Abstract

Early manifestation of Antiphospholipid Syndrome (APS), include Dermatological features which aid in early diagnosis, before occurrence of any life threatening complications. However, digital gangrene is rare skin phenomenon in APS and even rarer as initial presenting feature of APS. So we herein report a series of three cases of APS, including one case of primary APS in young female, whose was occurrence of with digital gangrene as first manifestation of the disease.

Keywords: ***Antiphospholipid Syndrome, Anti-Phospholipid antibody, Digital gangrene, Skin manifestations.***

Introduction

Antiphospholipid Antibody Syndrome (APS) is an acquired thrombophilic disorder. APS is characterized by episodes of thrombosis, obstetric complications and presence of Antiphospholipid Antibodies (APL) [1]. Around 50% of the patients with APS are not with any associated systemic autoimmune disease, and are labeled as Primary APS, while rest of the APS syndrome cases are secondary to some connective tissue disorders. About 4% to 55% cases of APS show some or other kind of Dermatological involvement and it is presenting feature in about 30% cases of APS [2]. However, initial presentation of APS as digital gangrene is very rarely reported. [2,3]. Here we report case series of both primary and secondary APS with digital gangrene as its presenting feature.

Case report

Case 1

A 20 years old female visited OPD in 2019 with presenting complaints of severe pain and numbness over fingers and toes, since over 15 days, and blackish discoloration of multiple digits of over 10 days duration. There was no preceding history of exposure to extreme cold, drug intake or fever. Also, there was no past history of raynaud's phenomenon, skin rash or ulceration. On examination, her Blood Pressure was 112/76 mm Hg in right arm in supine position, Pulse Rate was 82 beats/ minute and all major peripheral pulses were palpable. Except for right thumb and index finger, all the other digits were cold to touch, extremely tender. Black dry gangrene was noted on the tips of digits (**Figure 1**). Rest of her general physical and systemic examination was unremarkable. Laboratory investigations at our hospital revealed: Complete Blood Count (Hb 12.4 gm/dl, TLC 8950 cell/µl, Platelet Count 1.97×10^3 cells/µl), Blood Urea, Serum Creatinine, Liver Enzymes were within limits, and urine analysis showed trace proteinuria. ANA, antibodies against DsDNA, p-and c-ANCA, Anti-topoisomerase Antibodies, Anti-Centromere Antibodies, Antibodies against U1RNP were negative. Cryoglobulin assay was negative. Doppler ultrasound showed complete cessation of blood flow in digital arteries in affected digits. In view of diagnostic difficulty and presence of thrombotic episode, Anti-Phospholipid Antibody assay was done. It was positive for IgG anticardiolipin antibodies (45.6 GPL unit/ml). Thus diagnosis of primary APS was considered and patient was started on oral Warfarin therapy, along with low molecular heparin for initial 7 days. She was discharged with PT-INR of 3.2. A target INR of 3 to 3.5 was instructed to be maintained during her subsequent follow ups. After 3 months repeat IgG Anticardiolipin Antibody was done which was also positive with a titer of 39.4 GPL unit/ml) and hence, diagnosis of primary APS was confirmed. Patient is in regular follow up and there has been no recurrence of gangrene or other features of disease activity till last follow up.

Figure 1: Generalized digital gangrene in a case of primary antiphospholipid syndrome.

Received: January 03, 2025; **Revised:** February 13, 2025; **Accepted:** February 16, 2025

Case 2

A 37 year old man presented with a 2-week history of pain in the index and second finger of his left hand. A bluish discoloration in the fingers was also noted by him. The above symptoms had developed gradually over the period of time and were not accompanied by any other relevant symptoms. Past medical history was insignificant. General Physical examination, showed the distal segments of both above mentioned fingers were deeply cyanosed and cold, with presence of ulcerative patches (**Figure 2**). Both the radial and ulnar pulse was palpable. Rest of physical examination was unremarkable. The Blood Work Up included a CBC, ESR, biochemical screen, LFT, RFT, glucose, proteins, thyroid function, lipid profile were within normal limits. His Antinuclear Antibody was positive at titres of 1:320 with a negative double stranded DNA. His lupus anticoagulant was positive with a test ratio of 3.1 and a control ratio of 1.7. The IgG Anticardiolipin Antibody assay was positive with the titer being 49.0 GPL unit/ml. The IgM level was within normal limits (< 0.3 GPL unit/ml). Serological tests for syphilis were negative. This led to diagnosis of secondary Antiphospholipid Antibody syndrome. He was prescribed Apixaban, Nifedipine, and Steroids. After regular follow up for about 12 months, there is improvement in raynaud's phenomenon, the digital gangrenous patches have healed with scarring, and there was no recurrence.

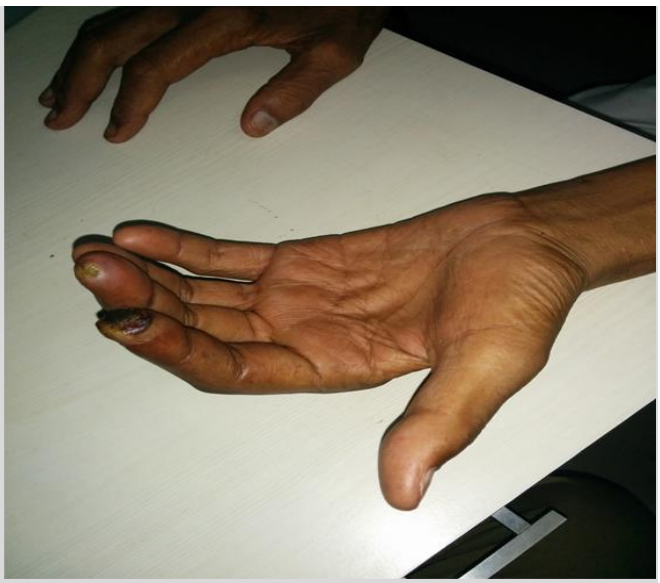

Figure 2: Digital gangrene of two fingers of left hand in male with secondary antiphospholipid syndrome.

Case 3

A 32-year-old woman presented with complaints of pain, swelling and ulcer over left index and middle fingers since one month. She was a known case of SLE for last 2 years. General Physical Examination revealed two erythematous ulcers with a hyperkeratotic base, located on distal palmar aspect of the fingers (**Figure 3**). Renal biopsy two years ago had revealed diffuse proliferative glomerulonephritis (WHO class IV lupus nephritis). There were no other systemic manifestations of SLE. She had achieved a complete remission of lupus nephritis and presently she was on medication including Mycophenolate Mofetyl 2 gram/day and 5 mg/day Presnisolone. She also denied a history of any previous Thrombotic Event or Miscarriages or Preeclampsia. The patient denied a history of smoking and having any symptoms associated with Raynaud's phenomenon. Clinically significant laboratory findings included positive anti Ds DNA antibodies at a titer of 25 U/ml (normal < 7 U/ml), positive lupus anticoagulant test (ratio of 2.9 vs. control ratio of 1.7), and positive IgG Anticardiolipin Antibody assay with the titer being 62.0 GPL unit/ml. A diagnosis of secondary Antiphospholipid Antibody syndrome was established. Oral anticoagulation in form of Warfarin was started. She was advised every month follow up and during the last 3 months of follow up, there was no new lesion and the existing lesions were healed with residual scarring.

Figure 3: Digital gangrene of left-hand fingers in case with antiphospholipid syndrome.

Discussion

Anti Phospholipid Syndrome (APS) also known as Huges Syndrome is an acquired autoimmune disorder that manifests clinically as recurrent venous or arterial thrombosis and /or fetal loss [1]. Characteristic laboratory findings in APS include persistently elevated levels of antibodies directed against membrane anionic phospholipids (i.e. IgG or IgM Anticardiolipin Antibody, antibodies against their associated plasma proteins (predominantly beta 2 glycoprotein) and /or evidence of circulating anticoagulant (lupus anticoagulant), on 2 different occasions, spaced at least 12 weeks apart. Up to 5% of healthy individuals may show presence of APL, with higher prevalence in pregnant females and elderly persons [4]. Hence, presence of APL alone is not diagnostic tool of APS.

Both primary and secondary APS presents identical features, although dermatological manifestations are more commonly seen in primary APS [5]. Prevalence of dermatological involvement varies from 4 to 55% [2]. Study by Frances et al reported that skin manifestations were present in 49% of patients [2]. While in the series reported by Alegre *et al.* [8] the cutaneous lesion developed as the first manifestation of Anti-Phospholipid Syndrome in 41% of APS cases. Various skin manifestations include; livedo reticularis (most common), livedo racemosa, primary anetoderma, cutaneous ulcerations, atrophie blanche, acrocynosis, sub-ungual splinter, hemorrhage, dermographism, raynaud's phenomenon, superficial venous thrombophilitis, pseudovasculitis, and digital gangrene [2,6]. Presence of digital gangrene is extremely rare in primary APS. In secondary APS, apart from presence of APL, some other pathogenic mechanism like; vasospasm, vasculitis, or atherosclerosis, may play causative role. The overall prevalence is reported to be 3.3-7.5% of APS patients [9]. In a study involving 200 cases of APS, including 100 patients of primary APS; presence of digital gangrene was seen in only 3 patients, and among them, only one patient had presence of digital gangrene as initial manifestation [2]. Moreover, wide spread involvement of almost all digits, as seen in our first case, is not commonly reported.

To conclude, we presented a case series of three APS patients with the patients having digital gangrene a rare clinical manifestation of APS as the initial complaint. All patients reported well to oral anti-coagulants and there was no recurrence. Digital gangrene could be a presenting feature of APS.

Abbreviations

APS: Antiphospholipid Syndrome
APL: Antiphospholipid Antibodies
OPD: Out-patient department
Hb: Hemoglobin
ANA: Anti-nuclear Antibody
Ds DNA: Double stranded DNA
ANCA: Anti neutrophilic cytoplasmic antibody
U1RNP: U1 Ribonucleoprotein particle
CBC: Complete blood count
ESR: Erythrocyte sedimentation rate
LFT: Liver function test
RFT: renal function test
SLE: Systemic lupus erythematosus
WHO: World health organization.

Declaration

Ethics approval and consent to participate

Written informed consent was obtained from all patients. Ethics committee approval was not required.

Consent for publication

I on behalf of all co-authors, hereby give my consent for publication of the manuscript in your esteemed journal.

Availability of supportive data

If needed, we give consent to provide supplementary Data.

Competing Interests

None

Funding Statement

None

Author's contributions

Surendra Singh Rathore was clinical incharge of all cases, and was responsible for diagnosis and clinical management of the cases. *Kumari Nirja, Garima Jeswani, and Sunita Choudhary* contributed in data collection, literature search, preparation of manuscript, and editing of the final version of manuscript.

Acknowledgement

None

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