

Case study

CATASTROPHIC ANTI-PHOSPHOLIPID SYNDROME PRESENTING WITH SYMMETRICAL PERIPHERAL GANGRENE

ABSTRACT: A case of 12 years old female who presented to the Emergency with discoloration of arms and legs and later developed gangrene which then auto-amputated. Anti-cardiolipin antibodies were found to be positive and skin biopsy findings were consistent with APS. she was diagnosed with catastrophic anti-phospholipid syndrome. However anti- ds antibodies were found to be negative.

KEYWORDS: ANTI-PHOSPHOLIPID SYNDROME, CARDIOLIPIN ANTIBODIES, GANGRENE, AUTO-AMPUTATION

INTRODUCTION: Anti-phospholipid syndrome(APS) is an acquired auto-immune thrombophilia. It can be primary or secondary¹⁻³. It can be associated with other auto-immune conditions most common of which is SLE and if not then it may later on in life lead to development of SLE⁴. Clinical manifestations of this syndrome are heterogenous. It is more common in adult females presenting with recurrent miscarriages and is very rare in children⁵. Even the largest APS cohort study reports APS onset in children aged less than 15 years in only 2.8% of population.⁶

The adult diagnostic criteria for APS revised in 2006 include one laboratory and one clinical criteria for confirmed diagnosis (as shown in table 1). Recently, adult diagnostic criteria is used for diagnosis of APS in children however some studies suggest that there should be separate diagnostic criteria for children aged less than 15 years of age because some children donot match this criteria.⁷

Rarely APS presents with skin manifestations. Skin lesions seen in APS are mostly manifestation of another variant of APS known as catastrophic anti-phospholipid syndrome (CAPS) which is characterized by multi-organ involvement along with microvascular occlusions. Some other skin lesions associated with CAPS include livedo reticularis, acrocyanosis, large cutaneous necrosis, palmar erythema, digital gangrene and ischemic ulcers⁸. Few studies report gangrene associated with anti-phospholipid syndrome however this presentation is very rare⁹. More commonly gangrene in anti-phospholipid syndrome is associated with SLE¹⁰.

CASE HISTORY: 12 year old female patient with no-comorbid presented to the Emergency room in critically ill condition with swelling and discoloration of upper and lower limbs. She previously had episode of loose motions and vomiting for which she was treated in her locality after which she developed blackish discoloration of upper and lower limbs. On examination her respiratory rate was 35 breaths/min, pulse 150 bpm, temperature 38degree centigrade, blood pressure 100/60. She had no previous history of such episode. She denies history of any drug intake, breathlessness or hemoptysis. Upper and lower limb pulses were not palpable. Rest of the systemic examination was unremarkable.

Investigations revealed Hb 4.8 gm/dL, platelet count 42×10^9 , neutrophils 63%, lymphocytes 33%, eosinophils 2%, basophils 2%, Urea 116 mg/dL, Creatinine 3.5 mg/dL, calcium 5.1 mg/dL, sodium 138 mg/dL, Potassium 3.2 mg/dL, chloride 105 mg/dL, magnesium 1.06 mg/dL, albumin 2.8, raised CRP (24 mg/L). Urine DR showed positive leukocyte esterase (>25 Leuc/uL), protein traces and occult blood. Total bilirubin was 7.6, direct bilirubin 3.2, ALT 165 u/litre, ALP 249 u/litre. Direct and indirect Coombs test were negative. PT was 13.7 seconds (control 11.4), APTT was 27.4 seconds (control 26.6 seconds). ANA, AMA, ASMA, AGPCA, c-ANCA, p-ANCA, anti-ds DNA were negative. Anti-cardiolipin IgG was positive (24.1), cardiolipin IgM was also positive (13.1).

Ultrasound of arms and legs revealed no flow below cubital fossa and popliteal fossa respectively. Discoloration of arms developed into symmetrical gangrene in both upper and lower limbs below the elbow and knee joint respectively as shown in figures. Overtime gangrenous parts got auto-amputated. Skin biopsy reports were consistent with findings of anti-phospholipid syndrome. Echocardiograph was normal (Ejection fraction 60%, normal sized atria and ventricles and no valvular abnormalities).

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DISCUSSION: This is an interesting presentation of CAPS in female child with symmetrical peripheral gangrene. This type of presentation clinically mimics Beurger's disease(11). Infection was found as a trigger for development of clinical manifestations. Patient was started on methylprednisone, cyclophosphamide and later methotrexate along with broad spectrum antibiotics. Treatment in APS in patient based. There is no modality of treatment currently developed to manage syndromes of APS. However improvements have been seen with anti-coagulation, plasma exchange, high dose corticosteroids with or without Immunoglobulins.(12) Currently there is no evidence of SLE in this patient however this patient is at high risk of development of SLE later in life. Lupus anti-coagulant would have been big help in diagnosis but couldn't be done due to financial constraints. There is much need of further research regarding diagnosis of APS in peadiatrics.

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91 **Table 1: Research criteria for defining the antiphospholipid syndrome. Adapted from Miyakis et al (2006). With permission,**
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Clinical criteria 1. Vascular thrombosis One or more clinical episodes of arterial, venous or small vessel thrombosis 2. Pregnancy morbidity (a) One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation (b) One or more pre-term births of a morphologically normal neonate before the 34th week of gestation because of: (i) eclampsia or severe pre-eclampsia or (ii) recognized features of placental insufficiency (c) Three or more unexplained consecutive spontaneous miscarriages before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded Laboratory criteria 1. Lupus anticoagulant (LA) present in plasma, on two or more occasions at least 12 weeks apart 2. Anticardiolipin (aCL) antibody of immunoglobulin (Ig)G and/or IgM isotype in serum or plasma, present in medium or high titre (i.e. >40GPL units or MPL units, or > the 99th centile), on two or more occasions, at least 12 weeks apart 3. Anti-β₂-glycoprotein I antibody of IgG and/or IgM isotype in serum or plasma (in titre >the 99th centile), present on two or more occasions at least 12 weeks apart Antiphospholipid antibody syndrome (APS) is present if at least one of the clinical criteria and one of the laboratory criteria are met

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