

CASE REPORTS

DIGITAL SYMMETRICAL PERIPHERAL GANGRENE: A RARE MALE PRESENTATION OF ANTIPHOSPHOLIPID ANTI BODY SYNDROME

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Abstract:

Anti-phospholipid antibody syndrome can be defined as the occurrence of venous and arterial thrombosis with or without recurrent miscarriage in association with laboratory evidence of persistent Antiphospholipid antibody / antibody to beta-2-Glycoprotein-1 / anti cardiolipin antibody / lupus anticoagulant (usually associated with SLE). It occurs usually in female who can present with recurrent miscarriage and fetal loss. Anti-phospholipid Antibody can be also found in some autoimmune diseases and post viral infections. Even certain drugs; e.g. phenothiazine, can cause it. Arterial thrombosis may lead to peripheral limb ischemia, stroke, and myocardial infarct. And venous thrombosis may be found in the form of DVT, pulmonary embolism & thrombosis in vessels supplying the abdominal organ.

Key words: Digital peripheral gangrene, Anti-phospholipid antibody syndrome, Thrombosis.

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Introduction:

Symmetrical peripheral gangrene is a well-documented but rare clinical syndrome which is characterized by symmetrical digital ischemic damage leading to gangrene of 2/ more sites in absence of large vessel obstruction or vasculitis¹⁻³. The term 'purpura fulminants', often used synonymously, however does not adequately depict this specific scenario³, rather it is characterized by acute onset, rapidly progressive purpuric lesions leading to skin necrosis, gangrenous changes of limbs/digits and organ dysfunction⁴. Hutchison first described the symmetrical peripheral gangrene in 1891⁵. Although most of the cases of symmetrical peripheral gangrene have been documented as single case report, a few relative large cases series have been described recently^{6,7}.

Symmetrical peripheral gangrene is a cause of significant mortality & morbidity. It often requires multiple limb amputation in the survivors. Thus early recognition of the disease and its underlying cause may have profound impact on the management and its final outcome. The pathogenesis of symmetrical peripheral gangrene is not yet well understood. A wide array of infective and non-infective etiological factors has been linked with its development. It is clear, anyway, that a flow state is commonly present in association with hypercoagulable vesospastic situation leading to microcirculatory occlusion. The ischemic changes begin distally and may advance proximally to involve of whole extremity.

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Existing data showed that DIC might be associated with 85% to 100% of causes of symmetrical peripheral gangrene^{3,6}. DIC most commonly occurs due to sepsis^{2,3}. In case of sepsis, activation of neutrophils and release of vasoactive substance play a contributing role to develop peripheral gangrene. Pneumococcus is the most common organism responsible⁶ here. Other organism such as staphylococcus aureus, neisseria meningitidis, Streptococcus pyogenes, klebsiella pneumoniae, mirabilis, pasteurilla multocida, pseudomonas, Enterococcus faecalis, carhocytophaga, Plasmodium Falciparum, mycobacterium tuberculosis, rubeola virus and varicella zoster, have been implicated as the causative agents of symmetrical peripheral gangrene. The patients of symmetrical peripheral gangrene may be either healthy/ immunosuppressive prior to the onset of this syndrome.

Cold induced vasospasm may be an additive factor in causation of gangrene. In a recent prospective study, most of the patients of symmetrical peripheral gangrene (10 out of 14) were seen during winter season⁶. Other non-infective causes includes myocardial infarction, pulmonary embolism, supraventricular tachycardia, hypertension, cardiac failure, hypovolaemic shock, systemic lupus erythematosus, polymyalgia rheumatica, decrease level of protein c and protein s, antiphospholipid antibody syndrome, cryoglobinaemia, acute lymphatic leukemia, dog bite, appendicitis, sickle cell disease, hypernatraemic dehydration, small cell Ca, drugs- adrenaline, nor adrenaline, dopamine and many others. Asplenia, immunosuppression, diabetes mellitus, rheumatic fever are among the other aggravating factor.

Treatment of digital symmetrical peripheral gangrene is multidisciplinary. No specific treatment has been shown to consistently prevent progression to reverse the gangrene. A team involving internist, critical care specialist, surgeon & dermatologist should undertake the management of symmetrical peripheral gangrene. The patient should

ideally treat in an intensive care unit. Identification & treatment of the underlying cause is the most important part of the treatment. Vasopressor agents, commonly used in the management of sepsis-induced hypotension, may aggravate this condition. Disseminated intravascular coagulation should be corrected as appropriate, its cause should be found out & treated aggressively. Intravenous-fluid and appropriate parenteral antibiotics should be started early. Management of DIC should be guided by basic tests of coagulation. If bleeding is the predominant factors are replaced. On the other hand in cases where thrombosis is predominant, several anticoagulants are tried. Use of heparin was not been proven to improve survival. Randomized trials failed to show any encouraging results regarding use of antithrombin. Recombinant activated protein C, plasmapheresis, intravenous immunoglobulin, continuous plasma ultrafiltration, and continuous veno-veno haemofiltration have also been used with variable success rate. Other measures that might be helpful are sympathetic blockade in the form of ganglion block or intravenous trimethaphan therapy, intravenous nitroprusside therapy, topical nitroglycerine ointment, local or intravenous infusion of an α_1 blocker (phentolamine, chlorpromazine) and intravenous infusion of prostaglandin (epoprostenol). Papaverine, reserpine, streptokinase, dextran and hyperbaric oxygen therapy have not been shown to be beneficial. Inter digital padding and protection from trauma may also decrease tissue injury. Amputation of the gangrenous area may be inevitable, but initially a non-surgical approach to management is preferred to allow time for the patient's condition to stabilize to allow the gangrene to become demarcated. Later on, skin grafting maybe needed. Early physiotherapy may restore joint mobility and range of motion. Treatment success has been reported for individual patients who received epoprostenol, tissue plasminogen activator and sympathetic blockade, combination of plasmapheresis, antibiotic, anticoagulant & heparin or warfarin with aspirin. Amputation

of the affected area may be undertaken, once demarcation develops and when patient is stable.

Case Report

A 45 years old smoker, normotensive, non-diabetic, non-asthmatic gentleman was admitted to the medicine unit with complaints of sudden onset of severe pain & blackening of fingers & toes of all four limbs for 8-10 days with ulceration of index and middle fingers of right hand & great toe of left foot for 2-3 days. The pain was sudden in onset, moderate to severe in nature, persisted throughout the day and present in all postures. Movement and cold exacerbated the pain and there was no relieving factor. No history of such type of pain was available. The pain was so severe that he was unable to do his daily activities.

The blackening of fingers and toes was also sudden in onset. It initially involved the fingers of right hand and gradually extended to the fingers of left hand than involved toes of lower limb on both aspects. Blackening didn't spread beyond wrist and ankle. There had been no previous history of such type of attack. There was also ulceration of left great toe and 2 fingers of right hand; ulcer is not associated with bleeding or excoriation. There is no radiation of pain, joint pain, wasting, stiffness, deformity, nodule, restricted movement, tingling, numbness, paraesthesia, fever, breathlessness, chest pain, hemoptysis, allergic condition, bleeding manifestation, unconsciousness, nasal crusting, proptosis or abdominal pain, hematuria, hearing loss, vision abnormality,

dry eyes & skin, oral & genital ulceration were also absent.

On examination, nail was found brittle with alternation of shape. Blood pressure on arm was 130/80 mmHg, on ankle was 100/70 mmHg, and pulse was 88 beats per minute. Pulse of both lower limb was present symmetrically but feeble, temperature was increased on both limbs & bilateral symmetrical blackening of fingers & toes with ulceration. All other system was normal. On investigation complete blood count showed neutrophilic leukocytosis with high ESR, positive anticardiolipin IgM Antibody & lupus anticoagulant antibody. Other investigation reports are C-reactive protein, C3, C4, Serum Electrolyte, Serum Creatinine, lipid profile, HbA1C, viral marker's, P-ANCA (Perinuclear Anti neutrophilic Cytoplasmic Antibody), C- ANCA(Cytoplasmic Anti neutrophilic Cytoplasmic Antibody), blood culture, ultrasonogram of whole abdomen, colour duplex study of both limbs, ECHO, anti-phospholipid IgG & IgM, APTT, bleeding time, clotting time, prothombin time, VDRL, magnetic resonance angiography of both lower limb, cryoglobulin precipitin test reveals' normal findings. Initially we treated the patient with LMWH for five days and then started oral anticoagulant, peripheral vasodilators, Calcium Channel Blocker and oral steroid. But pain didn't resolve. Rather ulcer and gangrenous condition was progressing. Then we consulted with surgery department and amputation was done. The patient is now having regular follow up with us. He does not have any more blackening or any new ulcer. However his pain is still persisting.



Discussion

Symmetrical peripheral gangrene carries a high mortality rate with a very high frequency of multiple limb amputation in survivors.⁸ It may manifest unpredictably with a broad spectra of clinical presentation. In this case, we have dealt with a middle aged smoker and diabetic patient. He presented with features of acute limb ischemia which were more complicated with digital gangrene. Examination revealed dry gangrene in some of his fingers and toes with feeble peripheral pulse. So we considered him as irreversible acute limb ischemia.

We approached to the acute management besides searching for the underlying cause. Hydration, nutrition maintenance and infection control as well as pain management were done. Moreover,

we looked minutely with frequent follow-up whether his blackening were deteriorating or not.

Fortunately it was static.

As the patient had no previous similar history and his symptoms took hours to days to develop, also he had no cardiac problem, so clinically we suspected it can be a thrombotic limb ischemia.⁵

We did his all base line investigations to rule out diabetic complications. All those came normal. Even his neurological examination was normal. Later we decided to screen other cause of thrombosis. We excluded septicemia earlier. Normal duplex study of his limbs and normal MRI of lower limbs make the scenario more complicated. Anyway high ESR and High CRP still points to any underlying condition. Later, we decided to antibody profile along with ANA. Though ANA came negative, positive anti-cardiolipin IgM Antibody & lupus anticoagulant antibody were highly conclusive.

So we diagnosed him as a case of anti-phospholipid syndrome. Possibly the thrombus lodged into small digital arteries. As he is a

smoker, we also ruled out any suspicion of malignancy. Meanwhile, we had talked to the surgery department and they advised for amputations. To prevent other complications, we treated him oral anticoagulant and steroids for long time.

Conclusion

Digital symmetrical peripheral gangrene due to anti-phospholipids antibody syndrome is a rare condition. But in medical science nothing is impossible; several kinds of reason are behind every disease whether it is usual or unusual. Whatever happens, symmetrical peripheral gangrene carries a high mortality & morbidity. High index of suspicion & prompt management with usual measures may limit the progression of the disease or gangrene. In our case the medicolegal aspects of associated gangrene & amputation must be born in mind.

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