GANGRENE OF ALL 20 DIGITS: REVIEW OF LITERATURE WITH RARE PRESENTATION OF TWO CASES
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ABSTRACT: Gangrene all 20 digits is a very rare clinical presentation. There are various diagnostic challenges faced while managing the cases of gangrene of all 20 digits. We report two cases of this rare presentation in a 40 year old female and a 60 year old male. There is plethora of etiologies of gangrene and with different treatment required for different causes as mentioned in the literature. But no cases of sickle cell trait with gangrene of all 20 digits have been mentioned in literature. So in evaluation of these patients, extensive blood investigations and imaging modalities are required as no single test is diagnostic of the underlying cause and may not be present in the literature.

KEYWORDS: Peripheral arterial disease (PAD), Gangrene, Sickle cell trait (SCD), Connective tissue disorder (CTD), Vasculitis, Infection

INTRODUCTION: PREGANGRENE: It is the changes in tissue which indicates that blood supply is inadequate to keep the tissues alive and presents with rest pain, colour changes, oedema, hyperaesthesia with or without ischaemic ulceration.¹

GANGRENE: It is macroscopic death of tissue in situ with or without putrefaction.¹

Etiology of gangrene is attributed to atherosclerosis, diabetic vascular disease, smoking and Buerger’s disease.² The past 20 years have unveiled a gamut of etiologies of vasculopathies including inflammatory or prothrombotic conditions. In 1969, homocysteine and thrombosis correlation was considered but its importance in thrombophillic conditions is realized only in the recent decade. Other important milestones in the vasculopathies are in 1982: ANCA and vasculitis and in 1983: APLA syndrome. Research on etiology of vascular diseases is concentrated on common and potentially lethal diseases like CAD and CVA. PAD has been definitely ignored. There are certain practical issues with the diagnosis of these conditions especially vasculitis, as serologic test like ANCA is not yet included in the diagnostic criteria of any vasculitis. Also there is ANCA negative vasculitis. Hence for confirmatory diagnosis of vasculitis, biopsy or angiography is necessary. Regarding biopsy diagnosis, the yield is poor (<40%) from most sites but for open lung biopsy (yield 90%), which is practically difficult. Investigations for prothrombotic conditions are expensive hence deferred. Moreover gangrene is often admitted in surgical ward for emergency intervention where the focus is on immediate relief and less on etiology.

CASE SUMMARY: A 60 year old male, a labourer, came with complaints of discoloration (blackening) of fingers and toes of all four limbs since 7 days, pain and swelling in both lower limbs since 7 days. (Figure 1 & 2) The patient gives h/o trauma to right foot 10 days back followed by
fever with chills. The patient is a chronic bidi smoker since 30 years. H/o consumption of alcohol, occasionally, present. Another 40 year old female, a housewife, came with chief complaints of discolouration (blackening) of fingers and toes of all four limbs since 15 days. (Figure 3 & 4) Pain and swelling in all toes since 15 days. The patient gives h/o malaria 20 days back for which the patient took treatment and the fever was relived.

PARAMETERS STUDIED: Detail history of fever, weight loss, rash, arthralgia, oro-genital ulcers, asthma, sinusitis, abdominal pain, anorexia, weight loss, smoking, drug intake and clinical examination was performed in all patients. Doppler study of lower and upper limbs, blood sugar, haemoglobin, complete blood count, ESR, urine routine, HIV, HBsAg, anti-HCV, lipid profile, serum homocysteine, ANA(anti-nuclear antibody), ANCA by IF (antibodies towards mpo and pr3 by ELISA if ANCA positive), ACLA(anti-cardiolipin antibody), LA(lupus anticoagulant), C3, C4(complement), Cryoglobulins, X-ray chest, 2D-Echo were done in all cases. Angiography, CT scan and biopsy were done.

MANAGEMENT: In both the cases, general physical examination and routine investigations were done. On local examination there was blackish discolouration of all digits of all four limbs with gangrenous changes. All the peripheral pulsations were normal of both upper and lower limbs. There was local rise of temperature with signs of chronic ischaemia. Lipid and coagulation profile were within normal limits. USG Abdomen showed no abnormality. Arterial Doppler of all four limbs showed normal triphasic flow with normal wave pattern and normal velocity in all arteries (Femoral, poplitial, anterior tibial, posterior tibial, brachial, ulnar and radial artery). Echocardiography was within normal limits with no evidence of any clot or vegetation. In spite of all the routine investigations, the cause for the gangrene could not be established so the patient was evaluated further. Arterial biopsy was s/o atherosclerotic changes. Skin biopsy was s/o small vessels vasculitis. Rhematoid factor–Negative, ANA and pANCA–Negative. On Hb electrophoresis–AS pattern was found. Intravenous antibiotics, analgesics, vasodilators, ecosprine and blood transfusion was also given. After treatment inflammation reduced and there appeared a clear line of demarcation with subsiding of pain and swelling.

DISCUSSION WITH REVIEW OF LITERATURE: Gangrene may be the first presentation of a systemic CTD or thrombophillic state. Younger age of onset (< 41yr), fever, weight loss, multiple limb involvement, anemia, high ESR, abnormal urine routine– proteinuria and RBCs all point towards a systemic connective tissue disorder. Laboratory tests for a systemic CTD and thrombophilia work up should be done in all non-diabetic PAD patients. Timely treatment of underlying cause will prevent damage to vital organs like the kidney in CTD patients and to the heart or brain in patients with hyperhomocysteinaemia and antiphospholipid antibody. Dactylitis is one of the earliest manifestations of SCD. The clinical findings are typically reversible, but roentgenograms may show bony destruction and permanent shortening of the digits can occur. A 7-month-old African American boy with sickle cell disease (SCD) and painful swelling of the hands and feet was treated with immersion of the hands in ice water. Thrombosis complicating dactylitis was reported once previously when a patient with SCD treated with sponge baths for
fever developed gangrene in all four extremities.\(^5\) Exposure to cold is a known precipitating factor for vaso-occlusive crisis by promoting vasoconstriction, de-oxygenation of hemoglobin and increased red cell viscosity.\(^6\) Therefore, the use of cold to treat dactylitis is clearly inappropriate. The diagnosis of protein S deficiency in this patient is intriguing. There is evidence that activation of coagulation plays a role in SCD. Decreased levels of the anticoagulant proteins are frequently reported; however, a correlation with disease severity has not been proven.\(^7\) Other diseases which can cause gangrene of extremities include systemic lupus erythematosus, progressive systemic sclerosis, Henoch-Schonlein purpura, anti-neutrophil cytoplasmic antibody associated vasculitis, Takayasu arteritis, infective endocarditis, gangrene associated with procoagulant states due to malignancy, anticardiolipin antibody syndrome, and disseminated intravascular coagulation.\(^8\) Rare causes of gangrene include heparin-induced thrombocytopenia, hemolytic uremic syndrome and HIV infection.\(^8\) Infections such as tuberculosis and cytomegalovirus, occlusive disease due to a hypercoagulable state, vasculitis are some of the mechanisms suggested for gangrene of the extremities.\(^8\) Widespread digital ischemic changes and gangrene of the hands and feet is an uncommon presentation in patients with HIV infection.\(^9\) HIV-associated gangrene may be associated with a known pathogen or trigger, or may occur in the absence of an obvious identifiable agent.\(^9\) Even though rare, vasculitis can lead on to devastating consequences. HIV associated vasculitis should be one of the differential diagnosis for patients presenting with gangrene of the extremities.\(^10\) Infective causes including tuberculosis, cytomegalovirus, Epstein-Barr virus, varicella zoster virus, herpes simplex virus toxoplasmosis, pneumocystis and salmonella.\(^11\) The two major mechanisms by which infection is thought to induce a vasculitis are direct microbial invasion, with resultant damage of the vessel wall, and immune mediated injury (both humoral and cellular).\(^12\) In Polyarteritis nodosa (PAN)-like vasculitis, the target organs that are usually involved are muscles and nerves, although skin and the gastrointestinal tract can also be involved.\(^13\) In general, there are two modes of presentation: Either as a peripheral neuropathy or with digital ischemia. It is well recognized that classic PAN can be associated with viral infections, especially hepatitis B virus (HBV).\(^14,15\) In both our cases, there was a consistent and pronounced involvement of the microcirculation particularly of limbs. Immune complex depositions have been implicated in pathogenesis. Hypersensitivity vasculitis like Henoch-Schonlein purpura, drug induced hypersensitivity vasculitis, and cryoglobulinaemia have all been postulated in these. It also includes angiocentric immune proliferative vasculitis, primary angitis of the central nervous system, large vessel (aorta, femorals, and carotids) vasculopathy and non-specific vasculitides; which do not fit into any of the characteristic patterns. These include non-specific or mononuclear inflammatory vascular disease. The treatment in patients with acute thrombosis type of occlusive disease depends on the clinical presentation. In those patients where the limb cannot be salvaged, primary amputation is done. Where the limb is salvageable, treatment options include endovascular procedures such as thrombectomy and thrombolytic or bypass procedures. Patients with infection with widespread ischemic necrosis and gangrene may require treatment with corticosteroids (in the event of possible vasculitis), thrombolytic agents (for the thrombotic component).

**SUMMARY:** **CONCLUSION:** Thus in this study we have tried to enumerate the diagnostic challenges faced while managing the cases of a gangrene of all 20 digits. Other highlight of the
study is that we have not came across any case in literature having an underlying AS pattern with gangrene of all 20 digits. Yet there were limitations of this study as complete work up for prothrombotic state like Protein C, protein S, antithrombin III, factor V Leiden mutation were not done due to financial constraints.

REFERENCES:

Fig. 1 & 2: Showing pre and in treatment of the male patient

Fig. 3 & 4: Gangrene of all the digits in female patient
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