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Case Report

A CASE OF SYMMETRIC PERIPHERAL GANGRENE.

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Abstract: A 50 – year old male, farmer, presented with complaints of abnormal sensations, pain and discoloration of hands & feet for last 7 months. He was a tobacco smoker with 15 pack – years of smoking. He had tachycardia, asynchronous pulses, dry purplish black toes, fingers and parts of adjacent hands and feet on examination. Investigations revealed leucocytosis, high ESR and protein S deficiency.

Keywords: Gangrene , Vasculitis , Smoking.

Case: A 50 – year old male, farmer by occupation presented with chief complaints of abnormal sensations, pain and discoloration of hands & feet for last 7 months. Patient was apparently alright 7 months back when he started with abnormal sensations involving his toes in the form of tingling & sensation of pins & needles. This remained of the same intensity for about 2 -3 weeks, got aggravated when the patient did his routine work like farming & was slightly relieved while sitting or taking rest. It did not have any relation with temperature like exposure to cold or warm water and it never disturbed him during sleep. After 2-3 weeks, patient felt similar sensations involving his fingers & thumbs. Again his symptoms got aggravated during working & there were no symptoms during sleep. He persisted with this problem for about 2 months, with no further worsening during this time. By the end of 2 months, he felt worsening of his symptoms. Pain started appearing in his toes & fingers. It was burning in nature, gradually progressive and interfered with his activities. His pain & abnormal sensations used to get worsened by doing any sort of activities like farming, walking, washing face. He had these symptoms for about 3 more months following which he started with discoloration involving fingers & toes, almost 1-2 days apart, initially in feet. His fingertips & feet became bluish in colour, progressively involved more & more digits & colour darkened with time. Discoloration & pain progressed & he developed blisters in feet & soles. Patient's symptoms now interfered with his all activities & his sleep as well.

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He did not lose the sensation of feeling cold or warm water with his feet or hands, nor did he lose the ability to move his hands or toes. He used over the counter painkiller tablets but there was no relief. There was no relief or aggravation of symptoms by keeping affected parts elevated or dependent.

There was no history of any fever / fatigue / joint pains / loss of hair / bleeding from any site / chest pain / breathlessness abdominal pain / change in colour of urine or stools. There was no history suggesting Raynauds phenomenon / photosensitivity / oliguria / swelling of body / weakness of any body part / travel or any drug intake prior to illness. Patient consulted some doctor for his complaints who initially prescribed analgesics and Gabapentin but there was no relief.

There were no previous hospital admissions or any history suggestive of hypertension, diabetes, antitubercular drug intake, chronic obstructive lung disease or rheumatic heart disease .Patient had never received any blood transfusions and had no allergic diathesis.

He had a normal appetite and bowel – bladder habits. He was a tobacco smoker with 15 pack – years of smoking. He was married, living with 4 children. Staple food was rice and there were no food fads. He used boiled water for drinking. He had no pets or dairy at home. There was no similar or any other significant health related problems in family members. They were seven members in family and belonged to Kappuswami socioeconomic class Upper Middle (II).

On examination, patient was conscious, cooperative, well oriented with time, place & person. Pulse was 110 / min, regular, fair in volume (in right radial), synchronous with both femoral pulses. BP was 120/70 mmHg (supine) and 110/70mmHg (standing).Respiratory rate was 14/min, Temperature of 97.8 deg F; Wt was 58 kg; Ht was 157cm and BMI was 23.53. There was no pallor, edema or icterus. Cyanosis was present (peripheral type).Tongue was moist, pink. There was no thyromegaly /no carotid bruit or lymphadenopathy / clubbing / flap. Nose and oral cavity were normal. Chest / CVS / Per abdomen / CNS : all normal. Digital rectal examination was also normal.

Examination of pulses revealed palpable fair volume pulse in right radial, both femorals, low volume pulse in left radial, right dorsalis pedis and absent left dorsalis pedis arteries. There was loss of synchronicity and discrimination in pulses .Local examination revealed dry purplish black toes , fingers and parts of adjacent hands and feet .The photographs of the same are shown in Figures 1 and 2.

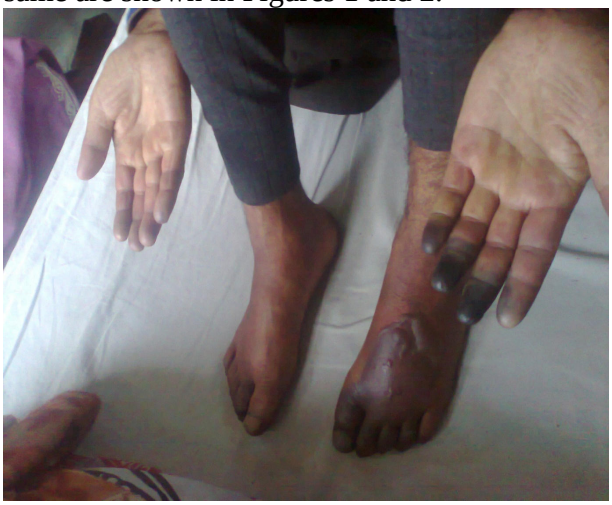

Figure 1. Peripheral gangrene.

Figure 2: Progression of gangrene.

We made the possibilities of (1) peripheral vessel disease; (2) vasculitis; (3) Buergers disease (4) Infection with DIC.

Investigations revealed Hb 12.5; Total leucocyte count of 17700; repeat 16800; Differential count showed N88 L10 M0.8; repeat N79L13M7 (N: neutrophils;M :mixed cells; L: lymphocytes);Platelets were 3.85 lac ; ESR was 35mm;Pripheral blood film was normal.PBF for malarial parasite negative; KFT

showed Serum urea of 44 and creatinine of 1.0; Blood glucose random 109 and fasting 90 mg/dl; Serum sodium 138 and potassium of 4.4.
Arterial blood gas analysis showed pH 7.45, pCO2 29, HCO3 21.9, pO2 62 , sO2 92.9 % and anion gap 17.1.
Urinalysis showed 10-12 pus cells per high power field with absent albumin and sugar. Cultures of blood and urine were sterile.
Liver function test : Bilirubin 0.8 ,total protein 6.8 ,albumin 3.5,alkaline phosphatise 146 ,SGOT 102 ,SGPT 84. Ca / P :8.6 / 3.7(mg/dL).
ANA: negative .Lipid profile :Total cholesterol: 96mg/dl (normal 100-200);TGs : 79 mg/dl (0-200);HDL : 40.3 (40-60);LDL :40 mg/dl(60-129)
HBsAg : neg ;IgG anti HCV : neg
ECHO ----N study.
MRI Cervical spine and brain :Age related cortical atrophy. Loss of cervical lordosis with degenerative spondylotic changes in cervical spine.There are marginal end plate osteophytes and dessicated internertebral discs with diffuse disc bulges at all levels.
Nerve conduction study revealed features of axonopathy in bilateral tibial nerves.Compression USG and Doppler of both lower limbs showed slowing of blood flow in all lower limb veins. All veins could be well compressed and showed no evidence of thrombus.There was no gross evidence of any peripheral artery obstruction or deep vein thrombosis.
Angiography: Coronaries normal.In left upper limb, there was cut off of radial artery flow at wrist level.In left lower limb, there was cut off of blood flow in distal arteries below ankle level.The findings are revealed in figures 3, 4 and 5.
Coagulation profile: PT 14; INR 1.07. Lupus anticoagulant panel :APTT : 31.60 sec (28.60 – 41.10);PTT – LA :33.40 sec (31.40 – 43.40);DRVVT : No evidence of Lupus Anticoagulant or deficiency of Factors (II ,V or X) detected.
Rheumatoid Factor (Immunoturbimetry) : 23.70 IU/ml (<14.00).
Cardiolipin Antibody Ig M serum (EIA):3.26 MPL U/ml (<10 neg) .
Cardiolipin Antibody IgG (EIA) : 2.87GPL U/ml (0.50 – 10.00).
Protein S Functional (Elecromechanical clot detection) :32.00% (normal 60.00 – 140.00 %)
Protein C Functional (Chromogenic) : 100.7% (normal 70.00 -140.00%)
Antithrombin activity Functional (Chromogenic) :90.00% (normal 80.00 - 120.00%)
Cryoglobulins Qualitative (Precipitation) :Negative
C3 Complement serum (Immunoturbimetry) : 168.00 mg/ dl (normal 90.00 -180.00)
C4 Complement serum (Immunoturbimetry) :73.00 mg/dl (normal 10.00 – 40.00) .
Final Diagnosis: Peripheral symmetric gangrene with doubtful etiology --? Buergers disease ..? Protein S deficiency.
Patient is planned for amputation and biopsy.
The patient was managed with parenteral antibiotics , aspirin , pentoxyphylline and cilostazol.
Patient was advised to protect his limbs from cold or trauma.
Discussion: Symmetric peripheral gangrene (SPG) is defined as the distal (acral) ischemic damage that occurs symmetrically in two or more sites (extremities) in the absence of a major vascular occlusion or vasculitis. It was first described by Hutchison in 1891 in a 37-year-old male who developed gangrene of fingers, toes, and ear lobules after shock [1]. The clinical picture of SPG with any etiology is suggestive of disseminated intravascular coagulation (DIC) as the final common pathway of its pathogenesis of which SPG is proposed to be a cutaneous marker[2]. Main causes of SPG include sepsis (due to a focus anywhere), low output states, shock, vasospastic conditions, myeloproliferative disorders, decreased level of protein C or protein S, faciparum malaria [3], viral gastroenteritis, malignancies like Hodgkin's lymphoma, paraneoplastic syndromes and hyperviscosity syndromes. Among infectious causes, most common are bacterial infections like pneumococcus, staphylococcus, meningococcus, and streptococcus [4]. The condition is aggravated by asplenism, hypothermia, vasopressor

infusion, immunosuppression, diabetes mellitus, renal failure, malignancy, ergot poisoning and increased sympathetic tone states. The hallmark of SPG in these conditions is microcirculatory failure. The hypercoagulable state, DIC, and vasospasm invariably coexist.The pathogenesis of SPG may be explained by Schwartzman reaction, bacterial endotoxin release and platelet plugging in peripheral arterioles due to vascular collapse and DIC.

In order to arrest the progression of pregangrenous changes to frank gangrene, we should recognise acrocyanosis early and quickly reverse the DIC. The underlying condition should be effectively managed and the patient should be stabilised hemodynamically. Starting anticoagulation with low dose heparin (300-500 IU/hour) may also be helpful in arresting the progression of pre-gangrenous changes to frank gangrene. Besides acrocyanosis, increase in serum lactate levels may indicate an impending SPG [5].Various modes of therapies for SPG include prostaglandin I 2 epoprostenol [6] and tissue plasminogen activator infusion, sympathetic blockade, the combination of plasmapheresis, leukapheresis and antibiotics and anticoagulation with heparin and aspirin [7]. Nitroprusside [8], topical nitroglycerine[9], papavarine, reserpine, streptokinase, dextran, hyperbaric oxygen, and sympathetic blockade (in the form of ganglion block) , intravenous trimethaphan therapy [10], local or intravenous infusion of an a-blocker (phentolamine, chlorpromazine)[11] have all been tried with variable and unequivocal success.Finally, amputation of the affected area may be undertaken once the patient is stable and develops demarcation of the gangrene. Examination of the amputated specimens often reveals thrombi concentrated in the small vessels with sparing of large vessels.

However, in our case, the patient is not that sick, has a subacute history over 7 months and is a smoker, so we think of Buerger's disease as a close possibility.

Thromboangiitis obliterans ,also known as Buerger's disease, and presenile gangrene [12] is a condition of progressive inflammation and thrombosis of small and medium arteries and veins of the hands and feet causing vaso occclusive phenomena. It is strongly associated with use of smoking tobacco products [13]. Buerger's disease was first reported by Felix von Winiwarter in 1879 in Austria [14]. The highest incidence of Buerger's disease is found in the natives of India, Korea, and Japan, along with Israeli Jews of Ashkenazi descent [15].

Olin's criteria [16] for diagnosis of Buerger's disease are shown below:

1. Typical presentation is a male between 20–40 years old [17].
2. Current (or recent) history of tobacco use.
3. Presence of distal extremity ischemia (indicated by claudication, pain at rest, ischemic ulcers or gangrene) documented by noninvasive vascular testing such as ultrasound.
4. Exclusion of other autoimmune diseases, hypercoagulable states, and diabetes mellitus by laboratory tests.
5. Exclusion of a proximal source of emboli by echocardiography and arteriography.
6. Consistent arteriographic findings in the clinically involved and noninvolved limbs.

The scoring system for diagnosing Buerger's disease is applied as indicated in Table 1 and Table 2 below. Our patient has a score of 5 with a medium probability of having the disease.

The arteriographic picture shows a "corkscrew" appearance of arteries particularly in the region of the wrists and ankles with collaterals giving "tree root" or "spider leg" appearance Angiograms may also show occlusions (blockages) or stenosis (narrowings) in multiple areas of both the arms and legs. Skin biopsies of affected extremities are rarely performed because of the frequent concern of poor healing of abnormally perfused biopsy site. Histologically, three stages of the disease are seen.In its acute phase,ther are highly cellular, segmental, occlusive, inflammatory thrombi, with minimal inflammation in the walls of affected blood vessels. Spread to adjacent veins and nerves is often observed.The polymorphonuclear leukocyte predominant inflammatory cellular aggregate may form

microabscesses and multinucleated giant cells.In the subacute phase, intraluminal thrombosis progressively organizes, but it may defer to vascular recanalization [18]. The end-stage phase is characterized by mature thrombus and vascular fibrosis.In all three stages of the disease, the integrity of the normal structure of the vessel wall, including the internal elastic lamina, is maintained that distinguishes it from arteriosclerosis and from other types of systemic vasculitis.

These patients have elevated serum anti–endothelial cell antibody titers, They also show an association with human leukocyte antigen (HLA)–A9, HLA-A54, and HLA-B5, suggesting a genetic component.

Most patients with Buerger's disease (70-80%) present with distal ischemic rest pain or ischemic ulcerations on the toes, feet, or fingers [19],[20].Smoking cessation has been shown to slow the progression of the disease and decrease the severity of amputation in most patients, but does not halt the progression. Among patients who stop using tobacco before progression to critical limb ischemia, the amputation rate is near 0%. In contrast, among patients who continue using tobacco, there is an 8-year amputation rate of 43%.

In acute cases, drugs and vasodilatory procedures are effective in reducing pain . Prostaglandins like Limaprost [21] are vasodilators and give relieve pain but do not help in changing the course of disease.Others include epidural anesthesia and hyperbaric oxygen therapy.In chronic cases, Lumbar sympathectomy may be helpful [22] by reducing vasoconstriction and increasing blood flow to the limb.Bypass can be helpful in treating limbs with poor perfusion secondary to this disease. Vascular growth factor and stem cell injections have also shown promise in clinical studies. Debridement is done in necrotic ulcers. In gangrenous or secondarily infected digits, amputation is frequently required. Streptokinase has been proposed as adjuvant therapy in some cases [23]. Medications to stimulate growth of new blood vessels (therapeutic angiogenesis), is considered experimental. Anti-inflammatory agents such as corticosteroids have not been shown to be beneficial in healing, but do have significant anti-inflammatory and pain relief qualities in low dosage intermittent form. Anticoagulation has also not proven effective.

Table 1. Scoring System for Diagnosis of Thromboangiitis Obliterans [24] proposed by Papa et al.

Positive Criterion	Positive Points
Age at onset	< 30 y (+2) 30-40 y (+1)
Foot intermittent claudication	Present (+2) By history only (+1)
Upper extremity	Symptomatic (+2) Asymptomatic (+1)
Migrating superficial thrombophlebitis	Present (+2) By history only (+1)
Raynaud phenomenon	Present (+2) By history only (+1)
Angiography; biopsy	If typical, both (+2) Either(+1)
Negative Criterion	Negative Points
Age at onset	45-50 y (−1) >50 y (−2)
Sex; smoking	Female (−1) Nonsmoker (−2)
Location	Single limb (−1) No lower extremity involved (−2)
Absent pulses	Brachial (−1) Femoral (−2)
Arteriosclerosis, diabetes, hypertension, hyperlipidemia	Discovered 5.1-10 y after diagnosis (−1) Discovered 2.1-5 y later (−2)

Table 2. Numerical Scores Defining Probability of Diagnosis of Thromboangiitis Obliterans.

No. of Points	Probability of Diagnosis of Thromboangiitis Obliterans
0-1	Diagnosis excluded
2-3	Diagnosis suspected (low probability)
4-5	Diagnosis probable (medium probability)
≥6	Diagnosis definite (high probability)

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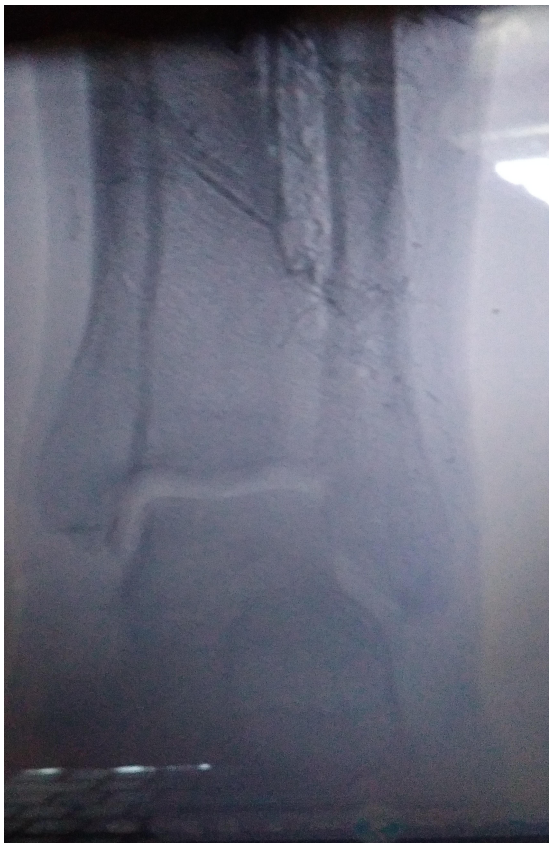

Figure 3

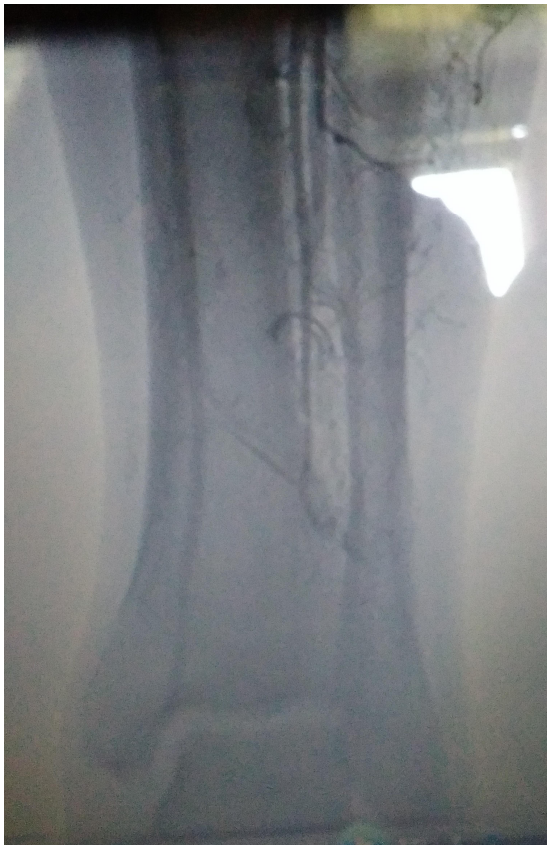

Figure 4

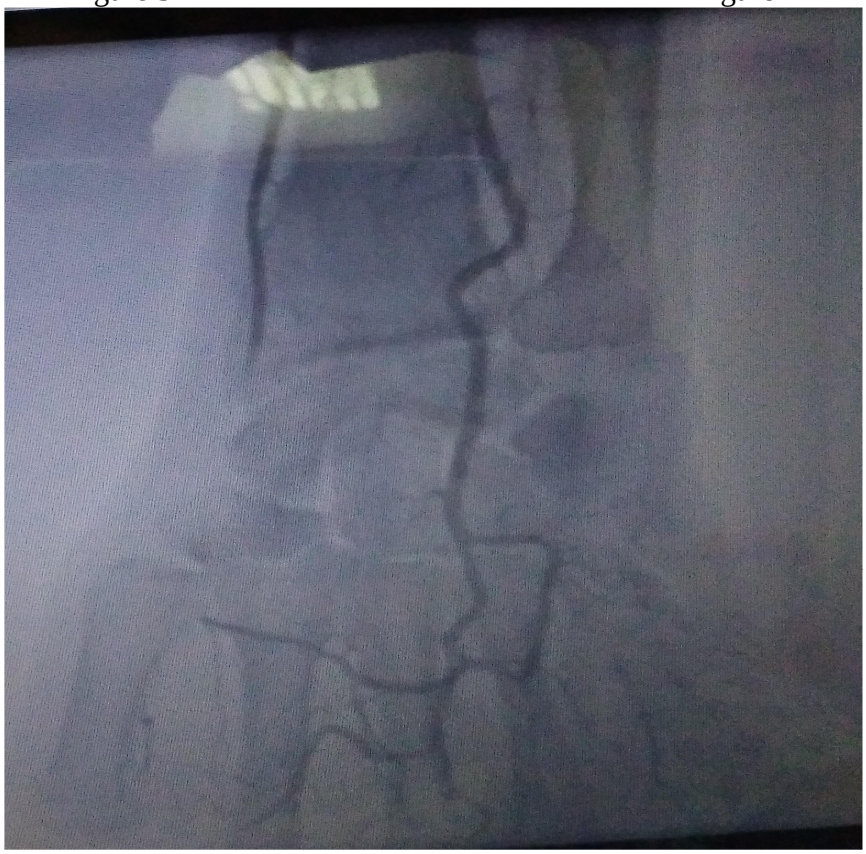

Figure 5