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Case Report

Internal Medicine Section

Rheumatoid Arthritis Presenting with Raynaud's Phenomenon in an Elderly: End of Road?

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ABSTRACT

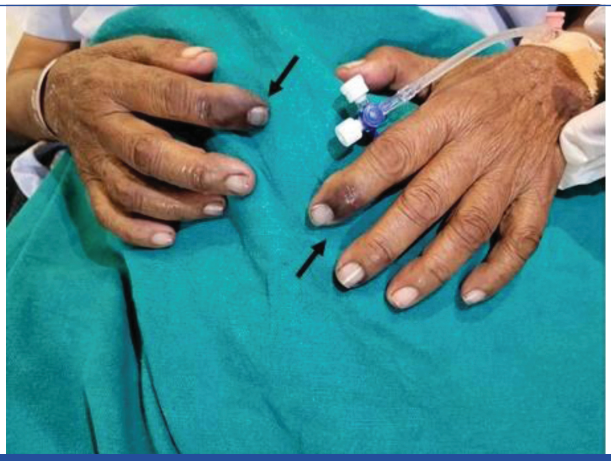
Rheumatoid Arthritis (RA) is an autoimmune and chronic inflammatory disorder where the immune system of the body attacks the healthy cells and causes inflammation. Raynaud's Phenomenon (RP) is a disorder of small blood vessels supplying the distal parts of the limbs where decrease in blood supply leads to infarction of that area. It occurs secondary to other disorders as in this case with RA. The report is about an 80-year-old female patient who presented with chief complaints of bluish discolouration over distal parts of hands and feet as well as pain in joints of all limbs. She had gangrene developing over the tips of fingers and toes, ulcer over the lower end of right foot, cold extremities, swelling over elbow and knee joints, oedematous hands and feet, and loss of pin prick needle sensations. With all the clinical presentations and investigation findings, the patient was diagnosed with RA presenting with RP. The patient was first started with the treatment for RA and then was managed symptomatically for vasculitis. Due to the old age factor and the advanced stage of the disease, the patient developed septicaemia and died due to cardiac arrest.

Keywords: Autoimmune, Connective tissue disorders, Joint pain, Vasculitis

CASE REPORT

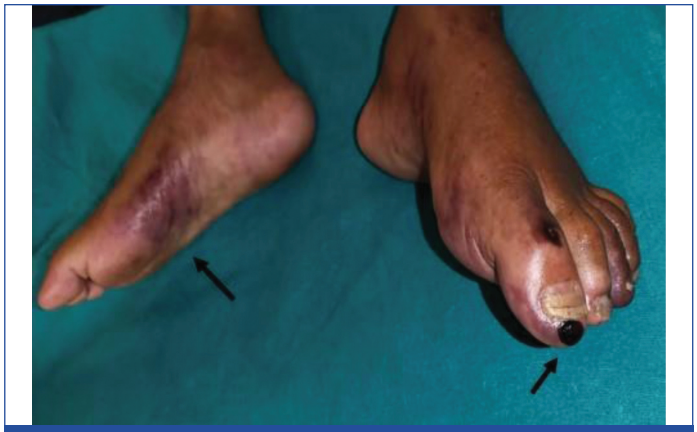
An 80-year-old female patient came to the hospital with complaints of pain in all joints and bluish discolouration of the distal parts of hands and feet for one month. She had swelling over distal parts of upper and lower limbs. She had breathlessness on exertion for two years and was prescribed medications for joint pain and breathlessness by the local general practitioner for two years. The patient was hypertensive and used to take tablet amlodipine 5 mg twice daily and was recently diagnosed with diabetes. She had no history of ischaemic heart disease or tuberculosis. She was a non smoker and non alcoholic.

Her physical examination revealed pallor, oedema under the neck and feet. There was tenderness over wrist and knee joints and bluish-black discolouration was present over distal phalanges [Table/Fig-1,2].



[Table/Fig-1]: Bluish-black discolouration of distal phalanges (Fingers).

On auscultation, pansystolic murmur was heard which radiated to the axilla. Her pulse was 86 beats per minute and regular blood pressure was 130/80 mmHg. The random blood sugar level was 133 mg/dL. She had an elevated total white blood cell count, increased rheumatoid factor, increased antinuclear antibody, positive anti Cyclic Citrullinated Peptide (anti CCP) antibody, increased C-reactive protein, increased troponin I and increased blood urea level, respectively. There was mildly elevated serum creatinine, aspartate aminotransferase and conjugated bilirubin [Table/Fig-3]. Tests were negative for Human Immunodeficiency Virus (HIV) and Hepatits B Surface Antigen (HBsAg).



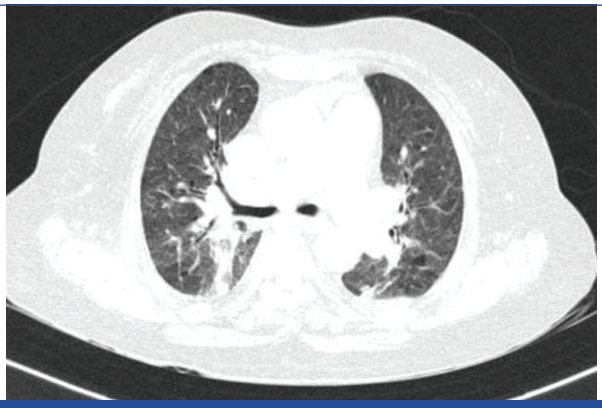
[Table/Fig-2]: Bluish-black discolouration of distal phalanges (toes).

Investigations	Observed value	Expected value
Random blood sugar (mg/dL)	133	<140
Total white blood cell count (cu.mm)	25800	4000-11000
Haemoglobin (gm%)	8.5, normocytic, hypochromic	12-16
Erythrocyte sedimentation rate (mm/hr)	74	0-30
Rheumatoid factor (IU/mL)	635.4	0-20
Antinuclear antibody (U)	1.1	≤1.0
Anti Cyclic Citrullinated Peptide antibody (anti CCP)	Positive	Negative
C-Reactive protein (mg/L)	293.78	0-10
Troponin-I (ng/mL)	75.4	0-0.04
Urea (mg/dL)	65	6-24
Creatinine (mg/dL)	0.4	0.7-1.2
Sodium (mEq/L)	131	131-145
Potassium (mmol/L)	3.8	3.6-5.2
Aspartate aminotransferase (U/L)	44	0-35

Alkaline phosphatase (IU/L)	106	44-147
Alanine transaminase (U/L)	38	7-56
Total protein (g/dL)	5.1	5.5-9
Albumin (g/dL)	2.5	3.5-5.5
Total bilirubin (mg/dL)	0.6	0.3-1.2
Bilirubin conjugated (mg/dL)	0.5	<0.3
Bilirubin unconjugated (mg/dL)	0.1	0.2-1.2
Globulin (g/dL)	2.6	2.0-3.5

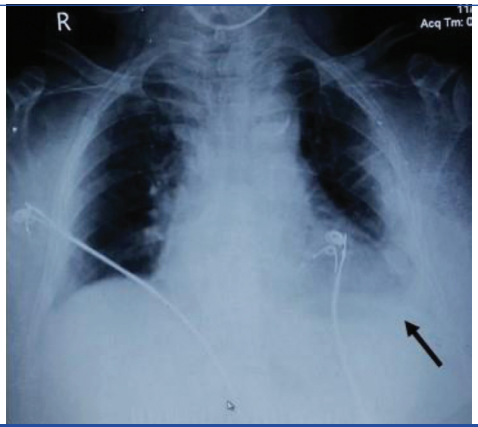
[Table/Fig-3]: Laboratory parameters.

The echocardiogram showed left atrial enlargement and hyperkalaemia. High-resolution Computed Tomography (HRCT) scan of thorax showed bilateral diffuse mild mosaic attenuation in lungs with few fibrotic stands and atelectatic bands in both lower lobes [Table/Fig-4].



[Table/Fig-4]: High-resolution Computed Tomography (HRCT) scan of thorax showed bilateral diffuse mild mosaic attenuation in lungs with few fibrotic stands and atelectatic bands in both lower lobes.

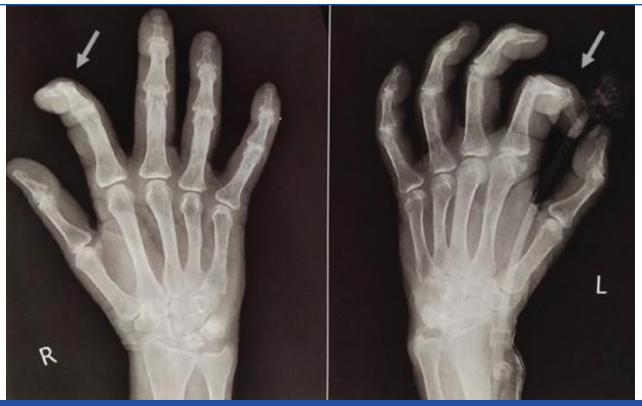
Mild cardiomegaly with dilated left heart chambers and mild pulmonary artery hypertension was observed. The 2D-ECHO showed hypertrophic obstructive cardiomyopathy, systolic anterior motion with severe mitral regurgitation. The chest radiograph showed consolidation in the left lower lobe of the lungs [Table/Fig-5]. X-ray right and left hand showing the typical Sausage digits (Kanavel's sign) [Table/Fig-6].



[Table/Fig-5]: The chest radiograph showed consolidation in the left lower lobe of the lungs.

Systemic rheumatoid autoimmune aetiology, for example systemic sclerosis and systemic lupus erythematosus and also, acral melanoma, osteoarthritis, polymyalgia rheumatica, bacterial infectious arthritis were the possible differential diagnosis.

The patient was kept on methotrexate 15 mg oral once daily, and pentoxifylline 400 mg oral 8 hourly but there was no improvement in her condition and she developed sepsis. In view of sepsis, patient was put on injectable antibiotics as pipracillin, tazobactum and lenozelid treatment for 2 weeks. Inspite of antibiotics and supportive measures, her blood pressure dropped to a level of being unrecordable. She was given ventilatory support and was also put on inotropic drugs. Despite these measures, the patient landed into sepsis with septic shock and succumbed after 2 weeks of therapy.



[Table/Fig-6]: X-ray right and left hand showing the typical Sausage digits (Kanavel's sign).

DISCUSSION

Important factors responsible for the development of RP are cold climate, prevalence in family, female gender, infections, haematological conditions, drugs such as beta blockers, ergot alkaloids, sympathomimetic drugs and rheumatological disorders like systemic sclerosis, systemic lupus erythematosus, and mixed connective disorders [1,2]. This phenomenon is rarely reported in RA especially in females and occurs below the age of 50. It has been recorded in 10% of the population, mostly in young women and has a definite history but, this is challenging to diagnose [3]. Uncertainty exists regarding the frequency of RP in RA. These could be attributed to variations in the research population, study design, and diagnostic standards for RP [4,5].

Some patients who have sensitive response to cold changes in the environment develop symptoms of RP relatively faster [6]. The index patient presented with all these factors, and were investigated and diagnosed for the same. She had joint pain followed by swelling and decrease in muscle tone of the distal parts of the limb. The patient experienced tingling sensations on the distal parts of the limbs involved and loss of function. Further, due to the development of vasculitis, gangrene starts to develop in the tips of fingers and toes [7]. Ravindran V and Rajendran S, reported a 19-year-old female who presented with gangrene on the index finger which was due to vasoconstriction of pre-capillary arterioles and digital arteries, and vasculitis [6].

A positive relationship between RA and RP has been well-established by Belch J et al., and his collaborators who studied 293 patients. Vascular spasm was reported in 11.3% of those patients and 2.7% of the 293 controls [3]. The co-morbid conditions of the index patient which added upto her condition were diabetes mellites, chronic hypertension, previous history of myocardial infarction or ischaemic heart disease and severe infection with corona virus.

A complicated interaction of genetic, neuronal, vascular, and intravascular variables results in the aetiology of RP. The genetic factors cause development of RP in half of the patients with positive primary RP history in the family with first degree relatives having RP. The pathophysiology of RP is primarily characterised by an increase in vascular tone, including vasospasm involving the digital arteries [8]. In this case, RP may be due to rheumatoid vasculitis. Postulated mechanisms are vasoconstriction compromising arteriovenous anastomoses and nutritional blood flow as well as intravascular factors, leading to increase the blood viscosity thereby precipitating RP [9].

Rheumatoid vasculitis is a late consequence of RA with a typical duration of 10 to 14 years [9]. It is an uncommon inflammatory disorder affecting the small and medium sized blood vessels.

This vasculitis mostly affects the skin, which can result in deep cutaneous ulcers and peripheral gangrene, as well as the peripheral nervous system, which can result in mononeuritis multiplex [10]. The complement system is activated when immune complexes, including rheumatoid antibodies, lodge on the blood vessel wall, causing vasculitis. Obliterative enteropathy is brought on by the proliferation of the vascular intima and media. Small vessel vasculitis or leukocytoclastic vasculitis results in cutaneous ulceration or palpable purpura [8].

The differential diagnosis is systemic rheumatoid autoimmune aetiology, for example systemic sclerosis and systemic lupus erythematosus and also, acral melanoma (discrete acral lesions and parallel ridge pattern is seen), osteoarthritis, polymyalgia rheumatica, and bacterial infectious arthritis. The diagnosis for RP is usually made with the help of detailed history and investigations. There are no typical signs which could help in ruling of the disorder [8]. Radiological examinations may help in ruling out certain differential diagnosis based on typical signs. Hypertension, Sjögren's syndrome, mixed connective tissue disease, undifferentiated connective tissue disease, fibromyalgia, carpal tunnel syndrome, cryoglobulinemia, dermatopolymyositis, vasculitis, thoracic outlet syndrome, hypothyroidism, and diabetes mellitus may be the possibilities in less than 5% cases [7].

Earlier, the aim for managing a patient with RA was to reduce the swelling and increase the mobility of the affected parts of the limbs. With incorporation of newer biological therapies which aim to achieve complete remission, prevention of tissue ischaemia and managing the disease progression such that the patient would be able to perform daily routine effectively [7]. Raynaud Condition Score (RCS) is used to measure the severity and frequency of attacks, the quality of life and the effect of RP on the individual [8]. The patients are managed conservatively at the early stages and only if there is no response to this management, pharmacological therapies are started. Now-a-days, the patients are prescribed combinations of Disease Modifying Anti-Rheumatic Drugs (DMARDs) with varying efficacy, side-effects and cost effectiveness. These include methotrexate, hydroxychloroquine, leflunomide, sulfasalazine, and biologic therapies [10].

CONCLUSION(S)

The Rheumatoid Arthritis (RA) does not frequently accompany Raynaud's syndrome, however this may be associated with certain other disorders, such as mixed connective tissue disease and scleroderma. Raynaud's syndrome patients should get special care for these disorders. RP is related to a significant morbidity and mortality. Early diagnosis and treatment in such conditions, especially in elderly can be prevented from early morbidity and mortality.

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