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Original Research Paper

General Medicine

EXTRAARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

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ABSTRACT Rheumatoid arthritis (RA) is a systemic autoimmune disease. The main characteristic of RA is persistent joint inflammation resulting in joint damage and loss of function. Rheumatoid arthritis may lead to a variety of extra articular manifestations. Extra-articular organ involvement in RA is more frequently seen in patients with severe, active disease and is associated with increased mortality. The occurrence of these systemic manifestations is a major predictor of mortality in patients with RA. [1] Our case series attempts to provide a glimpse into the various extra articular manifestations of Rheumatoid arthritis. In total, 3 patients have been included for this case series. All 3 patients were a known case of Rheumatoid arthritis who presented with extra articular manifestations at MGM hospital, Kamothe.

KEYWORDS :

INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory disease of unknown etiology characterized by a symmetric polyarthritis and is the most common form of chronic inflammatory arthritis. It is a systemic disease and may lead to a variety of extra articular manifestations.

Extra-articular RA is a serious condition, and rheumatoid arthritis patients with extra-articular manifestations should be aggressively treated and monitored. [3].

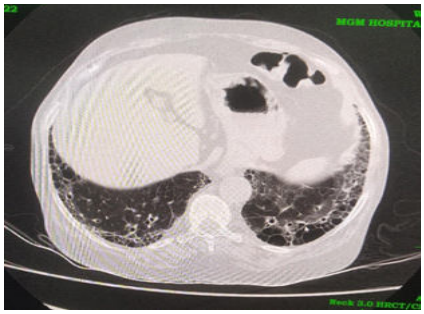
Patients with RA, who have high titers of rheumatoid factor (i.e., autoantibodies to the Fc component of immunoglobulin G are most likely to have extra-articular manifestations of their disease. [4,5,6] This case series seeks to highlight the wide ranging manifestations of Rheumatoid arthritis.

Case Reports

Case 1

A 63 year old female was brought with complaints of breathlessness, cough and fever since 2 days. Breathlessness was insidious in onset and progressive in nature. Patient had breathlessness at rest and resulted in difficulty in sleeping at night. It was associated with cough, dry in nature, without expectations. Patient had 1 episode of fever, not associated with any chills or rigors. Fever was relieved on taking medications. Patient was a known case of Rheumatoid arthritis since 20 years on Tab Methotrexate (2.5 mg twice daily on saturday and sunday) and Tab Folic Acid 5 mg once daily. On examination, patient had a pulse rate of 90 beats per minute, blood pressure of 110/70 mmHg, respiratory rate of 24 per minute with a saturation of 90% at room air.

On systematic examination, patient was conscious, well oriented to time, place and person. heart sounds were normal with no murmur heard. On auscultation, air entry was reduced on bilateral sides with bilateral coarse crepitations heard. A chest X-ray was done, which was suggestive of diffuse reticular Infiltrative lesions involving bilateral lung fields. Arterial blood gas picture was suggestive of respiratory alkalosis. A HRCT chest was obtained, which was suggestive of pulmonary fibrosis with subpleural interlobular septal thickening and peripheral honeycombing features, s/o Usual interstitial pneumonia type of interstitial lung diseases. ESR was 114 mm/h and CRP was 123mg/dl. Patient was started on Antibiotics and Tab Hydroxychloroquine 300mg bd, Tab Mycophenolate Mofetil 500 mg bd, Antifibrotics (Tab Nintendanib 200 mg bd)) and steroids (Tab Deflacort 0.5mg/kg/day). Gradually the condition of the patient improved and she was discharged.



Case 2

A 38 year old female was brought by relatives with complaints of weakness of left upper limb and lower limb since 1 month back. Patient was apparently asymptomatic 1 month back when she was doing her daily activities; she suddenly started complaining of weakness of left upper limb and lower limb. It was associated with slurring of speech. Patient was taken to a local hospital where her MRI brain plain with contrast was done, which was suggestive of left thalamic infarct with right cerebellar infarct with lumen occluding right vertebral artery thrombus. Patient was started on dual antiplatelets and anticoagulation and later referred to MGM. Patient was a known case of rheumatoid arthritis since 8 years, on Tab Methotrexate 7.5 mg (once daily on Saturday and sunday), Tab Folic Acid 5 mg once daily, Tab Hydroxychloroquine 300 mg once daily and Tab Methylprednisolone 4 mg once daily. Patient had associated complaints of appearance of maculopapular rashes over trunk and limbs with ulcer over knees, ankles and elbows since 2 months.

On arrival, pulse rate was 90 beats per minute, blood pressure was 110/70 mmHg, respiratory rate was 18 per minute with a saturation of 98% at room air. On systematic examination, patient was conscious, well oriented to time, place and person. Power was decreased in left upper limb and lower limb. Patient had slurring of speech. Patient's ANA came out negative, ANCA, APLA, ACPA were within normal limits while serum homocysteine levels were 20 Umol/L (Ref range : 5 – 15 Umol/L). Skin biopsy from ulcers was suggestive of acute on chronic granulomatous inflammation, indicating Pyoderma Gangrenosum. Patient was started on topical antibiotics and Cyanocobalamine tablets. Repeat MR angiography was suggestive of partial thrombus in right vertebral artery with

rest of the findings consistent with previous scan. Patient was later discharged on dual antiplatelets and was advised skin grafting.

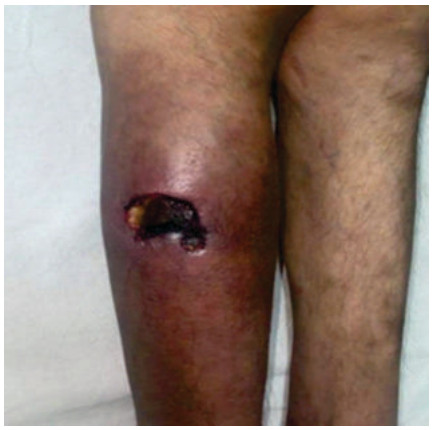


Figure 2 Pyoderma Gangrenosum seen over Right Lower limb - CASE 2

Case 3

58 year old female was brought by relatives with complaints of generalized weakness since 1 month, and skin lesions over lower and upper limbs. The skin lesions started on bilateral lower limbs and progressed to involve upper limbs. It was associated with itching over the lesions followed by peeling of skin over the affected area. There was no skin involvement anywhere else over the body. Patient had taken ayurvedic medications for 10 days. The lesions were followed by fever, insidious in onset, associated with chills and rigor. Patient had associated complaints of 4-5 episodes of vomiting – yellowish in colour, watery in consistency, containing food particles. There were no blood products in the vomitus. It was associated with 5-6 episodes of loose stools daily for 5 days – yellowish in colour and semisolid in consistency. Patient was a known case of rheumatoid arthritis since 10 years, not on any treatment. Patient was a known case of hypertension, diagnosed 1 year back on Tab Olmesartan and Tab Amlodipine. On arrival, patient had a pulse rate of 90 beats per minute, blood pressure of 80/60 mmHg, respiratory rate of 18 per minute with a saturation of 98% at room air. On examination, patient was found to have multiple, ill defined hyperpigmented plaques and scales over bilateral lower limb, including soles. Similar plaques were found on both the palms, suggestive of acute eczema with keratolysis exfolitia. On investigations hemoglobin was found to be 8.2 mg/dl with peripheral smear suggestive of microcytic hypochromic anemia. Serum Iron levels were decreased (3 mcg/dl), with raised serum ferritin levels (484 ng/ml), suggestive of anemia of chronic disease. CRP levels were raised (199.8 mg/dl). Patient was started on antibiotics, emollients and moisturizes. Blood and urine culture came out sterile. Serial haemoglobin levels were in decreasing trend. Patient later had 2 episodes of Haematemesis (~200 ml). Upper GI scopy was done, which revealed the presence of a duodenal ulcer (Forrest class 3) with mild hyperemic gastropathy, for which patient was started on PPIs and Syp Sucralfate and later discharged.

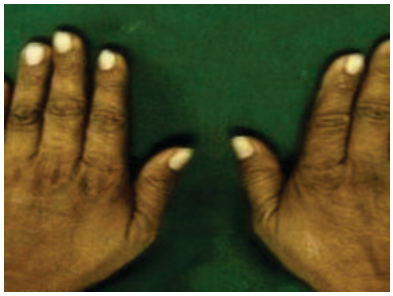


Figure: 3 Pallor Observed Over Hands

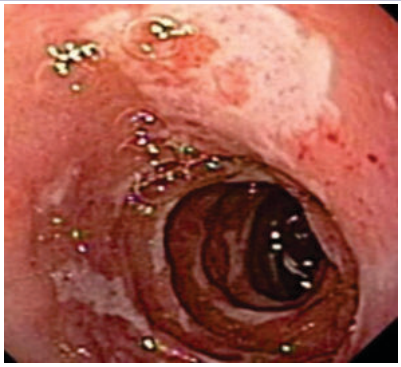


Figure 4: Duodenal Ulcer Observed During Ugi Scopy

DISCUSSION

RA affects ~ 0.5-1% of the adult population worldwide. Extraarticular manifestations may develop during the clinical course of Rheumatoid Arthritis in upto 40% of patients, even prior to the onset of arthritis. Subcutaneous Nodules, secondary Sjogren's Syndrome, interstitial lung diseases, pulmonary nodules and Anemia are among the most frequently observed extraarticular manifestations.[2] The prevalence of extraarticular manifestations of RA has declined in recent years, with the timing and pattern of the decline indicating that disease-modifying RA treatments may be changing the natural history of the disease. [7,8,9] Patients most likely to develop extraarticular disease have a history of cigarette smoking, have early onset of significant physical disability, and test positive for serum RF or ACPA. [2]

Cutaneous Manifestations

Subcutaneous Nodules can occur in 30-40% of patients. When palpated, the nodules are generally firm; non tender; and adherent to periosteum, tendons or bursae. These usually develop over forearm, sacral prominences, and Achilles tendon. They may also occur in lungs, pleura, pericardium and peritoneum. Other skin manifestations may include splinter haemorrhages, periungual infarcts, leg ulcers, digital gangrene and sharply demarcated painful ulcerations. .

Pyoderma gangrenosum is a rare disease characterized by chronic, recurrent ulceration of non-infective origin and usually associated with rheumatoid arthritis [1,2,14]. In our CASE 2, patient had maculopapular rashes over trunk and limbs with ulcera over knees, ankles and elbows on presentation, which were found to be pyoderma gangrenosum. The patient in CASE 3 had multiple, ill defined hyperpigmented plaques and scales over bilateral lower limb, including soles, suggestive of acute eczema with keratolysis exfolitia.

Haematological Manifestations

Haematological manifestations in RA may include anaemia, neutropenia, thrombocytopenia, thrombocytosis, eosinophilia, and haematological malignancies [10]. The cause of anaemia in RA is multifactorial-disease activity, drug-induced, nutritional, gastrointestinal bleed, bone marrow suppression, and ineffective erythropoiesis.

Anemia can be iatrogenic and caused by medications. [11]. Patients also have increased risk of Lymphoma, most common histopathological type being diffuse large B cell lymphoma. The incidence of felty's syndrome, a clinical triad of neutropenia, splenomegaly and nodular RA has declined. [2] In our CASE 3, the patient presented with generalized weakness and pallor and was found to be anemic.

Pulmonary Involvement

It includes pleuritis and pleural effusions. Pulmonary nodules can be seen, which may or may not be a part of Caplans

syndrome. Interstitial lung diseases may occur, generally found in smokers and patients with higher disease activity. Diagnosis is made by HRCT chest, showing infiltrative opacification or ground glass opacities, in the periphery of both lungs. Usual Interstitial pneumonia (UIP) is the most common pattern, showing progressive scarring of the lungs producing honeycomb changes in the periphery and lower portions of the lungs. The presence of ILD confers a poor prognosis. [2] In our CASE 1, the patient presented with breathlessness and was found to have UIP pattern of ILD on HRCT.

Other Manifestations

Cardiac Involvement

The most common cardiac Involvement in RA is pericarditis. Other conditions include pericardial effusion and Cardiomyopathy. Valvular abnormality like Mitral Regurgitation may be seen [2]

Oral Manifestations

Oral dryness and salivary gland swelling can also be found in patients with RA. These patients can also develop secondary Sjögren's syndrome. [3]

Gastrointestinal Manifestations

Primary involvement of the gastrointestinal tract, caused by mesenteric vasculitis leading to intestinal infarction, is very rare. [3]

Neurological Manifestations

Peripheral Neuropathy, due to small vessel vasculitis can be seen. Cervical Myelopathy caused by atlanto axial subluxation or pannus formation can be frequently seen.[12,13]

CONCLUSION

This case series describes 3 cases where patients, who were a known case of rheumatoid arthritis presented with extra articular manifestations. Although considered a "joint disease" rheumatoid arthritis is associated with involvement of extra-articular manifestations. The longer the duration of the disease will be, the larger the number of extra-articular manifestations. Extra-articular RA is a serious condition, and RA patients with extra-articular manifestations should be aggressively treated and monitored. [1]

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