RHEUMATOID ARTHRITIS ASSOCIATED WITH PULMONARY FIBROSIS IN NIGERIANS: TWO CASE REPORTS

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SUMMARY

Rheumatoid arthritis may sometimes present with extra-articular involvement, pulmonary involvement is not common. Rheumatoid arthritis has been reported among Nigerians and extra-articular manifestations are rarely seen. One of the patients was misdiagnosed and mismanaged as a patient with pulmonary tuberculosis. The study is to demonstrate that rheumatoid arthritis is not as rare as previously reported in Nigeria and its pulmonary involvement can mimic tuberculosis or other granulomatous lung disorder. Clinical and serological acumen are necessary to distinguish between the two. Two diagnosed patients with rheumatoid arthritis and pulmonary involvement seen at Olabisi Onabanjo University Teaching Hospital (OOUTH), are hereby presented.

INTRODUCTION

Rheumatoid arthritis are not commonly reported in Nigeria. There had been community based report which emphasised the rarity of rheumatoid arthritis as well as extra-articular manifestations (1). A recent study by Adelowo et al, gave a contrary result that Rheumatoid Arthritis may not be uncommon in Nigerians but confirms a low incidence of extra-articular manifestation and absence of pulmonary involvement in 200 patients studied (2).

Rheumatoid arthritis is usually diagnosed using the American College of Rheumatology Criteria (3) which has a high sensitivity and specificity. While rheumatoid factor are mostly associated with the extra-articular manifestation they are mostly negative among Africans with Rheumatoid arthritis without extra-articular features (4).

Various pulmonary manifestations have been reported in the developed world, these include diffuse interstitial fibrosis, pleural effusion, nodular lung disease, pulmonary vasculitis, alveolar haemorrhage, and pneumonitis (5).

Two cases seen in the chest unit of medicine department, OOUTH are presented as follows:

CASE 1

Mrs A.A was a 55 year old, non-smoking woman who presented with a six month history of cough productive of yellowish sputum. She had previously been diagnosed as arthritic by her general practitioner and had been placed on NSAIDs. She was also placed on anti-Koch’s which had not made her symptoms better.

Review at the clinic showed that she had a three year history of polyarthritis involving joints of the hands, elbows, shoulders, knees and ankles. She also complained of significant morning joint stiffness.

Physical examination showed a middle aged woman afebrile, pale and dyspnoeic. Cardiovascular system revealed pulse of 70bpm, BP 110/70 mmHg, Apex beat not displaced, heart sounds I, II and normal. Respiratory system examination revealed rate of 30 cpm, reduced chest excursion bilaterally, breath sounds reduced bilaterally and there were fine crepitations in both lung fields especially at the bases.

Musculoskeletal system revealed painful swelling of both wrists, ankles and knee joints. Tenderness in both metacarpophalangeal joints, shoulders and elbow. There was subcutaneous nodule
at the left elbow.
A diagnosis of rheumatoid arthritis was made based on the ACR criteria.

Chest x-ray showed widespread fibrosis of both lung fields. ESR was elevated 90min/hr (Westergren) rheumatoid factor positive titrate of 1:32. The lung function test showed a restrictive pattern: FEV1.5L/min, FVC1.8L/min with a ratio of FEV1/FVC 83%, PEFR 250ml/min.

She was placed on sulfasalazine 500mg tds, tab prednisolone 15 mg daily and diclofenac as required. She was stable and followed up.

CASE 2

Mrs O.D. was a 59 year old woman, nonsmoker who had previously presented to the clinic four years ago and had been diagnosed with rheumatoid arthritis using the ACR criteria. She had been on methotrexate tablets 15 mg once weekly and prednisolone with occasional NSAIDs. She however defaulted for one year before this presentation. She presented again in the chest clinic with a dry cough associated with breathlessness which had been worsening and associated with increasing incapacitation. The cough then became minimally productive of yellowish sputum.

Physical examination showed a wasted ill looking woman, pale and breathless. Cardiovascular examination was essentially normal. Chest auscultation showed presence of fine crepitations at the lung bases.

Musculoskeletal system examination revealed tenderness in both elbows and shoulders. She also had a boggy swelling in the left knee (effusion) and few swollen MCP joints. There were no subcutaneous nodules. Other systems were essentially normal. Laboratory investigations showed elevated ESR 68ml/hr. positive rheumatoid factors at titrate of 1:64.

Lung function test showed a restrictive pattern FEV1 1.6L/min, FVC 1.9L/min, FEV1/FVC 84.2%, PEFR 260L/min. Chest X-ray showed widespread fibrosis of both lung fields.

Methotrexate was withheld and was placed on cytosine arabinoside and cyclophosphamide for three months. She improved considerably. A repeat CXR showed less streakiness in the lung fields. She was also placed on flucloxacillin.

DISCUSSION

The reported cases are rare clinical condition of pulmonary manifestations of rheumatoid arthritis. Diffuse interstitial fibrosis has been described in approximately 40% of patients with RA (5-7). The disorder is initially characterised by chronic inflammatory changes in the alveolar walls and the presence of large mononuclear cells in the alveolar spaces. As the disease progresses, there is tendency to fibrosis with obliteration of the alveoli (7) and dilatation of the brochiole (8,9). The pulmonary areas primarily affected are the base of the lungs in the early stage of the disease and apices of the lung in more advanced stage.

Diffuse interstitial fibrosis occurs mostly in patients who have subcutaneous nodules and high titers of rheumatoid factor (5, 6, 7). The patients in question have high titers of rheumatoid factors and first patient has subcutaneous nodules. Symptoms include progressive dyspnea on exertion and a productive cough. The reported patients have productive cough and mild dyspnea on exertion.

Examination of affected patients can reveal an increased respiratory rate, clubbing, and crepitations particularly at the lung bases (8, 10).

Chest radiographs typically showed a reticulated pattern with progress to a fine nodularity and honeycomb fibrosis (11). The CXR of both patients showed widespread reticulated pattern (fibrosis) with some scattered honeycomb appearance in the first patient.

Therapeutic success depends on the amount of active inflammation or fibrosis present when treatment begins and also on availability of new proven effective treatment modalities (12).

Diffuse pulmonary fibrosis in patients with rheumatoid arthritis is in the absence of other known causes especially infective like Tuberculosis in our own environment is suggestive of rheumatoid lung. CXR is still the commonest means of diagnosis though recent reports have indicated that HRCT is more effective (13). This is however not available in our hospital. Lung biopsy is rarely indicated now. An evidence of erosive arthropathy is highly suggestive. Spirometry in rheumatoid lung can either be obstructive in the early phase or restrictive in the late phase as in the cases discussed. Gas transfer factor is diminished in rheumatoid lung except in those with alveolar haemorrhage. Protease inhibitor phenotype. HLA type, is also important. Rheumatoid lung is common in patients with HLA DRB1, those with PI MM protease inhibitor phenotype and those with tyrosine-phosphatase gene PTPN 22 (14, 15). Strongest susceptibility factor has been HLA DRBI*0404, however the marker for susceptibility to lung disease in rheumatoid arthritis is HLA B40 (14,15).

Medications typically given to patients with RA and interstitial fibrosis include corticosteroids, and other immune modulating agents such as sulfasalazine, hydroxychloroquine, cytotoxics like Azathioprim, cyclophosphamide, penicillamine and gold salts (5, 12, 16). Antibiotics are added to the treatment of patients with rheumatoid lung and chest infection. Patients with nodular lung needs repeated biopsies and monitoring of nodules for early detection.
of malignant transformation. Because of association of methotrexate with pulmonary fibrosis, patients with rheumatoid lung must not be given methotrexate (16).

New treatment strategies in rheumatoid arthritis: rheumatoid lung are targeted to interfere with critical inflammatory mediators like interleukin-1 beta and tumor necrosis factor α. Patients can be treated with intravenous TNF-α Inhibitor (infliximab). There is a reported sustained improvement in joint symptoms likewise (17, 18). Since April 2002, a recombinant human interleukin-1 receptor antagonist (Anakinra) is available in Germany (19).

Antioxidants such as selenium and Vitamin E as well as flavonoids can exhibit a novel anti-inflammatory action via the Complement-Neutrophils Activation Feedback (CNAF) mechanism (20). This may be better than immunosuppressives because the later increases the risk of life- threatening aspergillus infections (21).

The new treatment strategy was not administered in these patients because of non-availability.

Interstitial fibrosis is poor (22). Therapeutic success depends on the amount of active inflammation or fibrosis present at treatment initiation and also on the availability of new proven effective treatment modalities. The biologics- etanercept and rituximab, though available (2) were not used for the patients because they were not affordable to them.

CONCLUSION

This study highlights a pulmonary manifestation of rheumatoid arthritis namely interstitial fibrosis, the diagnosis which is made clinically.

It is also important for clinicians in the tropics particularly and world all over to keep an open mind when seeing patient with cough, not all cases are infective and due to tuberculosis. Connective tissue disorders are not common but definitely in existence and also affect blacks.

REFERENCES