Original Research Paper

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Pathology

HEMATOLOGIC MANIFESTATIONS OF RHEUMATOID ARTHRITIS IN A TERTIARY CARE HOSPITAL

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ABSTRACT Hematological manifestations of rheumatoid arthritis (RA) are very common. Blood dyscrasias and other hematological abnormalities are sometimes the first sign of rheumatic disease. In addition, novel anti-rheumatic biological agents may cause cytopenias. It is crucial that hematologists be aware of these presentations so that they are diagnosed and treated in a timely manner. A logical approach using easily available tests should allow straightforward decisions about diagnosis and therapy to be made, even in patients with some of the rarer hematological manifestations. An observational study was done in RA patients in a tertiary care hospital to study the prevalence and the type of hematologic manifestations from a pathologist's perspective. It was observed that anemia is the most common hematologic finding seen in RA, iron deficiency being the commonest cause of anemia, however hemolytic anemia was not seen. Leucocytosis was more common with predominant neutrophilia. Elevated platelet count, bicytopenia and pancytopenia were observed in RA along with raised ESR. Coagulation parameters were however within normal range. Bone marrow findings (where studied) included tuberculosis and plasma cell neoplasm. Summary: This study was conducted to estimate the proportion of patients with hematological abnormalities as the manifestation of RA and to study the nature of these various hematological problems, so that the empirical treatment can be started and also to inform the clinical rheumatologists about the common and rarer hematological manifestations of RA.

KEYWORDS : Hematology, Pathologist, Rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is the most common form of chronic inflammatory arthritis characterised by symmetric polyarthritis of unknown etiology. It is a systemic disease with extraarticular manifestations which includes fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis, and hematologic abnormalities.[1]

The common hematologic manifestations of RA is anemia of chronic disease (ACD). The anemia is predominantly therapy related particularly iron deficiency anemia (IDA) associated with chronic NSAID usage and direct bone marrow toxicity from DMARD therapy. Neutropenia is seen which is associated with Felty's syndrome , LGL syndrome and drug induced. Thrombocytopenia is related to autoimmune and drug induced etiology. Hematologic malignancy is also observed.[2]

METHODS

It was a retrospective study done in 63 cases of RA in a tertiary care hospital during the period of January 2018 to June 2019. CBC, complete blood picture evaluation, ESR and iron studies done in all the patients admitted to the department of Rheumatology with a clinical diagnosis of RA were included. Bone marrow examination and coagulation profile results(if done)were also retrieved.

After confirming homogenous distribution of data, it was entered using Microsoft Excel 2010 version and analysed. Data was summarized in percentages and proportions.

RESULTS

Out of 63 RA patients, 44 were female(69.84%)and 19 were male(30.15%),the female to male ratio being 2.3:1.

(I) RBCFINDINGS

Anemia was detected in 28 (44.44%) patients. The most common cause of anemia was iron deficiency seen in 16/28 (57.14%) patients followed by anemia of chronic disease seen in 12/28 (42.85%) patients. None of the patients had hemolysis as the cause of anemia.

(ii)WBCFINDINGS

WBC count abnormalities were seen in 21/63 (33.33%) patients of which 3/21 (14.28%) patients had leucopenia and 18/21 (85.71%) patients had leucocytosis. The most common abnormality was neutrophilia seen in 19/63 (30.15%) patients , followed by lymphopenia seen in 17/63 (26.98%) patients. 11/63 (17.46%) had lymphocytosis while the least common abnormality was neutropenia which was seen in 2/63 (3.17%) patients

(iii)PLATELET FINDINGS

Platelet abnormalities were seen in 23/63 (36.50%) patients of which increased platelet count was seen in 19/23 (82.60%) patients and thrombocytopenia was seen in 4/23(17.39%) patients. 8 patients showed increase in platelet count along with anemia while 11 patients had increase in platelet with normal hemoglobin.

SR.NO	PARAMETERS	LOW	NORMAL	HIGH	TOTAL
1	HEMOGLOBIN	28 (44.44%)	35 (55.55%)	00	63
2	TOTAL WBC	03 (4.76%)	42 (66.66%)	18 (28.57%)	63
3	LYMPHOCYTE	17 (26.98%)	35 (55.55%)	11 (17.46%)	63
4	NEUTROPHIL	02 (3.17%)	42 (66.66%)	19 (30.15%)	63
5	PLATELET	04 (6.34%)	40 (63.49%)	19 (30.15%)	63

(iv)BICYTOPENIA/ PANCYTOPENIA

In RA, 2 patients presented with bicytopenia and 1 with pancytopenia. Of these two, one patient had anemia and thrombocytopenia while other patient had leucopenia and thrombocytopenia. On further evaluation both had evidence of sepsis (raised procalcitonin). The patient with pancytopenia was further evaluated for bone marrow studies which showed hypocellular marrow with reduced cellularity, probably drug induced.

(v) COAGULATION FINDINGS

In RA, coagulation parameters were available in 10 patients (5 males and 5 females) of whom all patients had normal PT and aPTT.

(vi) ESR

59 (93.65%) patients had an elevated ESR while normal ESR was seen in 4 (6.34%) patients.

(vii)BONE MARROW FINDINGS

Bone marrow studies were done in 5 patients which had the following findings

- plasma cell neoplasm in one case
- necrotising epithelioid cell granulomas of Koch's aetiology (AFB positive) in one case
- hypoplastic marrow in one case
- reactive marrow hyperplasia in one case
- normal marrow with no significant findings in one case.

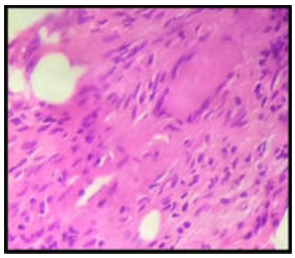

Image No. 1- Biopsy showing epithelioid cell granuloma (H&E x 40)

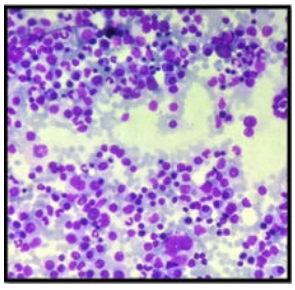

Image No. 2- Aspirate showing plasma cells(Leishman x 20)

DISCUSSION

Anemia was the most common hematologic manifestation present in 28 out of 63 patients (44.44%) . 16/28 (57%) patients had IDA while 12/28 (43%) patients had ACD. This was comparable with the study of Udayamma et al (2017) [3] who in her study of 50 RA patients found the most common hematologic manifestation as anemia seen in 60% of the patients. In her study IDA was more prevalent than ACD and was found in 33% of the anemic patients. In the study by Agrawal et al (2006) [4] anemia was present in 70.6% (151 out of 214) patients ,while in our study it was in 44.44%. They found ACD in 51.6% and IDA in 48.4% whereas in our present study IDA was more prevalent than ACD. In our study none of the patients had hemolytic anemia. This was comparable with the study of S. J. Bowman (2002) [2] where no direct association was found between hemolytic anemia and RA.

In this study 3 patients had leucopenia (14.28%) and 18 patients had leucocytosis (85.71%). Smyrnova V et al (2015) [5] in their study of 89 RA patients found that 13 (14.6%) patients had leucopenia, mainly caused by low lymphocytes level. This is comparable to our study. In our study lymphopenia was seen in 17 (80.95%) patients. 11 (52.38%) had lymphocytosis. This was comparable with the study of Fietta et al [6] who studied 66 patients of RA where lymphopenia has been observed in 15% (10/66) RA cases. Further studies on lymphopenia revealed marked reduction in T-cell numbers with normal circulating B-cell numbers. In our study there was no attempt to type the lymphocytes.

Thrombocytosis was seen in this study in 19 (82.60%) patients of whom 8 patients had anemia. Therefore the increased platelet count may be a reactive phenomenon in these 8 patients.[1] 11 patients had thrombocytosis without anemia (57%). This was comparable with the study of Hutchinson et al (1976) [7] who found thrombocytosis in 52% (39/75) RA patients. They stated highly significant relationship existed between the platelet count and disease severity and an inverse correlation with level of hemoglobin. However in the study by Udayamma et al [3] only 1 patient (2%) out of 50 was found to have thrombocytosis.

We found 2 patients of bicytopenia and 1 patient of pancytopenia probably related to immunosuppressive drugs. Fernando et al (2014) [7] found methotrexate induced cytopenia in their case report of a single patient.

No significant coagulation abnormality was seen in our study. This was comparable with the study of Conn D et al (1976) [8] who in their study of 41 RA patients found near normal partial thromboplastin time and prothrombin time.

93% of our patients had increased ESR. This is comparable to the studies of Vatulin et al (2015) [5] who in their study of 89 RA patients found an elevated ESR in all the patients and Prem Kumar et al (2014) [9] in his study of 346 patients of RA also found raised ESR in 305 (88%) patients. All our cases were in-patients with disease activity and 45% had anemia. Therefore corresponds to elevated ESR.

Of the 5 bone marrows available in RA, one patient had plasma cell neoplasm in our study. Similar finding was seen in the study by Agarwal V et al (2004) [10] who also reported one case of RA presenting with multiple myeloma. There is an increased risk of malignancy (Hodgkin's disease, non-Hodgkin lymphoma, leukaemia and MM) in RA independent of immunosuppressive therapy. IgA-λ light chain MM is reported more frequently however, MM of other immunoglobulin isotypes may occur. Increased exposure to radiation may predispose to MM. One patient had epitheloid granuloma of Koch's etiology. In the study done by Chong Hong et al (2016) [11] RA patients have 4-fold increased risk of TB disease as compared to general population. With the introduction of biological DMARDs and targeted DMARDs that act against the host defence immunities, the risk of TB disease is further increased. Bone marrow hypocellularity was seen in one case of the 5 cases. Abd El Hafez et al (2018) [12] also found 4 cases of hypocellular marrow of the 60 cases they studied. The comparison is not possible in our study due to the paucity of cases with bone marrow evaluation.

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