International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2017): 7.296

A 49 Years Old Woman with Disability Caused Byrheumatoid Arthritis Disease Progressivity: Case Report and Literature Review

Yoel Purnama[1], Cindy Christine[2], Sherly Desnita Savio[3]

[1, 2, 3]General Practitioner, RSUD Wangaya Denpasar, Bali-Indonesia

Abstract: ***Rheumatoid arthritis (RA) is a progressive inflammatory disease of unknown etiology, with a lifetime prevalence of up to 1% of world population. Onset peaks between 30 and 60 years old. RA can be marked by symmetrical peripheral polyarthritis which may lead to joint destruction and disability. Extra-articular manifestations include fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis, and hematologic abnormalities. The prognosis can be predicted based on clinical and laboratory evidences. New criteria for classification provides opportunity for earlier treatment. Initiation of early treatment of DMARDs is expected to prevent progressive and even change the natural course of RA.***

Keywords: Polyarthritis, Rheumatoid Arthritis

1. Introduction

Rheumatoid arthritis (RA) or rheumatoid disease is a chronic inflammatory origin and affects approximately 0.5% to 1% of the adult population worldwide, without distinction of races and being more common among females with 2-3:1 ratio. Interestingly, studies of RA from some of the Latin America and African countries show an even greater predominance of disease in females compared to males, with ratio of 6-8:1. Given this preponderance of females, various theories have been proposed to explain the possible role of estrogen in disease pathogenesis. Most of the theories center on the role of estrogens in enhancing the immune response like tumor necrosis factor α (TNF- α), a major cytokinein the pathogenesis of RA.[1,2]

This disease may start at any age, being more common from 30 to 60 years of age. To date, it has multifactorial etiology relating environmental, behavioral and genetic (HLA DDR4 and maybe DR1 in some populations) factors, immune unbalance and neuroendocrine changes. The genetic risk factors is the class II MHC haplotype of an individual. Single nucleotide polymorphisms (SNPs) in PTPN22 and PADI4 increase risk in some (but not all) racial and ethnic groups.[3-5]

RA is a systemic inflammatory disorder which may affect several tissues and organs, such as skin, blood vessels, heart, lungs and muscles, but it primarily affects joints producing inflammatory nonsuppurative synovitis which in general evolves to joint cartilage destruction and joint anchylosis.[1,2]

2. Case Report

A 49-year-old woman presented with pain, stiffness and deformity of the hand-wrist joints. Additional conditions included dyspepsia, gastroesophageal reflux (GERD), osteoarthritis of the hip, menopausal symptoms and hypertension. She was taking Mefenamic Acid 500mg three times a day, Captopril 25 mg three times a day, and Antacid three times a day.

She complained of nearly constant swelling, stiffness, and pain in her hands, wrists, elbows and hip joints. The pain and morning stiffness in her hands prolonged to around 1-2 hours and did not respond well to medications. She's had this disease since the last five years, beginning with mild symptoms, and been treated with NSAIDs in general clinic to relieve pain in her joints. She noticed a worsening of the symptoms by the inability to grasp and walk in the last 4 months.

At the visit, she reported her pain severity using Visual Analog Scale (VAS) as 6/10 (0= no pain; 10= greatest pain) and stated that the morning pain was frequently 4/10-6/10. Additional symptoms were fatigue, nausea and vomiting. She has had hypertension for the last 10 years. On physical examination, there was no swelling on the wrist joints; instead we found symmetrical deformities with contractures on the extensor side of both wrists **(Figure 1)**. Joint stiffness and tenderness to palpation of the metacarpophalangeal joint was present. The patient felt crepitation of the hip joints when she walked. There was no deformity found in knee examination.



Figure 1: Symmetrical deformities with contractures on the extensor side of both wrists

In laboratory investigation, the complete blood count (CBC) result was normal (WBC 3.41 x 10^3/uL, Haemoglobin 11.6 g/dL, Trombocyte 495 x 10^3/uL, Hematocrite 42.7%), ALT 187 U/LAST 178 U/L, BUN24 mg/dL SC0,8 mg/dL and Erythrocyte Sedimentation Rate (ESR) was found high (40mm/hour).Radiographic (X-ray) examination of the wrists showed severe destruction, joint narrowing and ero-

Licensed Under Creative Commons Attribution CC BY

sions of carpal bones **(Figure 2)**. X-Ray examination of the hips showed joint space narrowing, subchondral sclerosis, and osteophytes **(Figure 3)**.



Figure 2: Radiographic of the severe destruction, joint narrowing and erosions of carpal bones



Figure 3: Radiographic of the hips showed joint space narrowing, subchondral sclerosis, and osteophytes

The diagnosis of RA can be established based on anamnesis, clinical presentation, radiological investigation, and ACR criteria scoring system (diagnosis can be established with the score of more than 6). With these considerations, rheumatoid arthritis medication was given to this patient, including 5 mg of Prednison, twice a day; and 50 mg of Natrium diclofenac, twice a day.We then referred the patient to a hospital with more proper facilities in order to be given Disease-modifying antirheumatic drugs (DMARDs) therapy, rehabilitation, and further investigations.

3. Discussion

The delayed of diagnosis and absence of appropriate RA treatment can lead to joint destruction and disability. The primary target of the disease is the synovial membrane and tendon sheaths.Polymorphonuclear leukocytes engulf immune complex while extruding hydrolytic enzymes (such as cathepsin G, elastase, and collagenase) that can degrade proteoglycans and collagen of cartilage matrix, leading to joint destruction and chronic synovitis. Vascular proliferation andosteoclastic activity, most marked at the edges of thearticular surface, may contribute further to cartilagedestruction and periarticular bone erosion. [6-8]

The pathological changes in RA occur in 4 stages: [6,7]

1) Stage 1 – pre-clinical. Raised ESR, C-reactive protein (CRP) and RFmay be detectable years before the first diagnosis.
2) Stage 2 – synovitis. Early changes include vascular congestionwith new blood vessel formation, proliferation ofsynoviocytes and infiltration of the subsynovial layersby polymorphs, lymphocytes and plasma cells. Thereis thickening of the capsular structures, villous formationof the synovium and a cell-rich effusion into thejoints and tendon sheaths. In this stage, the disorder is potentially reversible.
3) Stage 3 – destruction. Persistent inflammation causesjoint and tendon destruction. Articular cartilage iserodedby proteolytic enzymes and by vasculartissue in the folds of the synovial reflections. Direct invasion of the cartilage by a pannusof granulation tissue creeping over the articularsurface also contributes. Pannus interferes with normal nutrition of articular cartilage from synovial fluid, and causes cartilage necrosis. Similar changes occur in tendon sheaths, causingtenosynovitis, invasion of the collagen bundles and,eventually, partial or complete rupture of tendons.
4) Stage 4 – deformity. The combination of articulardestruction, capsular stretching and tendon ruptureleads to progressive instability, subluxation, and dislocation. Granulation tissue is eventually replaced by fibrosis or scar formation, leading to joint contracture and deformity.

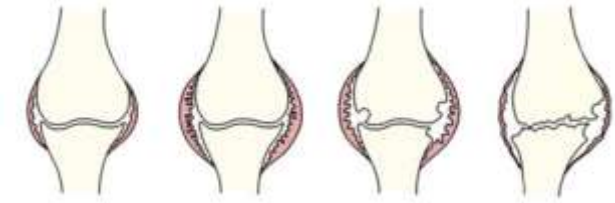


Figure 4: (a) Stage 1-pre-clinical. (b) Stage 2 – synovitis and joint swelling.(c) Stage 3 – early joint destruction with peri-articularerosions. (d) Stage 4 – advanced joint destruction anddeformity.[7]

Rheumatoid nodules can be found, consisting of a central necrotic zone surrounded by histiocytes and inflammatory granulation tissue. Nodules can occur under the skin, in the synovium, on tendons, in the sclera, and also viscera.[2] Around 30% of patients exhibit subcutaneous rheumatoid nodules, particularly in upper limbs.[6]Lymphadenopathy can happen in nearby or distant lymph nodes. Mild splenomegaly can also be found due to hyperactivity of the reticuloendothelial system. Vasculitis can be life-threatening, since it can lead to organ infarction. Muscle weakness occurs due to generalized myopathy or neuropathy. Visceral organs can be affected, including the lungs, heart, kidneys, gastrointestinal tract, and brain.[7]

Licensed Under Creative Commons Attribution CC BY

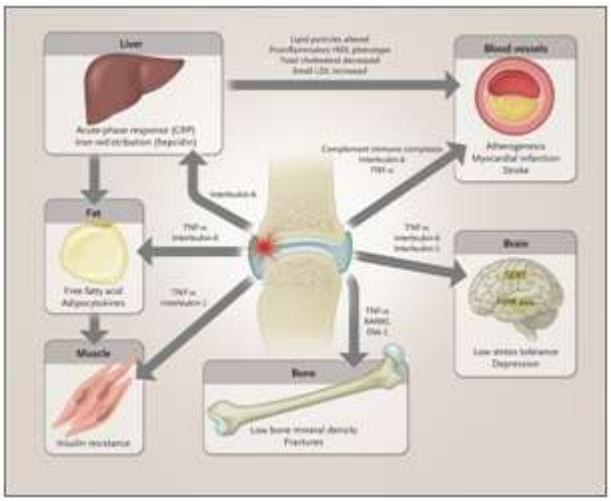


Figure 5: Pathogenesis of Rheumatoid Arthritis[9]

The diagnosis of RA can be made based on clinical manifestation, laboratory and radiographic changes modalities. Patient with RA typically present with pain and stiffness in multiple joints. The wrists, proximal interphalangeal joints, and metacarpophalangeal joints are most common involved. Morning stiffness can be lasting more than one hour suggests an inflammatory severity. Patient may also present with synovial thickening or synovitis that cac be palpable on joint examination. Sistemic symptoms of fatigue, weight loss, and low-grade fever may occur with active disease.[10,11]

New classification for RA (Table 2) have been made byAmerican College of Rheumatology in 2010. In this criteria, the presence of RA nodules or radiographic erosive changes are not included, which are less likely in early RA. The presence of symetric arthritis is not required, allowing for early asymetric presentation.[1,10,11]

Table 1: Classification Criteria Rheumatoid Arthritis[11]

		Score
Joint Involvement	1 large joint (shoulder, elbow, hip, knee, ankle)	0
	2-10 large joints	1
	1-3 small joint (MCP,PIP, thumb IP, MTP, wrists)	2
	4-10 small joints	3
	>10 joints (at least 1 small joint)	5
Serology	Negative RF and negative ACPA	0
	Low-positive RF or low-positive anti-CCP antibodies (≤3 times ULN)	2
	High positive or high-positive anti-CCP antibodies (≥3 times ULN)	3
Acute-phase Reactans	Normal CRP and normal ESR	0
	abnormal CRP and abnormal ESR	1
Duration of symptoms	<6 weeks	0
	≥ 6 weeks	1

Note: These criteria are aimed at classification of newly presenting patients who have at least one joint with definite clinical synovitis that is not better explained by another disease. A score of ≥ 6 fulfills requirements for definite RA. {ACPA, anti-citrullinated peptide antibodies; CCp, cyclic citrullinated peptides; CRP, C-reactive protein; E5R, erythrocyte sedimentation rate; IP, interphalangeal joint; MCp, metacarpophalangeal joint; MTp, metatarsophalangeal joint; Plp, proximal interphalangeal joint; RF. rheumatoid factor; ULN, upper limit of normal}. Source: D Aletaha et al: Arthritis Rheum 62:2569, 2010.

Autoimmune diseases such as RA are often characterized by the presence of autoantibodies. Rheumatoid factor is not specific for RA and may be present in patients with other diseases, such as hepatitis C, and in healthy older persons. Anti-citrullinated protein antibody is more specific for RA and may play a role in disease pathogenesis. Approximately 50 to 80 percent of persons with RA have rheumatoid factor, anti-citrullinated protein antibody, or both. Patients with RA may have a positive antinuclear antibody test, C-reactive protein levels and erythrocyte sedimentation. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are often icreased with active RA, and these acute phase reactants are part of the new RA classification criteria. CRP levels and ESR may also be used to follow evaluate the disease activity and response of the medication.[10,11]

The laboratory testing may help the physician to choose the optimal treatment for the patient (e.g., a patient with renal insufficiency or significant thrombocytopenia likely would not be prescribed a nonsteroidal antiinflammatory drug [NSAID]). Mild anemia of chronic disease occurs in 33 to 60 percent of all patients with RA. although gastrointestinal blood loss should also be considered in patients taking corticosteroids or NSAIDs. Methotrexate is contraindicated in patients with hepatic disease, such as hepatitis C, and in patients with significant renal impairment. Biologic therapy, such as a TNF inhibitor, requires a negative tuberculin test or treatment for latent tuberculosis. Hepatitis B reactivation can also occur with TNF inhibitor use.[10,11]

Radiological examination suchasX-ray remains the first choice for imaging in RA. Hands, wrists, knees, feet, elbows, shoulders, hips, and cervical spine should be assessed with radiography when indicated. X-ray done in early phase of the disease shows the features of synovitis, including periarticular soft-tissue swelling and joint effusion. Subsequently, regional osteoporosis, osteolytic erosions of subchondral bone, and joint space narrowing become more apparent. In advanced disease,articular destruction and joint deformity are obvious. Subluxation, dislocation, and bony ankyloses are the features of late and advanced RA.[6-8]



Figure 6: Radiographic changes in RA: (1) periarticular osteoporosis and soft tissue swelling. (2) Juxta-articular erosions. (3) Joint instability and deformity.[7]

Ultrasonographycan also be used to identify soft-tissue changes and earlyerosions within joints. Even though it is not yet the standard of care in patients with RA, ultrasound

Licensed Under Creative Commons Attribution CC BY

can be useful to detect thepresence of synovitis and early erosions. Additionalinformation on vascularity can be obtained with Doppler techniques. [2,3]Magnetic Resonance Imaging (MRI) offers earlier and more accurate assessment of joints than plain X-ray. MRI is used primarily in patients with abnormalities of the cervical spine.[7,8,12]

Several disorders of polyarthritis need to be differentiated from RA.Polyarticular osteoarthritis (OA) affecting finger joints may look similar to RA. The difference is that OA involves the distal interphalangealjoints and causes a nodular arthritis with radiologicallyobvious osteophytes, whereas RA affects the proximaljoints of the hand (wrist and MCP joints) and shows erosivefeatures in radiological examinations. The joint pain from osteoarthritis is also characteristically relieved by rest.[7,8]Polyarticular goutcan also be mistaken for rheumatoidarthritis. The diagnosis is made by identifying typical birefringent urate crystalsin the joint fluid or a nodular tophus.[7]Calcium pyrophosphate deposition disease affectslarge joints, but it may occur in the wrist and metacarpophalangeal joints as well. Crystals may be identified in synovialfluid or synovium.[7]Seronegative inflammatory polyarthritis likePsoriaticarthritis, Still's disease, systemic lupus erythematosusand other connective-tissue diseases have the feature of polyarthritis and need to be differentiated from RA.[7,8]Pyogenic arthritis is also can be presented like RA condition. It has the characteristic of fever and the causative organism can also be found in joint fluid examination.[8]

After RA has been diagnosed and an initial evaluation performed, treatment should begin. Recent guidelines have addressed the management of RA, but patient preference also plays an important role. There are special considerations for women of childbearing age because many medications have deleterious effects on pregnancy. Goals of therapy include minimizing joint pain and swelling, preventing deformity (such as ulnar deviation) and radiographic damage (such as erosions), maintaining quality of life (personal and work), and controlling extra-articular manifestations. Disease-modifying antirheumatic drugs (DMARDs) are the mainstay of RA therapy.[10,13,14]

DMARDs can be biologic or nonbiologic. Biologic agents include monoclonal antibodies and recombinant receptors to block cytokines that promote the inflammatory cascade responsible for RA symptoms. Methotrexate is recommended as the first- line treatment in patients with active RA, unless contraindicated or not tolerated. Leflunomide (Arava) may be used as an alternative to methotrexate, although gastrointestinal adverse effects are more common. Sulfasalazine (Azulfidine) or hydroxychloroquine (Plaquenil) is recommended as monotherapy in patients with low disease activity or without poor prognostic features (e.g., seronegative, nonerosive RA).[10,14]

Combination therapy with two or more DMARDs is more effective than monotherapy; however, adverse effects may also be greater. If RA is not well controlled with a nonbiologic DMARD, a biologic DMARD should be initiated. TNF inhibitors are the first-line biologic therapy and are the most studied of these agents. If TNF inhibitors are ineffective, additional biologic therapies can be considered. Simultaneous use of more than one biologic therapy (e.g., adalimumab and abatacept) is not recommended because of an unacceptable rate of adverse effects.[10,13,14]

Drug therapy for RA may involve NSAIDs and oral, intramuscular, or intra-articular corticosteroids for controlling pain and inflammation. Ideally, NSAIDs and corticosteroids are used only for short-term management. DMARDs are the preferred therapy.[10]

Remission is obtainable in 10 to 50 percent of patients with RA, depending on how remission is defined and the intensity of therapy. Remission is more likely in males, nonsmokers, persons younger than 40 years, and in those with late-onset disease (patients older than 65 years), with shorter duration of disease, with milder disease activity, without elevated acute phase reactants, and without positive rheumatoid factor or anticitrullinated protein antibody findings. After the disease is controlled, medication dosages may be cautiously decreased to the minimum amount necessary. Patients will require frequent monitoring to ensure stable symptoms, and prompt increase in medication is recommended with disease flare-ups.[10,13,14]

The purpose of surgical management is to achieve pain relief, deformity correction, and functional improvement.[3] In early progression of the disease, surgical management mainly consists of soft tissue procedures, such as synovectomy, tendon repair or replacement, and joint stabilization. In late rheumatoid disease, arthrodesis, osteotomy, and arthroplasty can be considered for patients with severe joint destruction, fixed deformity, and loss of function. Besides surgical management, occupational therapy, mechanical aids, and adjustments to home environment also play important roles in increasing patients' quality of life.[6,7]

In this patient the risk factors of RA include female and age between 30-60 years old. The symptoms found in this patient represented typical symptoms of RA, including swelling, stiffness, and pain in her hands, wrists, elbows and hip joints. The morning stiffness in her hands prolonged to around 1-2 hours. The American College of Rheumatology's (ACR) 2010 criteria was used to assess patient's condition **(Table 1)**; involvement of more than 10 small joints (score of 5) was found, along with the duration of more than 6 months of joint pain (score of 1) and the elevation of ESR or CRP (score of 1). Serological examination was not done due to the limitation of resources.

Table 2: ACR 2010 Criteria application from this patient's condition

		Score
Joint Involvement	>10 joint	5
Serology	-	0
Acute-phase Reactans	Abnormal ESR	1
Duration of symptoms	>6 weeks	1
Total Score		**7**

Note: A score of $\geq$ 6 fulfills requirements for definite RA.

The pathological changes found through radiological examination show deformity and destruction of both wrist joints, relevant to stage 4 RA. In this case, the main therapy of

Licensed Under Creative Commons Attribution CC BY

DMARDs was not available in our hospital. Therefore, the therapy given was corticosteroid and NSAID as temporary symptomatic management.

In this patient, late diagnosis and therapy caused progressive inflammation that leads to permanent deformity and disability. As the aim of RA treatment is mainly to prevent progressivity, this aspect may lower patient's outcome to conservative treatments, such as DMARDs and rehabilitation. The combination of DMARDs therapy may be considered. Surgical intervention might also be needed to repair the deformity and to restore the functionality of the joints.

4. Conclusion

A 49-years old female patient was presented in this case report, with the symptoms of swelling, prolonged stiffness, and pain in her hands, wrists, elbows and hip joints for the last five years. There was elevation of ESR and X-ray shows bone destruction and deformity of both wrist joints. Total score using ACR 2010 criteria is 7, fulfilling the requirements for the diagnosis of definite RA. The patient was treated with corticosteroid and NSAID initially, then referred to a hospital with more proper facilities to get DMARDs therapy. Surgical intervention should be considered to improve patient's quality of life.

References

[1] Heidari B. Rheumatoid Arthritis: Early diagnosis and treatment outcomes. Caspian journal of internal medicine. 2011;2(1):161.
[2] Fauci AS, Langford CA, Langford C. Harrison's Rheumatology, 3E. McGraw-Hill Publishing; 2013 Mar 22.
[3] Okada Y, Wu D, Trynka G, Raj T, Terao C, Ikari K, Kochi Y, Ohmura K, Suzuki A, Yoshida S, Graham RR. Genetics of rheumatoid arthritis contributes to biology and drug discovery. Nature. 2014 Feb;506(7488):376.
[4] Firestein GS, Zvaifler NJ. How important are T cells in chronic rheumatoid synovitis?: II. T cell-independent mechanisms from beginning to end. Arthritis & Rheumatism. 2002 Feb;46(2):298-308.
[5] Firestein GS, Budd R, Gabriel SE, McInnes IB, O'Dell JR. Kelley and Firestein's Textbook of Rheumatology E-Book. Elsevier Health Sciences; 2016 Jun 21.
[6] Salter RB. Textbook of disorders and injuries of the musculoskeletal system. Maryland: Lippincott Williams & Wilkins;1999. p.233-5.
[7] Solomon S, Warwick D, Nagayam S. Apley's system of orthopaedics and fracture. 5th ed. London: Hodder Arnold; 2010. p. 59-66.
[8] Smith HR. Rheumatoid arthritis treatment & management [Internet]. Medscape. 2018 [cited 2018 Jul 8]. Available from:https://emedicine.medscape.com/article/331715-overview
[9] McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med. 2011 Dec; 365(23): 2205-19. doi: 10.1056/NEJMra1004965
[10] Wasserman AM. Diagnosis and management of rheumatoid arthritis. American family physician. 2011 Dec 1;84(11):1245.
[11] Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham III CO, Birnbaum NS, Burmester GR, Bykerk VP, Cohen MD, Combe B. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis & Rheumatism. 2010 Sep;62(9):2569-81.
[12] Singh JA, Saag KG, Bridges Jr SL, Akl EA, Bannuru RR, Sullivan MC, Vaysbrot E, McNaughton C, Osani M, Shmerling RH, Curtis JR. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis & rheumatology. 2016 Jan;68(1):1-26.
[13] Singh JA, Saag KG, Bridges Jr SL, Akl EA, Bannuru RR, Sullivan MC, Vaysbrot E, McNaughton C, Osani M, Shmerling RH, Curtis JR. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis & rheumatology. 2016 Jan;68(1):1-26.
[14] Bijlsma JW, Welsing PM, Woodworth TG, Middelink LM, Pethö-Schramm A, Bernasconi C, Borm ME, Wortel CH, Ter Borg EJ, Jahangier ZN, van der Laan WH. Early rheumatoid arthritis treated with tocilizumab, methotrexate, or their combination (U-Act-Early): a multicentre, randomised, double-blind, double-dummy, strategy trial. The Lancet. 2016 Jul 23;388(10042):343-55.

Licensed Under Creative Commons Attribution CC BY