

## CASE REPORT

# The Difficult Rheumatology Diagnosis

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### OPEN ACCESS

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### ABSTRACT

**BACKGROUND:** Rheumatoid arthritis is a devastating condition. More so, the diagnosis of seronegative rheumatoid arthritis is often fraught off with much uncertainty and that leads to further suffering to the unfortunate patient.

**CASE DETAILS:** This is a case of Madam A, who presented with many non-specific symptoms and signs involving many systems which was finally diagnosed as seronegative rheumatoid arthritis. This case explores the challenges in reaching this uncommon diagnosis and how anti-inflammatory drugs can bring a miraculous relief to the patient's suffering.

**CONCLUSION:** The diagnosis of seronegative rheumatoid arthritis often presents a real challenge to the medical practitioner and often requires multiple visits and/or shared multidisciplinary care for confirmation of the diagnosis. Once diagnosed and treated with disease modifying anti-rheumatic drugs, often there is a miraculous relief to the patient's suffering.

**KEYWORDS:** Seronegative, rheumatoid arthritis, prednisolone, DMARD

### INTRODUCTION

The diagnosis of rheumatoid arthritis (RA) often depends on the constellation of clinical signs and symptoms based on the 2010 American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) classification (1). In this scoring definition, patients are diagnosed with definite RA if they achieve a score of  $\geq 6/10$ . However, in this scoring system, the score allocated to a positive Rheumatoid Factor (RF) is up to 3. This means patients who have seronegative RF may miss the boat for this diagnosis, thereby leading to a delay in diagnosis that will lead to progression of this devastating disorder and persistent in suffering of the patient. This brings us to a case of a 52 years old postmenopausal woman who presented with many atypical and anguishing symptoms and signs involving many body systems. After much delay, the diagnosis of seronegative RA was finally reached which allowed for subsequent miraculous treatment to be initiated on her that brought much respite to her.

### CASE REPORT

Madam A is a 52 years old woman who presented to the primary care clinic with history of intermittent chest discomfort and dyspnoea on exertion for three months associated with fatigue, anorexia, fever, intermittent bilateral leg swelling, occasional neck, shoulder, lower back and hipjoint pain. There was no paroxysmal nocturnal dyspnea, orthopnea or significant menopausal symptoms. There were occasional and worsening bilateral hand pain and swelling for the past two years. There was no morning stiffness.

On physical examination, the vital signs were normal. Systemic examination was also unremarkable. On joint examination, synovitis of the left wrist, proximal interphalangeal joints and metacarpophalangeal joints of the left index and middle finger was noted. There was also synovitis of the right ankle and tenderness over the right sacroiliac and right shoulder joints. There were no oral ulcers, alopecia or nail changes.

Initial investigation done previously at a general practitioner clinic showed normochromic normocytic anaemia with haemoglobin of 10.5 g/dL, normal fasting glucose, renal, thyroid and liver function tests, raised low density lipoprotein cholesterol (LDL-C) of 3.6 mmol/L, elevated high sensitivity C-Reactive Protein (hsCRP) of 29, and normal RF titer of only 4. For this visit, she was treated symptomatically with analgesics and given another appointment to two weeks where further investigations were ordered.

At her follow-up investigations showed a raised erythrocyte sedimentation rate (ESR) of 65 mm/hr with otherwise normal peripheral blood smear and connective tissue screening. Echocardiogram and electrocardiogram were also normal. Her Framingham Risk Score was only 5.3%. There was some diagnostic dilemma at this moment as even though she demonstrated symptoms suggestive of possible RA or polymyalgia rheumatica, the connective tissue screening was normal except for raised ESR. She scored 5/10 on the ACR-EULAR classification for RA. After discussion with a senior rheumatologist, diagnosis of seronegative RA was made which was confirmed on her subsequent visit to the rheumatology clinic two weeks later where X-rays of the hand and the feet showed early soft tissue swelling, periarticular erosion and joint space narrowing. She experienced tremendous improvement in her symptoms once Methotrexate 7.5 mg weekly was added to her oral prednisolone of 5mg daily at her second rheumatology clinic visit.

She is still under follow-up at both the primary care and rheumatology clinic to manage both her RA and hyperlipidaemia. At her latest follow-up after being diagnosed with seronegative RA for which two long years have passed, she was still on methotrexate 2.5mg weekly with hydroxychloroquine 200mg daily, which has rendered her virtually asymptomatic and able to carry on with her life without much interruptions.

## DISCUSSION

This case presented a huge diagnostic dilemma due to the many non-specific symptoms and signs that the

patient had. The only saving grace was the presence of joint symptoms which was also only intermittent. Investigation results further added to the diagnostic confusion, save for perhaps raised ESR and CRP.

Through multidisciplinary shared care with the rheumatology team, the uncommon and deceptive diagnosis of seronegative RA was reached. Subsequent treatment with oral prednisolone and later on with disease modifying anti-rheumatic drugs managed to relieve the patient of her sufferings.

The classical serological tests, RF and anti-cyclic citrullinated peptide (anti-CCP) may only be positive in 65% of cases of RA (2). This will adversely affect the diagnosis of RA when using the gold standard 2010 ACR-EULAR RA classification.

The diagnosis of seronegative RA, however, can be reached if patients are still able to demonstrate strong joint symptoms including pain, swelling and stiffness (3). Additional helpful findings include symmetrical polyarthritis, classic X-ray features and raised inflammatory markers. Seronegative RF implies that there are low levels of antibodies that is unable to warrant a seropositive response normally seen in RA (3).

DMARD treatment should be started as soon as possible to prevent the joints erosion that will lead to further disability in RA (4). In the absence of a positive RF, elevated CRP and joint changes including synovitis may be used as prognostic factors in RA (4).

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