A challenging case of rheumatoid arthritis-associated aortitis presenting with erythema nodosum after ST-segment elevation myocardial infarction: A case report

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Abstract
Rheumatoid arthritis is a systemic inflammatory disease that has many extra-articular manifestations. Cardiovascular involvement, including coronary vasculitis and aortitis and skin lesion of erythema nodosum are uncommon findings of patients with rheumatoid arthritis, and thus, it is challenging for diagnosis of this case from those unusual extra-articular presentation.

KEYWORDS
aortitis, erythema nodosum, myocardial infarction, rheumatoid arthritis, vasculitis

1 | INTRODUCTION

Erythema nodosum (EN) is a septal panniculitis that is a reactive process to various underlying etiologies, such as infections, inflammation, neoplasms, and medications. Coronary vasculitis is a rare cause of acute myocardial infarction and can be the first presentation of rheumatoid arthritis (RA). Here, we report an unusual case of RA associated with chronic aortitis presented with prolonged fever and EN after ST-segment elevation myocardial infarction (STEMI).

2 | CASE REPORT/CASE PRESENTATION

A 67-year-old Thai woman without an underlying condition presented with STEMI of the anterior wall. Coronary angiography revealed double vessel coronary artery disease with thrombotic occlusion at the mid part of the left anterior descending artery, Figure 1. She received percutaneous coronary intervention with drug-eluting stents at that occluded coronary artery. She experienced a prolonged fever that ranged between 37.8 and 39°C and...
chronic abdominal pain for 2 months since then. She was admitted to our hospital for further investigation. Fatigue, loss of appetite, and significant weight loss were also reported. Multiple painful skin nodules were found on her shins a week later. The patient was asked and only noted polyarthralgia and morning stiffness in her wrist joints for 1 year. Her current medication included baby aspirin, ticagrelor, omeprazole, enalapril, and carvedilol. She denied food and drug allergy, taking over-the-counter medication, antibiotics, oral contraceptive pills, and herbs.

On physical examination, the patient had bilateral symmetrical tender, non-ulcerative erythematous, warm nodules on the anterior part of both lower legs and left forearm, as shown in Figure 2. There was synovial thickening at both wrist joints and no signs of inflammation. The rest of a thorough multisystem examination was not remarkable. A 12-lead electrocardiogram recorded on admission showed sinus rhythm with a heart rate of 100 beats per minute, significant Q waves and inverted T waves in the V1-4 Chest leads. Transthoracic echocardiography demonstrated severe left ventricular systolic dysfunction (left ventricular ejection fraction 32%) with hypokinesia of the anterior wall, minimal pericardial effusion, and no vegetation. Septic examination did not show obvious sources of infection. Empirical antibiotic therapy with ceftriaxone and doxycycline and followed by carbapenem was prescribed. The fever was persistently high, and therefore, a skin biopsy was performed from one nodule on right shin, which showed chronic inflammatory cells, consisting of lymphocytes and histiocytes, infiltrating into the thickened fibrous septum of the subcutaneous tissue, when the epidermis and dermis were not noticeable as shown in Figure 3. Histological findings were consistent with the clinical diagnosis of EN. No organism was found and all cultures from skin tissue were negative.

To demonstrate the causes of EN, complete blood count showed leukocytosis (white blood cells 11,200/mm³), thrombocytosis (platelets counts 508,000/mm³), but abnormal white blood cells were not found. Bacterial
and fungal blood culture did not reveal growth. The polymerase chain reaction tests of the sputum and skin tissue for mycobacterium were negative. Serologic tests for hepatitis B and C were not detectable. Antinuclear antibodies, anti-DNase B, and anti-Streptolysin O tests were all in the normal range. Chest radiograph was normal. C-reactive protein levels of 105 mg/L (reference range: <5.00 mg/L), erythrocyte sedimentation rate >120 mm/h.

The main diagnostic hypothesis of EN in this case is rheumatoid arthritis. Further film X-rays of both hands were performed which showed bilateral juxta-articular osteopenia with narrowing carpal joint spaces at both wrists and soft tissue swelling (Figure 4). The rheumatoid factor was 9 IU/ml (reference range: <8 IU/ml) while the cyclic citrullinated peptide IgG test was negative at a level of 0.7 (reference range: 0.0–5.0 U/ml). Behçet’s and inflammatory bowel disease should be considered in the patients with EN who have arthritis; however, other characteristic features, that is, oral or genital ulcers, pyoderma gangrenosum and gastrointestinal symptoms of diarrhea were not found.2

To investigate the chronic abdominal pain, computed tomography of the chest and entire abdomen demonstrated surrounding soft tissue thickening and periaortic fat stranding without contrast extravasation around the abdominal aorta which is compatible for aortitis, as shown in Figure 5. While the major causes of aortitis are non-infectious, especially large-vessel vasculitis, the possibility of an infectious cause must be considered in which the serologic tests of treponemal, melioidosis, and salmonella showed all negative. This led large-vessel vasculitis to be considered as her cause of abdominal pain. Furthermore, late-onset RA, and giant cell arteritis may appear simultaneously or consecutively in elderly,3 but the characteristic findings of temporal arteritis include headache, jaw claudication, and visual loss were not seen. Thus, giant cell arteritis was excluded, and the final diagnosis of elderly-onset rheumatoid arthritis-associated aortitis was made.

The patient received intravenous dexamethasone 16 mg a day, hydroxychloroquine 200 mg per day and methotrexate 10 mg per week. Fever subsided within 48 h and other constitutional symptoms improved within 5 days. The EN was resolved with a saturated solution of potassium iodide 450 mg per day for 3 weeks. Her joint symptoms and abdominal pain were improved within a month after treatment. The erythrocyte sedimentation rate and the C-reactive protein also returned to normal.

3 | DISCUSSION/CONCLUSION

We report an unusual presentation of RA associated with aortitis. Both EN and STEMI are rare findings in RA, but both found in this case.

Erythema nodosum is a septal panniculitis that is a reactive process to various underlying etiologies such as infections, pregnancy, drugs, malignancy, and other systemic diseases.2,4,5 Streptococcal infection, primary tuberculosis, sarcoidosis, Behçet’s disease, medication, inflammatory bowel disease, and pregnancy were reported as common causes of EN.6 Skin manifestation is prevalent in RA patients, of which the rheumatoid nodule is reported to be the most common cutaneous expression. Accelerated rheumatoid nodulosis, granulomatous dermatoses, neutrophilic dermatoses, rheumatoid vasculitis, and pyoderma gangrenosum are all listed in association with RA.7 The association of EN with RA8 is relatively rare, and thus, it is quite challenging for diagnosis of this case after excluding other more common etiologies of EN, especially infection, such as tuberculosis, streptococcal infection, leprosy (in migrant workers), and viral hepatitis B.
Rheumatoid arthritis is a systemic inflammatory disease that has many extra-articular manifestations. Cardiac involvement in RA is not uncommon and can include pericarditis, cardiomyopathy, valvular disease, myocarditis, arrhythmia, stroke, congestive heart failure, peripheral arterial disease, aortic dissection, and coronary complications of stenosis, thrombosis, or aneurysm. Patients with RA can have coronary arteritis and impaired intrinsic endothelial function, which can lead to premature atherosclerosis, risk of myocardial infarction, and sudden cardiac death. Pericardial effusion is the most common cardiac involvement in RA which was also found in this case. Previous studies reported that it is less found (<10%) in patients with severe RA.

Coronary arteritis is seldom diagnosed during a patient’s lifetime. The prevalence of coronary arteritis among patients suffering from systemic vasculitis is largely unknown, and it is found more frequently at autopsy up to 20%. Patients with coronary arteritis can present acute coronary syndrome (ACS) and need emergent coronary reperfusion, and thus, sometimes it is not possible to investigate systemic vasculitis before. Her symptoms of active RA for a year, constitutional symptoms, associated aortitis, and persistently unexplainable high elevation of inflammatory markers (erythrocyte sedimentation rate and C-reactive protein) led us to suspect rheumatoid coronary arteritis as a possible cause of STEMI. We could not prove by histology or using intravascular ultrasound during coronary angiography. However, the thrombotic occlusion of left anterior descending coronary artery without evidence of any other stenosis in this vessel can reflect coronary arteritis.

Rheumatoid arthritis behaves as an accelerator for CAD. Patients with RA are at a twofold increased risk of myocardial infarction and stroke and up to 40% of all deaths in patients with RA are due to cardiovascular disease. The prevalence of lifetime myocardial infarction was 3.2%, when patients with RA and ACS presented with STEMI at the coronary intensive care unit was 35.3%. In addition, clinically significant coronary artery disease may be secondary to accelerated atherosclerosis from chronic rather than active inflammation of the arterial wall.

Furthermore, aortitis can be a manifestation of severe RA and is an isolated RA characteristic, with no other features of vasculitis. RA-associated aortitis is a rare entity. Small and medium vessel vasculitis are more commonly affected. However, RA is one of the causes to be considered in inflammatory aortitis. Laboratory investigation to rule out infectious causes of aortitis such as syphilis, tuberculosis, salmonellla were all negative and the clinical presentation of other autoimmune disease was less likely in this patient, therefore RA is the best explanation for aortitis in this patient. The clinical presentation of aortitis can vary from acute aortic syndrome, systemic inflammatory syndrome, thrombosis, pulse deficit, hypertension, abdominal, and back pain. It seems likely that the abdominal pain was the sole presentation of the aortitis in this hemodynamically stable patient. Fever, abdominal pain, and EN all resolved after treatment of RA suggesting that they were all parts of the same inflammatory disease.

The present case report demonstrates an unusual and complex presentation of rheumatoid arthritis. Physicians must be aware of not only erythema nodosum, but also all potentially serious extra-articular manifestations including coronary arteritis and aortitis.

**AUTHOR CONTRIBUTIONS**
Siripat Kaewnamchai and Bhakinai Temnithikul conceived and analyzed the case report. Siripat Kaewnamchai drafted the manuscript. Bhakinai Temnithikul and Teeranan Angkananard drafted and revised the manuscript.
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CONFLICT OF INTEREST
The authors declare that there is no conflict of interest regarding the publication of this article.

DATA AVAILABILITY STATEMENT
All data used during the current report are presented in the manuscript or available from the corresponding author on reasonable request.

ETHICAL APPROVAL
The study protocol conformed to the World Medical Association Declaration of Helsinki and is exempt from ethics committee approval as per the guideline of Srinakharinwirot University given that it is a case report, and informed consent was already obtained.

CONSENT
Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy.

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