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### Tuberculosis Arthritis Genu Sinistra with Drug-Induced Liver Injury, COVID 19 Confirmed

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#### ABSTRACT

**Background.** Tuberculosis is still a significant health problem, especially in developing countries. Although pulmonary tuberculosis is the most common form of the disease, extrapulmonary tuberculosis also contributes significantly to morbidity and mortality. 10-15% of extrapulmonary cases are due to tuberculous arthritis. The following is a case report of a 36-year-old woman with a diagnosis of genu Sinistra tuberculosis arthritis and drug-induced hepatotoxic injury due to OAT.

**Case presentation.** A woman, 36 years old, Muslim, addresses Banyuasin. The patient is a housewife, treated at Dr. Moh Hoesin General Hospital since October 11, 2021. The main complaint in the form of pain in the left knee has been getting worse since 1 week before being admitted to the hospital. 4 months before admission to the hospital, the patient complained of left knee pain, the pain felt like being stabbed, coming and going, especially when walking. In this patient, there was a complaint of nausea that was felt in the pit of the stomach. The results of laboratory examinations showed an increase in the transaminase enzyme and hyperuricemia, so it was suspected that the patient had DILI due to OAT drugs. Hepatocyte death in DILI can occur through two processes, namely processes mediated by apoptosis or necrosis. In apoptosis, cell shrinkage and fragmentation occur into small pieces with the cell membrane intact. These fragments are cleared by phagocytosis and generally do not stimulate the host immune response.

**Conclusion.** A patient diagnosed with arthritis tuberculosis genu Sinistra with Drug-Induced Liver Injury and Confirmed COVID 19.

#### 7 1. Introduction

Tuberculosis is still a significant health problem, especially in developing countries. Although pulmonary tuberculosis is the most common form of the disease, extrapulmonary tuberculosis also contributes significantly to morbidity and mortality. 10-15% of extrapulmonary cases are due to tuberculous arthritis.<sup>1</sup> The spread of tuberculosis germs to bone

structures can be through several ways, namely through blood vessels, through the lymphatic pathway, and the percontinuitatum pathway. Vascular (hematogenous) and percontinuous pathways are common pathogenesis pathways in tuberculous arthritis, whereas lymphatic pathways are rare in this condition. The diagnosis of tuberculous arthritis is

usually delayed because the possibility of tuberculosis is often overlooked in the differential diagnosis of joint disease. In addition, the classic constitutional symptoms of tuberculosis such as fever, night sweats, and weight gain are usually absent in patients with tuberculous arthritis, accounting for only 20-30% of cases. This disease involves large joints, especially the hip, knee, and ankle joints. In tuberculous arthritis, the course of the disease is slow, chronic and usually only affects one joint, and there is a decrease in joint function that interferes with activity.<sup>1,2</sup> The supporting examinations that can be performed are imaging, microscopic examination, biopsy, and culture. Microscopic examination is the fastest examination but is not sensitive, only 10-30% of cases have a positive smear. A biopsy is the gold standard examination in tuberculous arthritis.<sup>3</sup> The following is a case report of a 36-year-old woman with a diagnosis of genu Sinistra tuberculous arthritis and drug-induced hepatotoxic injury due to OAT. This case was appointed because it is rarely found and the diagnosis requires high clinical suspicion so that it can be used as a lesson in how to make a diagnosis, appropriate treatment, and know the prognosis in this patient so that it can be useful for the patient and all of us.

## 2. Case Presentation

A woman, 36 years old, Muslim, addresses Banyuasin. The patient is a housewife, treated at Dr. Moh Hoesin General Hospital since October 11, 2021. The main complaint in the form of pain in the left knee has been getting worse since 1 week before being admitted to the hospital. 4 months before admission the hospital, the patient complained of left knee pain, the pain felt like being stabbed, coming and going, especially when walking. Swollen knee joint, redness, feeling warm and stiff in the morning is absent. Fever, cough, weight loss, night sweats, and decreased appetite are absent. Hair loss, red face, and getting redder when exposed to the sun and often canker sores are absent. A history of falls and trauma to the knee

was denied. The patient has not been treated, only bought painkillers at the pharmacy, the complaints are slightly reduced.

1 month before admission, the patient complained of knee pain getting worse than before. Knee feels an enlarged, palpable lump, and pain like being pricked. The patient has difficulty exercising. There is redness and warmth in the knee. Fever is present, the temperature is not measured, and is relieved by fever-reducing medication. Decreased appetite accompanied by weight loss is present, the patient feels through his slightly loosened clothes. The patient then went to a clinic in the Sembawa area and was said to have arthritis. The patient was given painkillers and antibiotics. The patient forgot the name of the medicine, the complaints did not decrease.

1 week before admission, the patient complained of pain in the knee that was getting worse than before. The knee feels increasingly enlarged, the patient cannot bend the leg, the pain is like being stabbed. The patient is no longer able to work at home. The patient went to the Internal Medicine Rheumatology Polyclinic and was taken from the joint fluid. The fluid was found to be ± 30 cc, yellowish-green in color, and odorless. Then, the patient is advised to be hospitalized.

General condition looks very ill, sensorium compos mentis, blood pressure 124/86 mmHg, pulse 92 beats/minute, regular, adequate content and voltage, respiration rate 22 times/minute, temperature 36.3 C, numeric rating scale (NRS) 5, height 158 cm, weight 60 kg, body mass index 24.09 kg/m<sup>2</sup>, normal weight. Examination of the head, neck, thorax, abdomen within normal limits. Examination of the extremities in the left genu region looks swollen, there is tenderness, limited active-passive range of movement (ROM), there is a balloon sign. On laboratory investigations, it was found that the leukocyte value was increased by 13.070/mm<sup>3</sup>, the neutrophil value increased by 74% and the lymphocyte decrease was 17%, and the quantitative CRP value increased to 97 mg/L.



Figure 1. Regio genu sinistra

In this case, because the primary diagnosis of tuberculous arthritis had not been established initially, antibiotics could be given temporarily while waiting for the test results because based on epidemiology, the bacterial cause was found to be the highest. Delay in giving antibiotics can cause germs to rapidly multiply and will cause permanent damage to joint cartilage, causing hematogenous spread and ultimately leading to sepsis which can lead to death. Another thing to do is to perform a synovial fluid puncture/aspiration to remove as much pus as possible. If aspiration fails, surgical drainage is necessary. In giving antibiotics, several things need to be considered such as the severity of the disease, the age of the patient, the pattern of germs in the hospital concerned, as well as existing risk factors, such as rheumatoid arthritis, SLE, intravenous drug abuse, receiving immunosuppressive drugs or an immunocompromised state. The duration of antibiotics varies. In general, in uncomplicated septic arthritis, antibiotics are given for 2 to 4 weeks. In severe cases, the use of antibiotics can be longer up to 6 weeks.<sup>7,8</sup> After the diagnosis of TB arthritis has been successfully established with AFB examination, anti-tuberculosis drugs (OAT) can be given. Early administration of OAT can promote healing, maintain joint function, and prevent further damage. Based on the TB treatment guidelines in Indonesia, the treatment for TB arthritis is 2RHZE/10-16RH and should be given 1 year to 18 months in some cases. Dosage according to patient weight. This patient weighs 60 kg so he is given 4 tablets for 1 year. In addition to

pharmacological therapy, non-pharmacological therapies such as walking aids and surgery can be performed, therefore this patient was consulted for orthopedics.<sup>10,15,16</sup> This patient has a diagnosis of COVID-19. The patient was given supportive management in the form of vitamin C and vitamin D because he had no symptoms so no antiviral or antibiotic therapy was indicated. COVID-19 patients must be isolated for a maximum of 10 days from the time the confirmed diagnosis specimen is taken or if there are symptoms, the maximum isolation is 10 days plus 3 days free of symptoms of fever or respiratory problems.<sup>17</sup> Drug-induced liver injury (DILI), or drug-induced hepatotoxicity, is a liver injury caused by exposure to a drug or non-infectious agent. In this patient, there was a complaint of nausea that was felt in the pit of the stomach. The results of laboratory examinations showed an increase in the transaminase enzyme and hyperuricemia, so it was suspected that the patient had DILI due to OAT drugs. Hepatocyte death in DILI can occur through two processes, namely processes mediated by apoptosis or necrosis. In apoptosis, cell shrinkage and fragmentation occur into small pieces with the cell membrane intact. These fragments are cleared by phagocytosis and generally do not stimulate the host immune response. On the other hand, necrosis causes loss of mitochondrial function and ATP depletion leading to cell swelling and lysis that stimulates local inflammatory processes. The main treatment for DILI is delaying the drug that may be causing it. In most cases, spontaneous recovery occurs

without the need for any treatment. In this case, OAT was delayed until liver function returned to normal and clinical symptoms such as nausea and abdominal pain disappeared. Then when DILI has been completed, OAT can be given one by one.<sup>18-20</sup>

### 3. Discussion

Tuberculous arthritis is an infection of the joints caused by *Mycobacterium tuberculosis* which is the result of hematogenous spread from a primary distant focus infection. Constitutional symptoms such as fever, night sweats, and weight loss are usually absent in patients with tuberculous arthritis. The classic presentation of the disease is monoarthritis with pain (with or without movement), stiffness, and decreased function over weeks or months.<sup>2,10</sup> Joints that are often affected are large joints such as the hip or knee joints. Other joints that can be affected are the sacroiliac, shoulder, forearm, ankle, carpal, and tarsal joints. On physical examination, swollen joints may be found with or without a feeling of warmth. Limited movement due to pain and swelling due to synovial hypertrophy and effusion may also be present. In developing countries, the diagnosis of bone and joint tuberculosis can be established by clinical and radiological examination. Clinical examination is carried out by looking at the signs and symptoms that exist and performing laboratory tests (elevated ESR, BTA sputum test, tuberculin test). Radiologically, the process of tuberculous arthritis can begin in the synovium or the bone. In the early stages, the atypical signs that appear are thickening of the joint capsule, the joint looking gloomy and the joints are slightly widened due to intra-articular effusion, osteoporosis in the bones around the joint due to hyperemia.<sup>12,13</sup>

### 4. Conclusion

A patient diagnosed with arthritis tuberculosis genus Sinistra with Drug-Induced Liver Injury and confirmed COVID 19.

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