Dermatomyositis with Hepatic Impairment: A Rare and Intriguing Case Report Unveiling the Diagnostic Challenges and Treatment Dilemmas

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Abstract

Background: Dermatomyositis is a rare idiopathic inflammatory myopathy (IIM) characterized by skin lesions and systemic manifestations.
Case Presentation: A 32-year-old Indonesian man who was consulted by the neurology department presented with upper and lower limbs weakness for three months. Based on the results of history taking, physical and supporting examination, the diagnosis of dermatomyositis was made. The initial therapy comprised azathioprine 50 mg (2-0-1), methylprednisolone 4 mg (5-4-4), and hydroxychloroquine 1x200 mg. Azathioprine was used instead of methotrexate due to elevated liver enzymes. However, after one month of treatment, azathioprine was found to be ineffective. As per the guidelines, if the patient does not respond after four weeks of initial treatment, the therapy should be changed to mycophenolic acid. At present, the patient has shown improvement in clinical symptoms and laboratory examination and is still being followed up.
Conclusion: Dermatomyositis is a rare disease that is difficult to diagnose due to various differential diagnoses that must be ruled out. Prompt diagnosis and effective management of dermatomyositis are essential to improve patient outcomes. This case highlights the importance of considering alternative therapies for patients with dermatomyositis and elevated liver enzymes.

Keywords: Dermatomyositis; Polimyositis; Muscle weakness

1. Introduction

Dermatomyositis (DM) is an idiopathic inflammatory myopathy (IIM) condition characterized by skin lesions and other systemic manifestations.[1,2] Less common skin lesions include mechanical hands (hyper-keratosis of lateral fingers and palms), panniculitis, cutaneous vasculitis, urticaria, flagellate erythema, follicular hyperkeratosis, erosive or vesiculous lesions, and exfoliative erythroderma. Calcinosis may also occur, particularly in cases of juvenile dermatitis, a subset of patients who are defined as usually having the onset of disease before the age of 16 years.[3]

Dermatomyositis is a rare condition. A retrospective study conducted between 1967 and 2007 in Olmsted County, Minnesota, estimated an incidence rate of 9.63 per 1,000,000 people. The same study also found that 21% of all cases were of the amyopathic subtype. Dermatomyositis generally affects people between the ages of 40 and 50 with a mean age at diagnosis of 44.0 ± 18.3 years. This condition is more

common in women than men, with incidence rates of 3.98 and 4.68 per 1,000,000, respectively.[4] In Europe, a higher prevalence of dermatomyositis has been noted in Southern Europe compared to Northern Europe.[3] A study conducted in Quebec showed a higher prevalence of dermatomyositis in urban areas. A cohort study conducted in Pennsylvania also demonstrated a group of clinical amyopathic dermatomyositis (CADM) in areas with high air pollution. These studies indicate the possibility of environmental factors acting as a trigger for the condition.[5]

In dermatomyositis, muscle involvement is clinically similar to polymyositis but is accompanied by a unique set of skin findings. Proximal muscle weakness, elevated muscle enzymes, myopathic changes on electromyography, and inflammatory changes on muscle biopsy are diagnostic criteria for polymyositis. The presence of a characteristic rash in the presence of the above features defines dermatomyositis. This diagnosis is made by meeting these criteria in combination and excluding other potential etiologies for this test abnormality.[6]

Dermatomyositis occurs in patients with genetic susceptibility induced by sun exposure, infection, and malignancy. The clinical manifestations are divided into classic dermatomyositis and clinical amyopathic dermatomyositis. In classic dermatomyositis, the patient has skin and muscle complaints, whereas in clinical amyopathic dermatomyositis, there are no muscle complaints. Skin disorders in dermatomyositis can occur before or after muscle complaints. As many as 30-50% of patients experience skin complaints 3-6 months before the onset of muscle complaints, while in 10% of patients, there are muscle complaints before the lesions on the skin.[1,7]

Investigations for the diagnosis of dermatomyositis are autoantibodies, muscle enzymes, electromyography (EMG), magnetic resonance imaging (MRI), skin and muscle biopsies.[7] Before deciding on a specific therapeutic intervention program, patients should have a thorough evaluation to determine the presence and extent of muscle disease, the presence of other systemic involvement, including cardiac, pulmonary, and/or gastrointestinal dysfunction, and the presence of malignancy. Prompt detection of the underlying malignancy in a newly diagnosed patient is one of the most important therapeutic interventions; however, removal or treatment of the accompanying malignancy does not always result in remission in dermatomyositis patients.[3]

The management goals of dermatomyositis are focused on treating muscle weakness, skin disease, and other underlying complications. The first-line treatment of muscle disease in dermatomyositis is systemic glucocorticoids with or without immunosuppressants. Although no standard systemic steroid regimen is defined for dermatomyositis, the general principles of therapy are the same. Once an adequate response occurs, systemic steroid administration is gradually tapered over time. The total duration of therapy with systemic steroids usually ranges between nine and twelve months. It is important to note that administration of high doses of glucocorticoids for more than six weeks can lead to glucocorticoid myopathy.[4]

2. Case Presentation

A 32-year-old Indonesian man came to the rheumatology outpatient clinic in Haji Adam Malik General Hospital, Medan on September 15th, 2022, presenting with weakness in the upper and lower limbs since three months ago. The weakness was getting more severe gradually, involving from proximal to distal muscles progressively, and persisted throughout the day. The patient found it difficult to lift both hands and difficult to get up from a sitting position. Other presentations include stiffness in both hands for approximately 30 minutes in the morning, itching sensation and rashes on the face and body, swelling of the face, and jaw stiffness until it is difficult to open the jaw and difficult to swallow. Other presentations such as pain in the upper and lower limbs, hair loss, cough, dyspnea, fever, nausea, and vomiting were all denied by the patient. Past medical history such as hypertension, heart disease, diabetes, and other autoimmune diseases

were also denied by the patient. The history of family members with similar presentations or autoimmune diseases was denied. A history of smoking or alcohol consumption was denied by the patient.

Initially, six months ago, the patient experienced an itching sensation and rash appearing all over the body, especially on the abdomen area then spread to the upper limbs area. Three months later, the symptoms continued with the appearance of weakness in the lower limbs, starting from proximal and continuing to distal. Upper limb weakness was experienced two weeks later. The upper and lower limb weakness was getting worse over time. Then, the patient went to see a local neurologist and was treated together with an internist in Kalimantan but his conditions did not improve at all. After two months with his condition not improving, the patient moved to Medan and continued his treatment at Haji Adam Malik General Hospital, Medan. The patient was then admitted to the neurology department of Haji Adam Malik General Hospital, Medan on August 15, 2022, with a diagnosis of lower motor neuron tetraparesis caused by neuropathy suspect or CIDP suspect and had been given prednisolone but stopped because the patient's face became swollen. The patient was then consulted to the Hepato-Gastroenterology division of internal medicine with acute liver injury and multiple cholelithiasis and to the skin department with xerosis cutis. In the end, the patient was then consulted to the rheumatology division one week after starting to get therapy at Haji Adam Malik General Hospital, Medan with suspicion of autoimmunity.

On general physical examination, vital signs were found normal. On physical examination, a reddish-purple rash was found on both upper eyelids (heliotrope eyelid rash), reddish rash on both cheeks (malar rash), nasolabial folds (Figure 1), erythema papules and macules on the neck, upper chest, and upper back (shawl sign), erythema papules on the metacarpophalangeal (MCP) joint area (gottron's papules) (Figure 2).

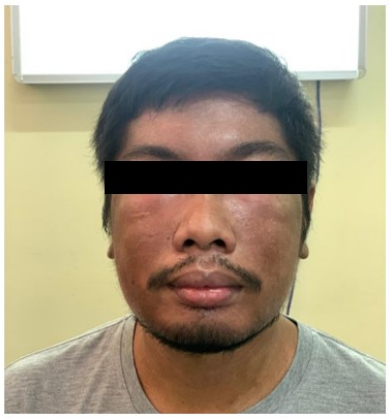

Figure 1. Classic clinical presentation seen on the dermatomyositis patient's face: Heliotrope eyelid rash, malar rash, nasolabial folds.

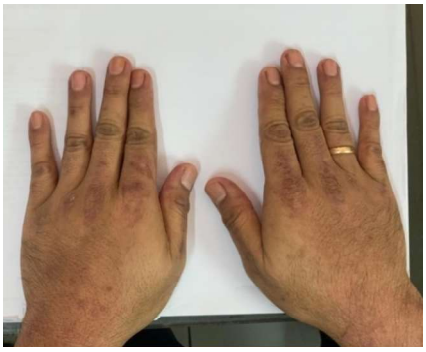

Figure 2. Dermatological changes including Gottron's papules that were seen on the surface of MCP joint in this patient who had tan skin.

Examination of the eye, ear, nose, throat, respiratory, cardiovascular, and abdominal systems were normal. In the neurological examination, the muscle strength was found to be 4433 / 4433 in the upper extremities and 4433 / 4433 in the lower extremities. In laboratory examination, hemoglobin, leukocytes, platelets, C-reactive protein (CRP), and renal function (urea and creatinine) were found within normal limits. There was also an increase in liver function including SGOT 197 U/L, SGPT 121 U/L, increase in muscle-related enzymes including CK-MB of 859 U/L, CK-NAC 8140 U/L, LDH 1091 U/L. The ANA IF was found to be speckled with titer 1:1000 and the anti-Jo-1 antibody test was negative. In the electromyography test, diffuse myogenic lesions were found indicating the condition of myopathy (Figure 3). In MRI examination of the left and right thigh muscles, a diffuse signal increase was found in the muscles of the right and left thigh muscles which was consistent with the clinical symptoms of dermatomyositis (Figure 4). Muscle biopsy was performed and the histopathological examination of the biopsied left thigh muscle tissue found a non-specific chronic inflammatory process in the lesion with the infiltration of inflammatory cells of lymphocytes and macrophages, muscle tissue lined with round to spindle nuclei, slightly increased N / C ratio, smooth chromatin, some of the nuclei were prominent, eosinophilic cytoplasm and had muscle fibers (Figure 5).

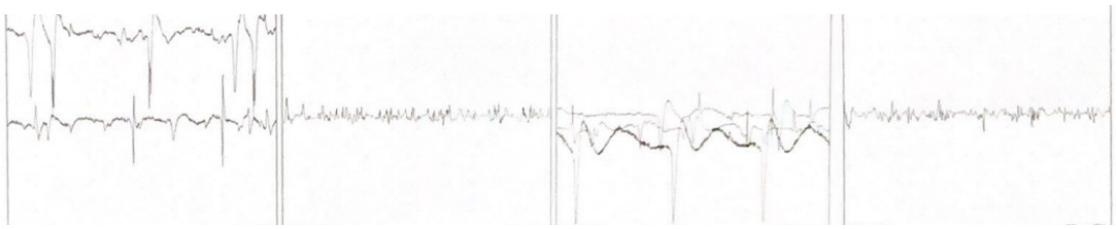

Figure 3. Electromyography examination found myogenic lesion with spontaneous activity in the right biceps muscle and left anterior tibialis muscle.

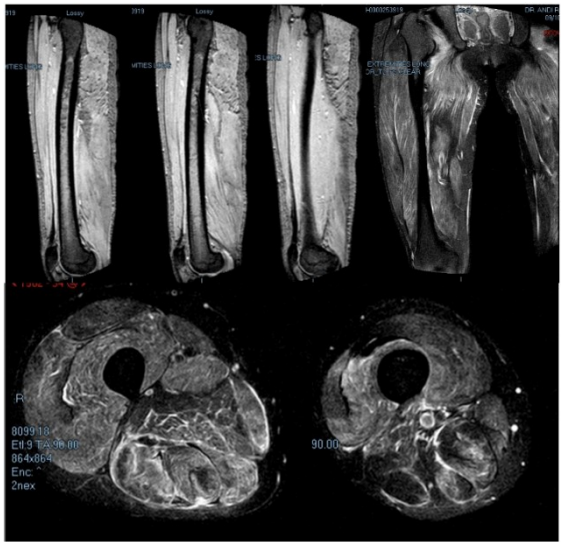

Figure 4. MRI findings of patient's left and right thigh muscles.

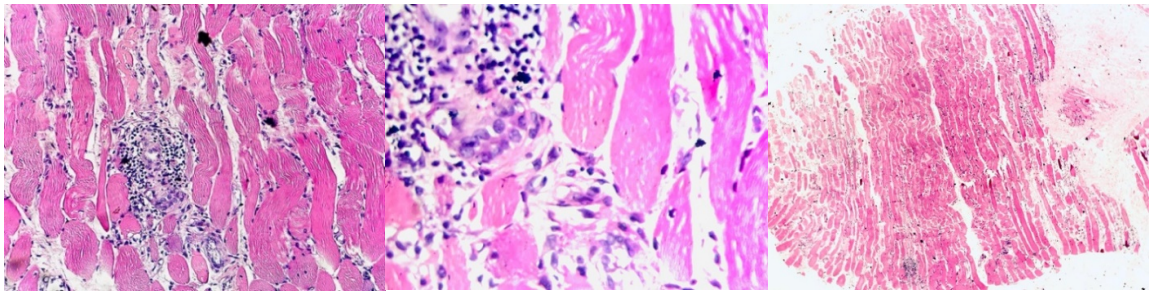

Figure 5. Histopathologic features of the left thigh muscle (non-specific chronic inflammatory process) supporting the diagnosis of dermatomyositis.

Based upon the results of history taking, physical examination, and supporting examination, the diagnosis of dermatomyositis in this patient was made. The patient also got a 15,9 score on The European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for adult and juvenile idiopathic inflammatory myopathies which could be interpreted as Definite IIM with 100% probability as IIM and with Dermatomyositis as the subgroup. Therefore, resulting in dermatomyositis as the diagnosis of this patient.

The patient was then given Azathioprine 50 mg (2 tab – 0 tab – 1 tab), methylprednisolone 4 mg (5 tab -4 tab – 4 tab), and Hydroxychloroquine 1x200 mg. One month after the treatment, the swollen face and facial redness had subsided but the patient still complained of weakness in the limbs. The patient still had difficulty raising hands and standing up from a sitting position. On physical examination, the reddish rash on the face had subsided. Subsequently, the therapy was changed to Mycophenolic Acid 2x360 mg, Hydroxychloroquine 2x200 mg, methylprednisolone 4 mg (5 tab – 4 tab – 3 tab) tapering down, calcium lactate 2x500 mg.

Another 2 weeks after the medication, symptoms of weakness in the extremities were still present so Mycophenolic sodium dose was increased to 2x720 mg. After the adjustment dosage, the motoric movement showed improvement to normal condition with CK level of 573. In the follow-up examination in December, the patient's complaint of weakness in the extremities diminished. The level of CK-MB (130 U/L), CK-NAC (683 U/L), and LDH (461 U/L) also showed improvement. In January, the patient was having a better improvement in symptoms and laboratory examination. It was found that the levels of AST (26 U/L), ALT (30 U/L), and CK-NAC (185 U/L) were normal. At present, the patient is still orally administered the previous therapy mentioned above and is still being followed up.

3. Discussion

Dermatomyositis is the most common subset of IIMs with the presence of skin lesions and symptoms of myositis.[3] Classic dermatomyositis: Symptoms of dermatomyositis are usually intense itching, especially on the scalp, tight skin, a burning sensation as if something is creeping under the skin, and tingling. Skin eruptions are chronic and progressive, leaving scars of dyspigmentation, atrophy, and telangiectasia. Pathognomonic lesions are purplish pink papules on the dorsal hand with a predilection for the metacarpals and interphalangeal joints (gottron's papules); purplish-pink erythema of the upper eyelid, edema which may be accompanied by erythema of the lateral and medial canthus or adjacent nasal wall (heliotrope sign); and erythematous or pinkish-purple macules at the interphalangeal joints, olecranon process, patella, and medial

malleolus (Gottron's sign). As many as 30% of patients with dermatomyositis have ulcers on the surface of the extensor joints, namely above the Gottron papules, Gottron's sign area, fingertips, and periungual. In necrotic ulcers, anti-MDA5 autoantibodies or malignancies are often present.[8]

For the patient who presents with cutaneous features that are consistent with DM, investigation for concomitant muscle disease should be performed. Due to the possibility of subsequent development of muscle disease, patients without myositis should be evaluated with a muscle examination and serum creatinine kinase and aldolase levels every two to three months.[9] The patient showed typical features for diagnosis of dermatomyositis such as progressive muscle weakness in the upper and lower limbs, stiffness in both hands for approximately 30 minutes in the morning, itching sensation and rashes on the face and body, swelling of the face and jaw stiffness until it is difficult to open the jaw and difficult to swallow. In the physical examination of this patient, the pathognomonic signs of DM were also found which included the Gottron papules and heliotrope rash. Also, other skin findings such as facial erythema and shawl signs were found in this patient. The patient's anti-Jo showed a negative result. The myositis panel examination may show other positive antibody results, but our hospital facility does not have the myositis panel examination yet. The patient was having an improvement in motoric movement to normal condition with CK level of 573 in October and CK level of 130 in December. Then, the patient showed a better improvement with normal AST and ALT levels in November.

Treatment overview for dermatomyositis consists of aggressive photoprotection to reduce the exacerbating effects of ultraviolet light, antipruritic agents to manage the associated pruritus, topical corticosteroids or topical calcineurin inhibitors for local treatment of skin manifestations, and systemic medications aimed at attaining sustained control of the disease. Pruritus can interfere with sleep patterns and activities of daily living and should be treated aggressively with topical or oral antipruritic agents. Topical antipruritic therapy containing pramoxine, menthol, or camphor may provide temporary symptomatic relief. The use of oral sedating antihistamines such as hydroxyzine, cyproheptadine, or doxepin, cyproheptadine, or doxepin, or other agents such as amitriptyline or gabapentin, is often necessary to improve pruritus.[10]

Clinical experience supports the use of topical corticosteroids for reducing the erythema and pruritus associated with DM. In general, topical corticosteroids are considered adjunctive as most patients will require systemic therapy to adequately treat their DM skin disease. High-potency topical corticosteroids are often used to treat the hands, extensor surfaces, and scalp, where the risk of corticosteroid-induced cutaneous atrophy is low, while lower-potency agents are used for disease in areas that are more prone to atrophy, such as facial erythema and the heliotrope eruption. Topical calcineurin inhibitors (most often tacrolimus 0.1% ointment) are typically utilized for patients who do not improve with topical corticosteroids or for long-term topical therapy in areas that are prone to cutaneous atrophy. Topical calcineurin inhibitors are applied to the affected skin twice daily. Improvement in erythema and symptoms may be evident within the first month of treatment. Most patients require systemic therapy to achieve satisfactory suppression of cutaneous disease. The goals of systemic treatment are to achieve resolution of pruritus and skin changes or to achieve a level of improvement in which mild, residual disease can be successfully managed with topical therapy. The clinical presentation influences the approach to treatment.[10]

The patient was given Azathioprine 50 mg (2 tab - 0 tab – 1 tab), methylprednisolone 4 mg (5 tab – 4 tab – 4 tab), and Hydroxychloroquine 1x200 mg. The Azathioprine was given instead of MTX because this patient's liver function was decreased. Hydroxychloroquine was given for the patient's cutaneous manifestation. One month later, the swollen face and facial redness had subsided but the patient still complained of weakness in the limbs. The patient still had difficulty either raising hands or standing up from a sitting position. On physical examination, the reddish rash on the face had subsided. After one month of treatment, Azathioprine was not really responsive, so the treatment was replaced by Mycophenolic acid. Following the guideline, if the patient is resistant or not responding after 4 weeks of initial treatment, then the

treatment should be changed to Mycophenolic acid. Subsequently, the therapy was changed to Mycophenolic Acid 2x360 mg, Hydroxychloroquine 2x200 mg, methylprednisolone 4 mg (5 tab – 4 tab – 3 tab), calcium lactate 2x500 mg. Two weeks later, the dose was adjusted to Mycophenolic Acid 2x720 mg. At present, the patient showed improvement in the clinical symptoms and also in the laboratory examination, and still being followed up until now.

4. Conclusion

Dermatomyositis is an idiopathic inflammatory myopathy condition characterized by skin lesions and various other systemic manifestations. Dermatomyositis is a rare disease and difficult to diagnose due to various differential diagnosis that must be ruled out. The first line of therapy is corticosteroid and the second line of therapy is methotrexate for skin and muscle symptoms. The initial therapy was then given Azathioprine 50 mg (2-0-1), methylprednisolone 4 mg (5-4-4), and Hydroxychloroquine 1x200 mg. Azathioprine was given instead of MTX because this patient's liver function was decreased. After one month of treatment, Azathioprine wasn't so responsive. By the guideline, if the patient is resistant or not responding after 4 weeks of initial treatment, then the treatment should be changed to Mycophenolic acid.

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