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Case Report

Combination Therapy of Prednisone, Azathioprine, and Hydroxychloroquine in Patient with Dermatomyositis

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ABSTRACT

Introduction: Dermatomyositis (DM) is an autoimmune disease with manifestations of inflammatory myopathy accompanied by cutaneous involvement. In patients with cutaneous DM, for the first line of therapy can be given photoprotection, topical steroids, Hydroxychloroquine (HCQ) or Chloroquine and Quinacrine, while the gold standard in DM myopathy is systemic corticosteroids. Inadequate therapeutic regimens can result in morbidity or complications, especially calcinosis.

Case Presentation: A 29-year-old woman on dermatological examination of the facial region, right and left manus, erythematous patches, multiple, ill-defined borders, irregular edges, varied in shape and size were found. Sontheimer's proposed diagnostic criteria: major criteria: heliotrop sign (+), gottron papule (+), gottron sign (+). Minor criteria: v-neck sign (-), shawl sign (-), holster sign (-). The patient underwent a histopathological examination with the results indicating dermatomyositis. In patients using diagnostic classification criteria of the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) which leads to the diagnosis of Dermatomyositis. Meanwhile, for the severity of Dermatomyositis, we use the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) which gets a total activity score of 15 which is included in the category of Moderate-Severe Dermatomyositis. The therapy given to the patient was PO Azathioprine 2x50 mg, PO Hydroxychloroquine 1x200 mg, PO Prednisone 1x5 mg and Olium olivarum 2 dd ue.

Conclusion: A combination of prednisone, azathioprine, and hydroxychloroquine is effective as a therapy for dermatomyositis. This can be proven by an increase in muscle strength and the red spots disappearing in this patient.

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INTRODUCTION

Dermatomyositis (DM) is an autoimmune disease with manifestations of inflammatory myopathy implicated with cutaneous [1]. The precise etiology and pathogenesis of DM cannot yet be decided, there's a theory that DM is caused by autoimmune disease and can be activated by natural components, such as drugs, infections, exposure to ultraviolet (UV) light, and pollutants. Prevalence of DM in adults (adult dermatomyositis) reported 6-7 cases per 100,000 people per year. The incidence of DM is 5-10 per million people per year [2–4].

Gold standard therapy for DM myopathy are corticosteroids systemic [5–6]. Meanwhile, moderate to severe DM specifically should be treated with a combination which contain steroids and immunosuppressants such as Methotrexate (MTX), Azathioprine (AZA) or Mycophenolate Mofetil (MMF). First-line therapy for cutaneous DM may include photoprotection, topical steroids, Hydroxychloroquine (HCQ) or Chloroquine and Quinacrine. Studies are showing that 41-75% of patients with DM are successfully treated with HCQ [7–9]. Providing therapy that is not carried out quickly and inadequately can cause various complications, one of

which is calcinosis [7]. So this case report was carried out to determine the effect of a combination of 3 drugs on patients with DM.

CASE PRESENTATION

A 29-year-old woman came to the skin and genital clinic consulted by the Internal Medicine department of Saiful Anwar Hospital with a diagnosis of Dermatomyositis. The patient complained of reddish spots on the face and hands since 2 months ago accompanied by itching with a VAS of 5/10. The reddish spots on both hands feel raised like swelling accompanied by pain with a VAS of 7/10. This complaint was also accompanied by pain in the hips, knees and elbows with a VAS of 7/10 making it difficult for the patient to walk.

On dermatological examination of the facial region, right and left manus, erythematous patches, multiple, ill-defined borders, irregular edges, varied in shape and size were found. Sontheimer' proposed diagnostic criteria: major criteria: heliotrop sign (+), gottron papule (+), gottron sign (+). Minor criteria: v-neck sign (-), shawl sign (-), holster sign (-). The patient underwent a histopathological examination with the results indicating dermatomyositis. In patients using diagnostic classification criteria of the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) which leads to the diagnosis of Dermatomyositis. Meanwhile, for the severity of Dermatomyositis, we use the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) which gets a total activity score of 15 which is included in the category of Moderate-Severe Dermatomyositis. The therapy given to the patient was PO Azathioprine 2x50 mg, PO Hydroxychloroquine 1x200 mg, PO Prednisone 1x5 mg and Olium olivarum 2 dd ue.

On the 28th day of treatment, most of the red spots on the patient's face had faded, some had become blackish-brown spots, and the itching on the red spots was no longer present. Pain in the hips, knees and elbows was said to be reduced, with a VAS of 5/10. Categories of responses before and after therapies are summarized in **Table 1**. Dermatological status shows erythematous patches, some hyperpigmentation, multiple, indistinct borders, irregular edges, variable shape and size.

DISCUSSION

Dermatomyositis (DM) is an idiopathic inflammatory myopathic disease characterized by varying degrees of skin disease accompanied by muscle weakness. The cardinal sign of DM is a skin eruption accompanied by symmetrical weakness and proximal muscle pain. Periorbital edema including the bridge of the nose and eyelids is a commonplace of the skin sign in the acute stage. It is accompanied with symmetrical erythema that is described as pink-purple or purple (heliotropic erythema). This redness can moreover develop on the chest (v-sign) or the back of the neck (shawl sign). In a few cases, red-purple erythema shows up on the lateral side of the thigh (holster sign) [3,4].

Flat papules are also characteristic of DM, usually found proximal to the interphalangeal and metacarpophalangeal joints on the extensor side of the hand (Gottron papules), or sometimes in the elbow, ankle or knee area, in these cases it is more often in the form of erythema or plaque (Gottron sign). Periungual telangiectasis may also occur, showing up as dilated capillaries on capillary microscopy and now and then associated with bleeding from dilated vascular loops. This is typically related to nail crease induration that's excruciating when retracted (forehead sign). Additional signs of DM include increased photosensitivity, non-scarring alopecia, and severe pruritus of the scalp and other areas of the body. Hyperkeratosis and linear papules such as Rhagade can develop on the hand, on fingers 1, 2 and 3, this is called "Mechanic's Hands".

Table 1. The Severity of Myopathy in Dermatomyositis Patients, before Therapy and after Therapy

Area	Pre-Therapy		Post-Therapy	
	Right	Left	Right	Left
Deltoid Middle (shoulder abductors)	10	10	10	10
Biceps Brachii (elbow flexors)	8	8	10	10
Wrist Extensor (extensor carpi ulnaris/radialis)	10	10	10	10
Quadriceps Femoris (knee extensors)	5	5	8	8
Ankle Dorsiflexors (tibialis anterior)	10	10	10	10
Neck Flexors (scalenes, sternocleidomastoid)	10	10	10	10
Gluteus Medius (hip abductors)	7	7	9	9
Gluteus Maximus (hip extensors)	7	7	9	9

Similar hyperkeratosis can also occur on the feet, usually spreading to the plantar and toes (Hiker's Feet) [5].

As of now, the main goal of providing treatment to DM patients is to increase muscle strength and everyday activities, as well as improve systemic symptoms. The main therapy for DM is immunosuppressants, physical therapy, monitoring side effects of drugs and preventing complications. Glucocorticoids remain the first line therapy option for DM with the choice of oral prednisone 1mg/kgBW/day. In patients who rapidly deteriorate, intravenous methylprednisolone 1000 mg/day for 3-5 days is recommended before starting therapy with oral glucocorticoids. High-dose corticosteroids (>0.5 mg/kg BW/day) are the main therapy for DM [3,5,6].

The American Academy of Dermatology (AAD) recommends systemic corticosteroids for initial therapy for muscle weakness at a dose of 0.5-1.5 mg/kg/day. After muscle complaints improve, the dose can be reduced gradually. The AAD does not specify when and how much the dose can be reduced. Oddis and Medsger stated that patients were given corticosteroids 60 mg/day for leastwise 1 month, which would be continued for 2–4 weeks after serum creatinine kinase was normal, and reduced gradually by 10 mg/month.

This shows biochemical and good outcomes for patients. Other research also states that reducing the dose of corticosteroids can be done after heart enzymes are normal or can be reduced by half the initial dose within 6 months, with the target of stopping the dose in 2 years. Corticosteroids should not be continued forever, some patients may discontinue the therapy after at least 14 months. The steroid dose should be reduced slowly, 10 mg/day every 1-2 weeks until it reaches a dose of 20 mg/day. Maintenance doses can be given to patients to reduce symptoms and prevent remission, by administering a steroid dose of 2.5–5 mg/day every 1-2 weeks. In most cases, maintenance doses can be given at 5 mg/day for the long term. However, this study does not indicate how long maintenance doses of prednisone can be given [5–7,20].

Monotherapy with steroids can only be given in very mild cases. Meanwhile, moderate to severe DM specifically should be treated with a combination which contains steroids and immunosuppressants, such as Methotrexate (MTX), Azathioprine (AZA), or Mycophenolate Mofetil (MMF). In addition, patients who do not respond to the therapy of steroids and do not show an increase in muscle strength can also be given a combination of these drugs [5].

As many as 57–75% of studies show that DM patients improve with *AZA* therapy. On double-blinded randomized placebo-controlled study, AZA has been studied as first-line therapy in combination with prednisone [7]. The therapy algorithm indicates that hydroxychloroquine (HCQ) is the first-line therapy for cutaneous DM. As many as 41–75% of studies said that DM patients experienced clinical skin improvement with HCQ. Recent research shows that HCQ can cause retinal complications, so the latest guidelines recommend follow-up eye examinations every 5 years after using the first dose of HCQ in patients without complications. However, patients who experience complications (receiving HCQ therapy for >5 years, consuming a dose of HCQ greater than recommended, patients with high body fat levels, kidney and liver disorders, age >60 years) are followed up every year [15,17,18].

In this patient we diagnosed with dermatomyositis, there were reddish spots on the face, Gottron papules, Gottron sign dan Mechanic's hands with myositis of the hips, elbows and knees. The patient was given a combination therapy of prednisone, azathioprine (AZA) and hydroxychloroquine (HCQ). Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) is a measuring tool that can be used to measure the severity of dermatomyositis. This patient obtained a score of 15 which is included in the Moderate-Severe Dermatomyositis category. Meanwhile, to measure the severity of myopathy using the Manual Muscle Testing-8 (MMT-8) measuring instrument.

CONCLUSION

A combination of prednisone, azathioprine, and hydroxychloroquine is effective as a therapy for Dermatomyositis. This can be proven by an increase in muscle strength and disappearing red spots in this patient as measured using the CDASI measuring instrument.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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