Dysphagia as an Early Presenting Symptom in Dermatomyositis

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ABSTRACT

Dermatomyositis is a systemic disorder that frequently affects the esophagus, lungs, and the heart. Dermatomyositis diagnostic criteria involve evaluation of proximal muscle weakness, elevation serum levels of muscle enzyme, characteristic features of electromyography, typical muscle biopsy and classical skin rash of dermatomyositis. The prevalence of dysphagia in patients with dermatomyositis varied from 10-73%.

A 40-year-old male was admitted to Cipto Mangunkusumo hospital with chief complaint of difficult in swallowing. He had been well until he began to have muscle weakness, myalgia, fatigue, and obstructive symptom in his upper digestion tract. Physical examination showed general weakness and symmetrical rash on the face, chest and back. Laboratory examination revealed anemia, thrombocytopenia, and elevated transaminase serum level. Antinuclear antibody was positive. Esophagogastroduodenoscopy showed severe esophagitis. The gastric mucosa biopsy revealed non-active chronic gastritis, antral lymph atrophy, and non-dysplastic. Biopsy of esophageal mucosa showed Barret's esophagus with squamous epithelial cell and hard dysplasia focus. The electromyography result was suspected to a dermatomyositis. The deltoid muscle biopsy demonstrated dystrophy.

Dysphagia may be an initial presenting symptom and especially prevalent in patients with dermatomyositis or other inflammatory myopathy. Dysphagia associated with these myopathies primarily affects the skeletal muscle–activated oropharyngeal phase of swallowing. It may precede weakness of the extremities or present as the sole symptom. Recommended treatments used to treat inflammatory myopathy associated dysphagia are combination of medical, rehabilitation, and interventional. Dysphagia associated with nutritional deficits, aspiration pneumonia, decreased quality of life, and poor prognosis. Patients with inflammatory myopathy and dysphagia are reported to have a 1-year mortality rate of 31%.

Keywords: *dysphagia, dermatomyositis, inflammatory myopathy*

ABSTRAK

Dermatomiositis merupakan penyakit sistemik yang sering menyerang esofagus, paru-paru, dan jantung. Kriteria diagnosis dermatomiositis melibatkan kelemahan otot proksimal, elevasi serum enzim otot, gambaran elektromiografi yang khas, biopsi otot yang tipikal dan ruam kulit yang khas dermatomiositis. Prevalensi disfagia pada pasien dengan dermatomiositis bervariasi antara 10-73%.

Pada kasus ini dilaporkan seorang pria berusia 40 tahun dirawat di rumah sakit Cipto Mangunkusumo dengan keluhan utama sulit menelan. Keluhan diawali dari rasa lemah tubuh, mialgia, kelelahan, dan gejala obstruktif di saluran pencernaan atas. Pemeriksaan fisik menunjukkan kelemahan seluruh tubuh dan ruam simetris pada wajah, dada dan punggung. Pemeriksaan laboratorium menunjukkan anemia, trombositopenia, peningkatan enzim transaminase, dan antibodi antinuklear positif. Endoskopi saluran cerna bagian atas menunjukkan esofagitis berat. Biopsi mukosa lambung menunjukkan gastritis kronis yang non-aktif, atrofi kelenjar getah bening di antrum, dan non displasia pada mukosa. Biopsi mukosa esofagus menunjukkan Barret esophagus dengan sel epitel skuamosa dan fokus displasia keras. Hasil elektromiografi menunjukkan kecurigaan ke arah dermatomiositis dan hasil biopsi otot deltoid menunjukkan distrofi.

Disfagia dapat menjadi gejala awal atau merupakan keluhan utama dari dermatomiositis atau miopati inflamasi lainnya. Disfagia berhubungan dengan miopati yang mempengaruhi otot rangka yang mengaktifkan

fase orofaringeal pada proses menelan. Keluhan disfagia dapat mendahului gejala kelemahan ekstremitas atau sebagai gejala tunggal pada dermatomiositis. Rekomendasi terapi untuk tatalaksana disfagia pada miopati inflamasi merupakan kombinasi dari obat-obatan, rehabilitasi, dan terapi intervensi. Disfagia berhubungan dengan terjadinya defisit nutrisi, pneumonia aspirasi, menurunnya kualitas hidup, dan prognosis yang buruk. Pasien dengan inflamasi miopati dan disfagia dilaporkan memiliki mortalitas 1 tahun sebesar 31%.

***Kata kunci**: disfagia, dermatomiositis, miopati inflamasi*

INTRODUCTION

Inflammatory myopathies are acquired muscle diseases that are typically categorized into 4 groups; including polymyositis (PM), dermatomyositis (DM), inclusion body myositis (IBM), and an overlap syndrome with mixed characteristics. DM is an idiopathic inflammatory myopathy with common clinical features of slowly progressive symmetrical muscle weakness and cutaneus manifestations. The pathogenesis of cutaneus disease of DM is poorly understood; however the following factors have been implicated. DM rarely occurs in multiply members but may be linked to certain human leukocyte antigen (HLA), immunological abnormalities, viral infection, exposure to ultraviolet light, drug-induced myopathies and malignancy.[1]

DM can occur in people of any age. DM affects both children and adults, and female are more often than male. Diagnostic criteria and a classification scheme were based upon a combination of clinical, laboratory, pathological evaluation. DM diagnostic criteria involves evaluation of proximal muscle weakness, elevation serum levels of enzyme, characteristic features of electromyography (EMG), typical muscle biopsy histopathology, and the classical skin rash of DM. Dysphagia has been reported to occur in 10-73% of these patients.[1,2,3]

The dysphagia associated with these myopathies primarily affects the skeletal muscle–activated oropharyngeal phase of swallowing. It may precede weakness of the extremities or present as the sole symptom. Dysphagia is associated with nutritional deficits, aspiration pneumonia, decreased quality of life, and poor prognosis. In fact, patients with inflammatory myopathy and dysphagia are reported to have a 1-year mortality rate of 31%. A variety of medical, rehabilitation, and interventional treatments are used to treat inflammatory myopathy-associated dysphagia. The following case report presents a case of 40-years-old man with dysphagia as an early presenting symptom, which did not occur long enough for us to recognize that the patient's diagnosis was DM.[1,4]

CASE ILLUSTRATION

A male, 40 years old, was admitted to Cipto Mangunkusumo hospital with chief complaint of difficulty swallowing. He had been well until one month later, and then he began to have muscle weakness. He felt myalgia and fatigue, as well as loss of appetite; and he had lost 5 kg of weight. Two weeks before admission, he felt an obstruction developed in his upper digestion tract, which made him had difficulty swallowing. It was accompanied with a dry cough, hoarseness and hypersalivation. There was no chest pain, no difficulty to breath, no difficulty to pass urine, and no diarrhea or constipation.

Since 6 months prior to admission, the patient found a pruritic-papular rash in the face and then new rashes were developed along upper portion of the chest and back and the color became brighten. There was no history of hair loss, no oral ulcer, no chest pain, and no difficulty in breathing.

The symptoms persisted and worsen, patient could only eat soft and watery food, sometimes also get hiccup. Subsequently, the patient went to Division of Gastroenterology, Department of Internal Medicine at Cipto Mangunkusumo hospital, and then was planned to have esophagogastro-duodenoscopy (EGD). However, when the fatigue and difficulty swallowing were getting worse, he came to the emergency unit.

At the emergency unit, the patient consumed food through nasogastric tube. The patient was consulted to the Department of Ear, Nose and Throat and Department of Dermatology. Both departments concluded neurogenic dysphagia and seborrheic dermatitis.

There was no history of heart problem, pulmonary problem, and no history of allergy of food or medicine. He denied the same problem in her family. Patient was a public transportation driver and had been exposed to concrete dust and radiation. He had a 20-year smoking history. He had no recent exposure to ill persons and had not traveled recently.

Based on physical examination, the patient was appeared ill, compos mentis, and malnourished. The blood pressure was 100/60 mmHg, pulse rate was 80 beats/minute, body temperature was 36.6˚C, body weight was 43 kg, height was 160 cm and body mass index was 16.79 kg/m^2. On skin examination, we revealed rashes, which were symmetrical, erythematous, lenticular, placate with squama on the facial (ala nasi, naso-labial and bucal region), scalp, and neck. The conjunctiva was not pale, no jaundice.

Her lung sounded vesicular, which were normal. Neither rales nor wheezing was found. Her 1st and 2nd heart sound were normal, no murmur or gallop was found. Our abdominal examination found no distention and no tenderness. The liver and spleen were not palpable. No edema was found on both extremities.

Laboratory examination revealed hemoglobin level of 10.9 g/dL, hematocryt of 34.6%, the leukocyte count was 5,010/uL, platelet count was 89,000/uL, erythrocyte sedimentation rate (ESR) was 50 mm/hour, mean corpuscular volume (MCV) was 78 fl, mean corpuscular hemoglobin (MCH) was 27 pg, mean corpuscular hemoglobin concentration (MCHC) was 34 g/dL. The differential count showed following results: eosinophil 0, basophil 0, neutrophil 51.9%, lymphocytes 10%, and monocytes 3%. The peripheral blood film showed normocytic normochromic anemia, ureum level was 17 mg/dL, creatinine level was 0.3 mg/dL, aspartate aminotransferase (AST) level was 100 U/L, alanine aminotransferase (ALT) level was 40 U/L, albumin level was 2.70, globulin level was 3.00, creatine kinase (CK) level was 300 U/L, blood glucose level was 92 mg/dL, sodium level was 135 mEq/L, kalium level was 3.9 mEq/L, and chloride level was 97.1 mEq/L. Urine analysis results were normal. Electrocardiography (ECG) result was within normal limit, chest X-ray showed no infiltrate, no cardiomegaly. The hepatic seromarker was positive for hepatitis B surface antigen (HBsAg) and negative for anti hepatitis C virus (HCV).

The gastric mucosa biopsy demonstrated non active chronic gastritis, antral lymph atrophy, non-dysplastic and found no *Helicobacter pylori*. The liver biopsy demonstrated chronic hepatitis, piecemeal mild necrosis, focal moderate necrosis and fibrosis staging F3. Evaluation of EGD demonstrated grade C esophagitis with mild gastritis.

The esophagus mucosa biopsy demonstrated Barret's esophagus with squamous epithelial cells with hard dysplasia focus. The EMG demonstrated myogenic diffuse lesion with motor neuropathy axonal type in right ulnar nerve and left sural nerve, which were suspected to a DM. The patient underwent a deltoid muscle biopsy which demonstrated dystrophy. Antinuclear antibody (ANA) was positive and all profile of ANA including anti Jo 1 were negative. The CK was 300 U/L. The history, clinical findings and blood tests all supported to a DM and therefore methylprednisolone tablet 3 times 16 mg/day was commenced.

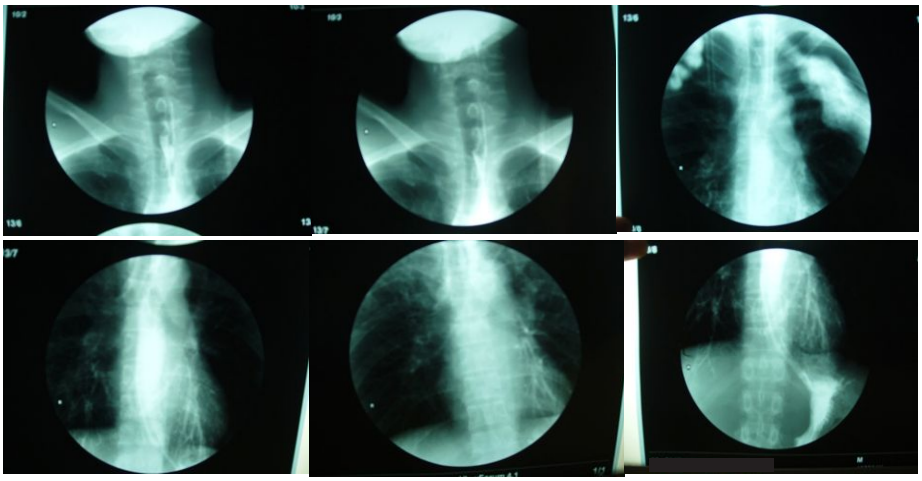

Figure 1. The barium-swallow X-rays with contrast showed normal oesophageal motility

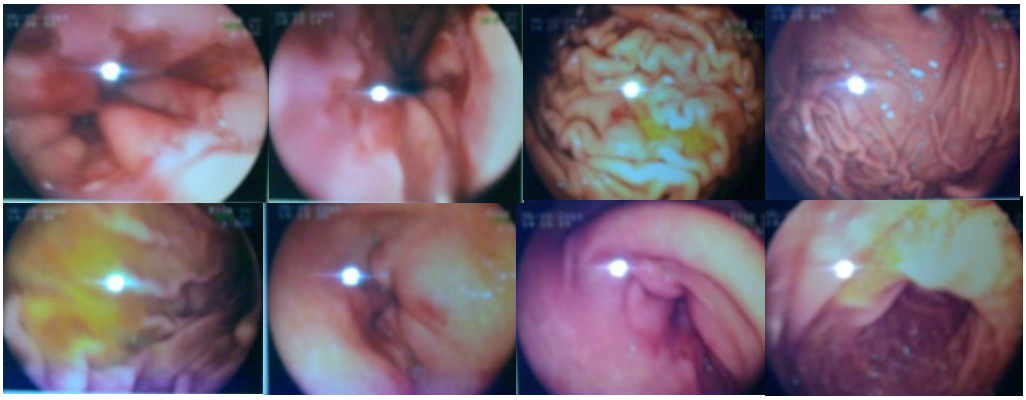

Figure 2. Endogastroduodenoscopy showed severe esophagitis with multiple ulcers in corpus and antrum

The patient was discharged 60 days later with significant improvement in symptoms and planned to be followed up by both the gastroenterologists and rheumatologists in daily clinic.

DISCUSSION

The idiopathic inflammatory myopathies are rare diseases. The prevalence of the inflammatory myopathies is estimated at 1 in 100,000. PM as a stand-alone entity is a rare disease affecting adults. DM affects both children and adults, and women are more often than men. IBM is three times more frequent in men than in women, more common in Caucasians than blacks, and is most likely to affect persons > 50 years of age.

The mechanisms that cause autoimmune reaction have not been known, but both genetic and environmental factors are likely to confer risk factors developing chronic inflammatory myopathies. Recent studies on pathogenesis of the myopathy have been controversial. Some suggest that the myopathy in DM is probably caused by complement-mediated (terminal attack complex) vascular inflammation. The strongest genetic association is HLA; while the most frequently associated environmental factor is viral infection. Other observations suggest the correlation between ultraviolet light exposure and myositis. Several drug may induce myopathies and increase the risk of having malignancy for patient with DM.[2,5,6,7,8]

Inflammatory myopathies are acquired muscle diseases that are typically categorized into 4 groups: PM, DM, IBM, and an overlap syndrome with mixed characteristics. The clinically suspected diagnosis of PM, DM, or IBM is confirmed by examining the serum levels of muscle enzymes, EMG findings, and muscle biopsy.[3,9]

DM is an idiopthic inflammatory myopathy, systemic disorders with characteristics of bilateral symmetrical muscle weakness and typical cutaneus findings.[10,11,12] The inflammatory myopathies, which are collectively often named as myositis, have common clinical features of slowly progressive symmetrical muscle weakness, decreased muscular endurance and fatigue.[6]

The diagnostic of myositis should be suspected in adult with sub-acute or insidious onset of symmetrical proximal muscle weakness. A diagnosis of myositis is supported by typical laboratory results of myopathy such as raised serum levels of CK or lactate dehydrogenase (LDH), myopathic change on EMG or a muscle biopsy with sign of myopathy. A definite diagnosis can be made when histopathological changes present in muscle biopsy. These changes include infiltrates of mononuclear inflammatory cells, regenerating and degenerating muscle fibres.[2,6,12]

Such criteria should be applied assuming that the possibilities of infectious, toxic, metabolic, dystrophic or endocrine myopathies have been excluded by appropriate evaluation. Several sets of criteria have been proposed for the diagnosis and classification of idiopathic inflammatory myopathies. All of them have limitation and none have been properly validated. Despite their limitation, the Bohan and Peter criteria often used for diagnosis and classification of idiopathic inflammatory myopathies.[12]

Based on the history of this patient, we found difficult swallowing with symmetrical and bilateral muscle weakness since 1 month prior to admission. He felt myalgia and muscle weakness that had worsen day by day. No history of oral ulcer, pain and joint swelling. Six months prior to admission, he felt altered skin condition accompanied with itching. First, the rash was on his face, then it ascended to upper portion of the chest and back and the color became brighter. It was also accompanied with a dry cough, hoarseness and hypersalivation. We suggested such condition as the signs of dermatomyosities.

Based on physical examination, we found pathognomonic or typical rash for dermatomyositis, which was similar to the heliotrope rash and poikiloderma that occurred in a V-shaped distribution over the anterior neck, upper chest and back region (the shawl sign). In some cases, it may dominate the clinical symptoms. The skin rash may precede the muscle symptoms by months or even years. In some other patients, the skin manifestations may be the only clinical sign of DM. Another characteristic skin rash in DM are the Gottron papules, that were found over bony prominences, particularly the metacarpophalangeal joints, the proximal interphalangeal joints and/or the distal interphalangeal joints, peri-ungual erythema, and calcinosis; which were not found in this patient. Others clinical features for DM include arthralgia and arthritis, lung fibrosis, cardiomyopathy, Raynound's phenomenon and Sjogren syndrome. Dermatomyositis has been linked to internal malignancy in 15-25% cases.[3,4,12,13,14]

Based on the laboratory results, we found normocytic anemia, increased ESR up to 50 mm/hour, increased AST level of 100 U/L, increased ALT level of 40 U/L, and increased CK level of 300 U/L. ANA was positive, but all profile of ANA including anti Jo-1 were negative. Autoantibodies are frequently found in patients with myositis. Antinuclear antibodies were found positive in 30% DM patients and 90-100% in patients with systemic lupus erythematosus (SLE). A number of autoantibodies in DM have been detected, including Jo-1 and anti M-2, as myositis antibodies were directed as cytoplasmic antigen. Anti Jo-1 was

positive in 20% of patients with DM. Anti Jo-1 is associated with myositis and pulmonary involvement and is not the only marker of disease.[7,14,15] We also found hypoalbuminemia (2.70) with albumin globulin ratio less than 1. Positive HBsAg was also found that we assessed as chronic hepatitis B.

The most important investigation were the measurement for serum levels of muscle enzymes, EMG, and muscle biopsy. CK was considered as the most sensitive and useful serum muscle enzyme to measure and maybe used in finding and assesing the progress of the disease. CK is not specific for myositis and may be seen in several other conditions. About 10-20% patients may have CK level within normal range. Other commonly used enzyme that may have elevated level in the serum for myopathic condition are ESR, LDH, AST, ALT.[3,12,13,15]

Patients with DM may mimic SLE in demostrating photosensitivity and malar rash. Skin biopsy in these two diseases share similar histophatological feature of "interface dermatomyositis". Skin biopsy in such patients cannot exclude the possibility of SLE.[8]

Electrocardiography (ECG) of the patient showed results within normal limit, no conduction abnormality and arrhytmias were detected by ECG. In DM, clinical manifestations of heart involvement are rare, subclinical manifestations are frequently reported.[2,8,14] The EMG results of our patient suggested myositis. EMG is part of diagnostic procedure. The myopathic changes include myopathic motor unit potentials with or without spontaneous discharge and fibrillation. However, normal EMG result does not preclude myositis. The sensitivity of EMG changes is uncertain; therefore, EMG is not recommended as an outcome measure during treatment.[3,12] Muscle biopsy is important to confirm inflammatory changes, to distinguish between PM and IBM, to exclude other myopathies. Needle muscle biopsy showed fiber necrosis and regeneration in association with inflammatory cell infiltrates with lymphocytes adjacent to the blood vessels and between muscle fibers. Notably, a positive muscle biopsy is required for establishing a definitive diagnosis of DM.

Dysphagia occurs in 10–73% of patients with inflammatory myopathies.[6] The dysphagia associated with these myopathies primarily affects the skeletal muscle–activated oropharyngeal phase of swallowing. It may precede weakness of the extremities or present as the sole symptom. Dysphagia is associated with nutritional deficits, aspiration pneumonia, decreased quality of life, and poor prognosis.[4,11,16,17]

Oropharyngeal dysphagia was defined as difficulty in swallowing together with one or more of the following deglutitive symptoms, including bolus hold-up, multiple swallows required to clear the pharynx, deglutitive coughing and/or choking, or post-nasal regurgitation.[17]

The skeletal-muscle activated oropharyngeal phase of swallowing is clearly affected, which lead to the increased incidence of aspiration pneumonia. It finally results in ineffective peristalsis and clinical manifestation of gastro-oesophageal reflux, gastroparesis and constipation due to colonic inertia. A multi-disciplinary approach is essential and the roles of dieticians, speech and language therapists are imperative. Assessment with video-fluoroscopic studies can help us to identify pharyngeal pooling, impaired tongue-base retraction, decreased laryngeal elevation and cricopharyngeal dysfunction. Esophageal and gastric radionuclide transit studies are safe, simple, non-invasive method of highlighting esophageal and gastric delay.[1,4,5]

Principal treatment for DM is immunosuppressive drugs. Treatment with glucocorticoid provides a substantial improvement in survival and reducing disability. High initial dose of glucocorticoid are recommended. Large prospective randomized controlled studies of steroids in polymyositis and dermatomyositis have not been performed. Hence, steroid therapy followed by other immunosuppressive agents is largely empirical but widely accepted. [2,4,11,14,18]

Clinical experience suggested that addition of immunosuppressive drugs to glucocorticoid is indicated in the majority of the patients. Many experts recommended early introduction of immunosuppressive treatment in severe case with poor prognosis and also in order to reduce the side effect of long-term glucocorticoid treatment such as steroid myopathies, osteoporosis, cataract, aseptic necrosis, etc.[7,14,15] Azathioprine, a purine analog that inhibits purine synthesis resulting in inhibition of deoxyribonucleic acid (DNA), ribonucleic acid (RNA), and protein synthesis, may decrease proliferation of immune cell leading to lower autoimmune activity. Chloroquine phosphate inhibits chemotaxis of eosinophils and locomotion of neutrophils as well as impairs the complement-dependent antigen-antibody reaction.[12,19] Intravenous immunoglobulin (IV IG) has been used in patients who are refractory to steroid-sparing treatment. IV IG has been shown to have positive effect on myopathy. The dose recommendation of 2 g/kg BW should be repeated six weeks depending upon clinical response. Rituximab have been seen effective for DM and the result of large controlled ongoing studies are being expected.[2,5,8,12,18]

A variety of medical, rehabilitation, and interventional treatments are used to treat inflammatory-myopathy associated dysphagia. Medical treatment emphasizes the control of disease process; whereas rehabilitation focuses on swallowing compensation techniques, exercises, and diet modification. Interventional measures include cricopharyngeal or esophageal

dilation, cricopharyngeal myotomy, and botulinum injections of the upper esophageal sphincter. Although some studies frequently find procedures such as cricopharyngeal myotomy is beneficial, however, the application of rehabilitation measures is far less clear. Swallowing compensation techniques also have an important role to play. Percutaneus endoscopic gastrostomy (PEG) tube insertion may be required if swallowing remains unsafe but the highest mortality has been described in such patients.[1]

Glucocorticoid therapy for our patient was initiated with methylprednisolone at a dose of 1 mg/kg/day (3 times 16 mg/day). For the first four to six weeks of therapy, methylprednisolone was continued at 1 mg/kg/day with ongoing assessment of the clinical response. After that, we will taper the dose. Maintenance of steroid dose at 1 mg/kg per day should not persist beyond six weeks because of the potential for the development of glucocorticoid myopathy. After four to six weeks at the initial dose, the steroid tapering down should begin.

Treatment for skin disease with sun avoidance and hydroxychloroquine has been beneficial. Rehabilitation and physical therapy are important in management of myositis. Physical exercise now has been recommended as combination therapy together with immunosuppressive treatment. Combining exercise with immunosuppressive therapy is safe and has clear beneficial effect on muscle function.[4,5,14,18]

Our patient took sun protection cream and steroid topical for his skin. For physical therapy, he did exercise supervised by the physician from the rehabilitation medic department. The goal of therapy was to improve muscle strength; thereby, improving the function in daily activities and ameliorate the extra-muscular manifestations. When strength improves, the serum CK level reduced concurrently, however the reverse is not always true. CK level is used to monitor disease activity, but the level may have poor correlation with clinical disability. Unfortunately, there is a common tendency to "chase" or treat the CK level instead of the muscle weakness, a practice that has led to prolonged and unnecessary use of immunosuppressive drugs and erroneous assessment of their efficacy.[5]

After treatment, the general condition of our patient has become better, the patient could consume food by oral route and the weakness slowly disappeared. From laboratory results, we found that the AST has decreased to 75 U/L and ALT has decreased to 44 U/L. CK, LDH, aldolase, AST, and ALT are the muscle enzymes that routinely been measured in the evaluation of myopathy.

The prognosis of dermatomyositis depends on the severity of the myopathy, the presence of malignancy, and/or the presence of cardiopulmonary involvement. Patients with dermatomyositis who have malignancy, cardiac involvement, or pulmonary involvement and those elderly patients with dermatomyositis (> 60 years) have a poorer prognosis. The disease may show spontaneous remission in approximately 20% of patients. About 5% of patients have a fulminant progressive course, with eventual death. Therefore, many patients require long-term therapy.[11]

The presence of dysphagia in patients with myositis infers higher mortality rate. Williams et al confirm the poor prognosis of this association. Despite multidisciplinary care of such cases, 31% of patients in their study died of their disease within 12 months of diagnosis and the mortality relates mainly to respiratory complications.[4] After optimal therapy of immunotherapeutic agents we expect resolution of dysphagia in patients with myositis.

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