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Case Report

Successful management of a 7-year-old female with juvenile dermatomyositis at a tertiary hospital in low-income country

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Juvenile dermatomyositis (JDM) is a rare chronic autoimmune disease belonging to idiopathic inflammatory myopathies. Pathological skin lesions and proximal weakness primarily characterize this entity, but clinical symptoms can be heterogeneous. Children are more likely to have long-term complications such as lipodystrophy, calcinosis, and vasculopathy. Calcinosis is one of the characteristic sequelae of JDM, despite recent advances in the treatment of JDM, about one-third of patients still develop dystrophic calcinosis. In low-income countries, the availability of medicines is very limited. In our case, a 7-year-old female diagnosed with JDM presented with calcinosis. Aggressive and adequate treatment with steroids, methotrexate, hydroxychloroquine, and aluminium hydroxide can treat the complications. It is challenging to establish an early diagnosis, treatment, prevention of long-term complications, and improved prognosis of JDM, which then will improve the patient's quality of life, especially in low income countries with limited drug availability. **[Paediatr Indones. 2024;64:X; DOI: https://doi.org/10.14238/pi64.6.2024.X]**.

Keywords: *Takayasu arteritis; vasculitis; hypertension; pediatric; percutaneous transluminal angioplasty*

Juvenile dermatomyositis (JDM) is a rare childhood systemic autoimmune disease characterized by unexplained chronic and proximal weakness and rash due to skin inflammation.[1] Juvenile dermatomyositis or juvenile polymyositis is part of idiopathic inflammatory myopathies (IIMs), it is a group of autoimmune muscle diseases with varied organ involvement and the most common inflammatory myopathy in children, accounting for about 85% of cases. Girls are more affected than boys at 2.3:1 ratio. The average age of onset is about 7 years.[2,3] Gottron's papules and heliotrope rashes are disease characteristics and can help confirm the diagnosis. Although the disease has many heterogeneous symptoms, calcinosis, abnormal deposition of insoluble calcium salts on the skin, subcutaneous tissue, or muscle, is probably the characteristic of the disease.[4]

Pathogenesis of JDM is an immune attack on the capillary endothelium of muscles, infiltration of plasmacytoid dendritic cells as a consequence of type I interferon response, and upregulation of major histocompatibility complex (MHC) class I on the surface of muscle fibers.[5] The clinical manifestations of JDM were first described in 1887. In late 1975, Bohan and Peter established five criteria for diagnosis. The diagnosis of possible JDM requires the presence of a pathological rash (Gottron's papules on the surface of the extensor muscles of the knuckles, elbows, knees, or ankles) or heliotropic rash and two other criteria. Definitive JDM requires a characteristic rash with three additional criteria. Generally, the first two criteria (proximal weakness and classic rash) are almost

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always present. Criteria 3 (i.e., increased serum levels of myoenzyme), 4 (i.e., changes in electromyography (EMG)), and 5 (i.e., histopathological changes) provide additional laboratory support for diagnosis.[6]

The case

A 7-year-old-girl came to the allergy immunology outpatient clinic with a chief complaint of body weakness. There was weakness in the legs for 2 years and getting worse since 4 weeks before the hospital visit. The weakness with pain in the thigh when walking has occurred since the first month, but now the pain was no longer exists. There was no fever, no leg stiffness, either swelling of the joints. She had difficulty bending her leg, squatting, and climbing stairs, but could wear her clothes independently. There was reccurent redness near the right eyelid and a wound in the right elbow area for 1 year, without history of trauma. There was no body weight gain for 1 year.

From the physical examination, we found a female with a body weight of 16 kg, body height of 116 cm, body surface area of 0,733m^2. The anthropometric measurements were plotted on the CDC growth chart. The CDC growth chart revealed weight for age at <P5, length for age at P10-25, weight for length at P5, 81% from ideal body weight.

Inspection of the head and neck area revealed no pallor, jaundice, cyanotic, or tachypnea. We found swelling and reddish-purple rash around both eyelid areas, as a heliotrope rash. Chest movement was symmetrical, with no retraction visible. Breath sounds were all vesicular without any rhonchi or wheezing. The first and second heart sounds were normal, with no murmur or gallop. Abdominal examination revealed a normal sound of bowel movement, and no hepatomegaly or splenomegaly was palpable. The female genitalia and anal were normal.

From the local examination, there was heliotrope rash in both edge eyelid areas, swelling, and redness of the periorbital (**Figure 1**). We found flat-topped, erythematous to violaceous papules and plaques at both elbow and fingers as a gottron's papules (**Figure 2**) also calcinosis in the elbow and both tight. There were deformities in the extremities. It was found that both legs were asymmetrical. The left leg looked longer.

We did not find any meningeal sign from the neurological examination, but motoric strength was lower (2/5) at the proximal extremity of both legs and

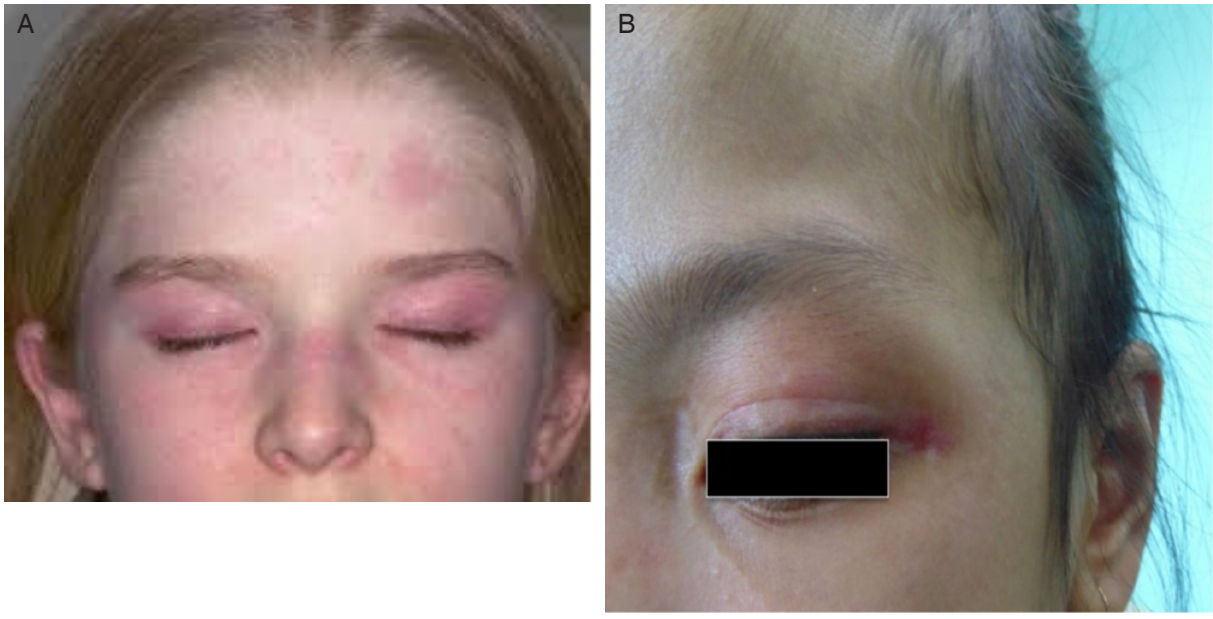

Figure 1. Erythematous rash around the left eye (heliotrope rash)
A. Illustration of heliotrope rash, B. Heliotrope rash in our patient

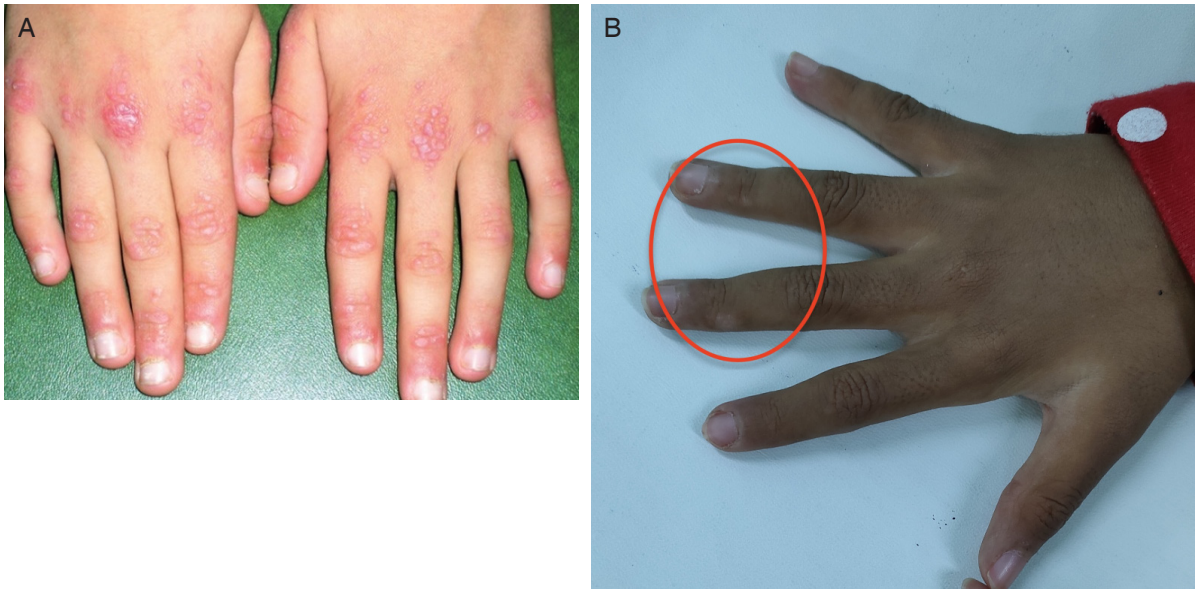

Figure 2. Gottron's papules
A. Illustration of Gottron's papules, B. Gottron's papules in our patient

hand. From the *paediatric Gait Arms Legs and Spine* (pGALS) examination, we found that the patient had asymmetrical legs. The spine examination revealed that the patient looked tilted to the left. We found calcinosis in the hand, elbow, and thigh. She scored 25/52 on the *Childhood Myositis Assessment Scale* (CMAS-14).

Laboratory evaluation revealed normal complete blood count (Hb 10.9 g/dL, WBC 7,290/L, platelet count 348,000/L), prolonged ESR (2-30 mm/h), normal CRP (<10 ng/L), normal CK (<190), high CK-MB (3.83 ng/mL), normal complement C3 and C4 (124mg/dL and 20.4 mg/dL, respectively), normal ANA test (<40 AU/mL), normal anti dsDNA (<30 IU/mL), and high LDH (323 U/L). Hip and thigh imaging (**Figure 3**) showed parenchymal soft tissue calcification at right L4-5 and calcification in soft tissue at the level of the proximal right and left femur on the lateral side, at the level of the right and left femur proximal to the distal side of the medial side, which is suspicious for soft tissue calcification in juvenile dermatomyositis. The results of the electromyography showed clinical axonal motor polyradiculoneuropathy with muscle denervation. MRI of the femur (**Figure 4**) revealed diffuse high signal intensity in musculus gluteus maximus bilateral, musculus vastus lateralis at intermedius et medialis bilateral, musculus adductor longus, musculus adductor brevis, musculus magnus bilateral, and musculus biceps femoris bilateral.

From tissue biopsy, we found greyish and solid tissue. The epidermal layer was found to have an atrophic appearance with basal cell vacuolar degeneration (**Figure 5**A). We performed a biopsy because it can help confirm JDM by revealing characteristic features like fiber degeneration, inflammation, and the presence of immune cells around blood vessel and within muscle tissue. It provides evidence inflammation and damage specific to JDM, which is crucial for differentiating it from other muscle diseases or conditions with similar symptoms. Biopsy offers a more precise picture of structural damage. The dermis layer was found to have lymphocytic inflammatory cell infiltration along the epidermal junction (**Figure 5B**). The results accord with the description of dermatomyositis.

We assessed this patient for juvenile dermatomyositis based on the history taking, physical examination, laboratory, and radiology findings. However, in our country, intravenous immunoglobulin (IVIG) is not included in the national health insurance system. In addition, probenecid is also not available. Therefore, this patient got prednisone

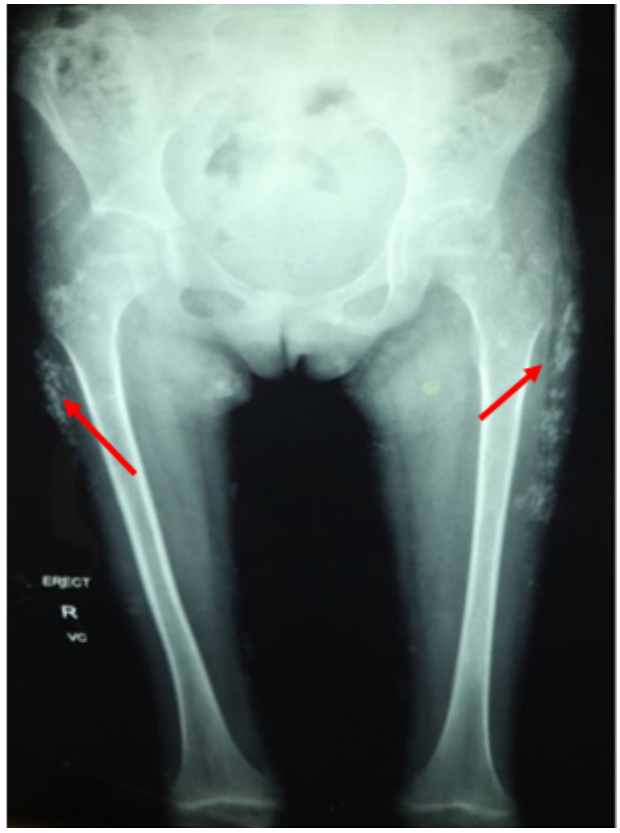

Figure 3. Plain X-ray showed soft tissue calcification in JDM

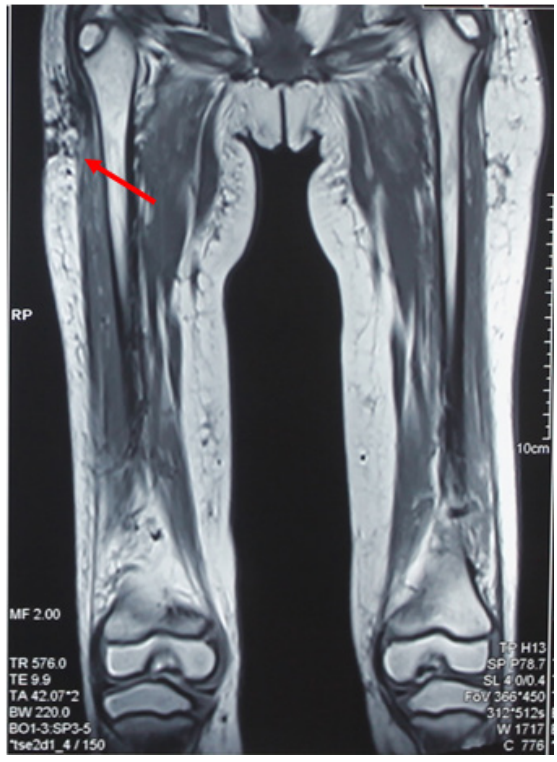

Figure 4. MRI of proximal legs showed hyperintense signal

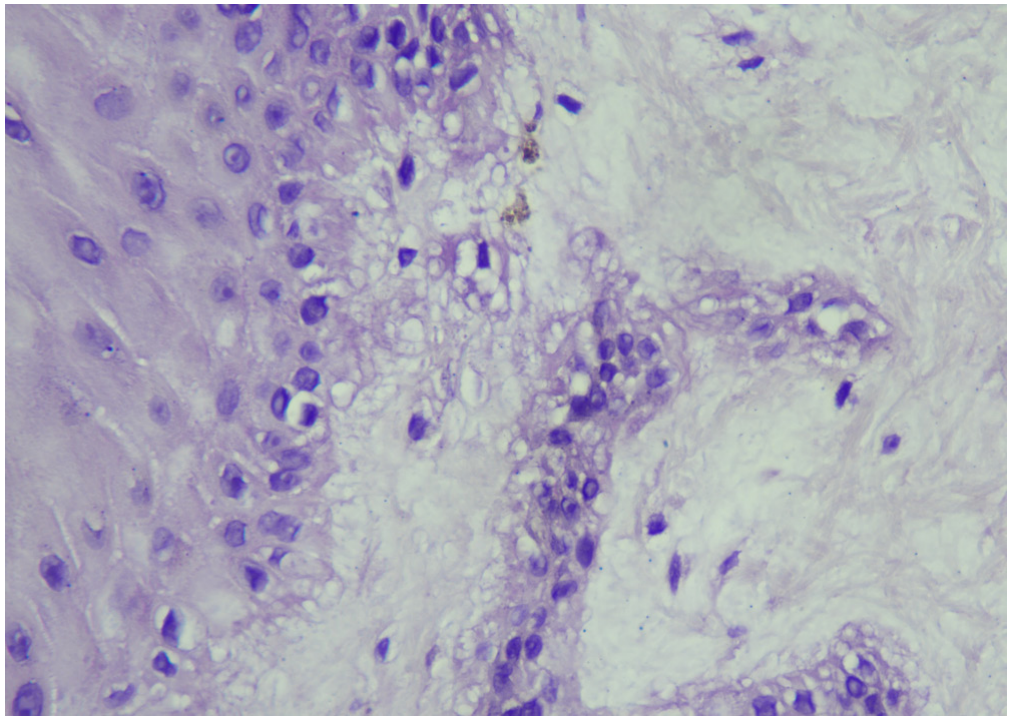

Figure 5A. Basal cell vacuolar degeneration of femoral area

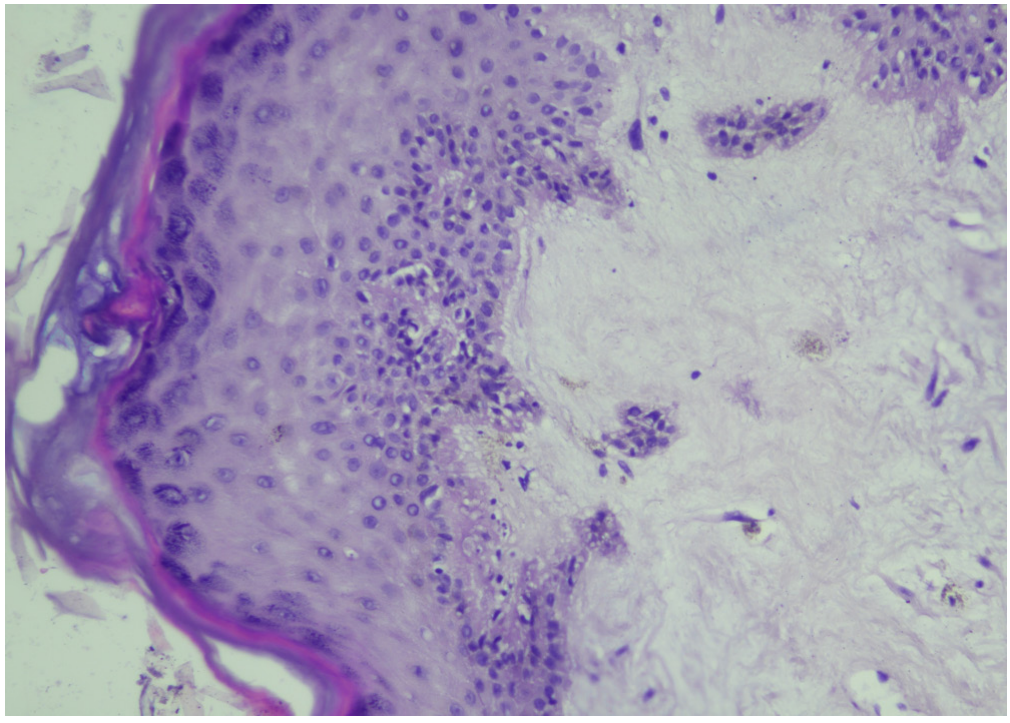

Figure 5B. Histopathology of dermal layer showed inflammatory cell infiltration along the dermoepidermal junction

5mg 6-0-0 tablets (2 mg/kg/day), methotrexate 2.5 mg 4 tablets every week (~15mg/m^2/week), folic acid 5 mg, vitamin D3 1x1000 IU tablets, calcium 2x500mg, hydroxychloroquine 1x100 mg, aluminium hydroxide 4x10 mL, as medical therapy. The patient also consulted with the Medical Rehabilitation Department to get physiotherapy management. After following up for 9 months, there was improvement in calcinosis and proximal motoric strength (4 out of 5). The laboratory results also returned to normal value. All examination procedures and therapies were done after receiving consent from the patient's guardian.

Discussion

Idiopathic inflammatory myopathies are a rare group of systemic connective tissue diseases. Symmetrical chronic inflammation and weakness of the proximal muscles are characteristic of these disorders. The most common inflammatory myositis in children is juvenile dermatomyositis. The most common age onset of JDM is 7-year-old, and it predominantly happens in females. It is characterized by weakness of the proximal muscles and characteristic skin symptoms, but the early signs are different and undetectable, making it difficult to get an early diagnosis. If the muscle weakness progresses, it can be difficult for the patients to climb stairs, comb hair, and be unable to roll in bed. Muscle weakness also may occur in the flexors of the neck.[2,7-10]

The most common skin features are heliotropic discoloration, papules or Gottron's signs, and capillary changes in nail folds. Calcification is often associated with a late diagnosis and the longer duration of untreated disease. Fever, weight loss, fatigue, myalgia, arthritis, lymphadenopathy, and abdominal pain are constitutional symptoms known to be associated with JDM. Damage to the gastrointestinal tract can cause vasculitis and intestinal perforation. Similarly, shortness of breath may occur due to airway involvement in the form of interstitial lung disease, pneumonia, or respiratory failure. Large organ involvement, severely debilitating, and ulcerative skin disease put patients at high risk, and these patients require urgent care and treatment under the supervision of a specialist. The characteristic rash facilitates early diagnosis but should be distinguished from other connective tissue disorders such as systemic lupus erythematosus.[8,11-14]

A pathognomonic rash such as heliotrope rash and Gottron's papule is required to diagnose JDM (according to the criteria made by Bohan and Peter), and 3 of 4 muscle features such as symmetrical muscle weakness, evidence of myositis on muscle biopsy, elevated serum levels of muscle enzymes, and myopathies on EMG. Muscle enzyme measurements should include CPK, lactate dehydrogenase, alanine aminotransferase, and aspartate aminotransferase.[3,15]

The diagnosis of JDM requires strong clinical suspicion. A negative result on an initial test does not rule out a diagnosis of JDM. Muscle enzymes may be normal in many cases. Muscle biopsies are rarely done for children with JDM due to the availability of MRI.[16] MRI T2-weighted imaging provides a non-invasive method to evaluate inflammation, it now replaced the gold standard of invasive muscle biopsy tests.[15,17]

The JDM treatment plans based on *Children's Arthritis and Rheumatology Research Alliance* (CARRA) working group include hydroxychloroquine 5 mg/kg/day (up to 400 mg) as monotherapy for treatment option A. Treatment plan B includes the addition of parenteral methotrexate (preferred) at a dose of 15 mg/m2 or 1 mg/kg (up to 40 mg) once a week. Treatment option C includes oral corticosteroids (prednisone 1-2 mg/kg/day up to 60 mg) in combination with weekly methotrexate and daily oral hydroxychloroquine at doses similar to treatment option B. This patient used treatment option C. Oral aluminium hydroxide is administered at a dose of 10 mL four times a day. Clinical improvement in this patient occurred within 9 months.

Remission times have decreased due to a superior safety profile compared to monotherapy. Other medications, such as intravenous immunoglobulin, may be used in severe cases or when the response to existing treatments is inadequate, IVIG may be used in JDM, particularly in severe, refractory, or steroid-resistant cases. It is not always the first-line treatment but is an important option in managing difficult cases. However, those medicines are not available in health insurance in low-income countries. Calcium and vitamin D3 supplements are also prescribed to correct the loss of bone density. When the patient shows clinical improvement, the steroid should be gradually reduced.[9,15]

Mortality is less than 2%, but 51-73% of JDM presented with the disease after a mean follow-up of 16.8 years.[18] The disease remains serious and has higher mortality rates in developing countries. Delayed diagnosis and treatment are some of the most important factors associated with a poor prognosis and increased risk of calcinosis. Calcinosis occurs in approximately 40% of patients with JDM. Calcinosis is a dystrophic disorder that usually occurs in areas of damaged tissue where serum calcium and phosphorus levels are normal. The elbows, knees, torso, arms, feet, hips, and head are most affected but can occur almost anywhere on the body. The onset of calcinosis most often occurs 1 to 3 years after onset. Calcinosis is polymorphic and can appear in various forms. The calcium deposition on any surface area can lead to joint contracture and stiffness.[3]

Aluminum hydroxide can decrease the intestinal absorption of phosphate, which can lead to decreased serum calcium-phosphorus products and consequently decreased tissue calcium deposition. Several case reports have demonstrated that oral aluminum hydroxide therapy significantly improved JDM-related calcinosis after 8 months of treatment.[3]

Plain radiography is recommended as an initial imaging test to detect calcinosis. Calcinosis is one factor that is often used to evaluate myositis. Dysregulation of calcium metabolism-related proteins, local tissue injury, and active inflammation are thought to play a role in calcinosis. Calcinosis is also commonly associated with active JDM and the proinflammatory process surrounding the lesion. Several reports describe macrophage and proinflammatory cytokines, including interleukin-6 (IL-6), IL-1, TNF-α, soluble TNF receptors, neopterin, and IL-18. Many therapeutic strategies have been attempted to treat calcinosis in JDM, including drugs that affect calcium metabolism, anti- inflammatory drugs, and surgical resection.[2,3,15,19,20]

Establishing an early diagnosis, treatment, prevention of long-term complications, and improved prognosis of JDM is challenging. This, in turn, improves the patient's quality of life, especially in low income countries where drugs are limitedly available. Early aggressive treatment is the important key to a better prognosis.

Conflict of interest

None declared.

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