

Sodium thiosulfate for the treatment of calcinosis secondary to juvenile dermatomyositis

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ABSTRACT

We report the successful use of sodium thiosulfate in a patient with juvenile dermatomyositis complicated by ulcerative skin disease and progressive calcinosis. This therapy may have a role in improving calcinosis, even if more studies are necessary to determine the safety and efficacy of this treatment in juvenile dermatomyositis-related calcinosis.

Introduction

Juvenile dermatomyositis (JDM) is an inflammatory myopathy with a predilection for proximal muscles and skin. It is characterised by insidious progression of malaise, easy fatigue, muscle weakness, fever and rash that may predate diagnosis by 3 to 6 months (1, 2). Although many clinical studies have concentrated on muscular features, the cutaneous manifestations of JDM can be serious and difficult to treat and may progress to ulcerative disease and/or subcutaneous calcification, impacting seriously on quality of life in the long term (3). Current treatment of JDM includes early aggressive use of corticosteroids coupled with immunosuppressive drugs such as methotrexate, cyclosporine and intravenous immune globulins (IVIG) (4). Delay to diagnosis and inadequate treatment increase the risk of developing calcinosis. However, once established, this complication is difficult to treat.

Case report

We describe a case of JDM with severe skin manifestations including ulcerations and diffuse calcinosis. A Caucasian boy presented at the age of 3 years and 10 months with malaise, fatigue, arthralgia, heliotrope rash, Gottron's papules on PIP joints, elbows and knees, shawl sign, and periungueal telangiectasia. There was weakness of proximal muscles and elevation of aldolase (11.0 U/L, normal <7.3 U/L), while serum lactate dehydrogenase (LDH) and creatine kinase (CK) levels were normal. Magnetic resonance imaging (MRI) demonstrated diffuse muscle oedema of proximal muscles and electromyography showed a myopathic pattern. So a diagnosis of JDM was made and treatment with steroids pulses was started,

followed by daily oral steroids and hydroxychloroquine. During the following months, clinical manifestations and abnormal laboratory findings improved. However, skin ulcerations of the upper and lower extremities and widespread calcinosis appeared one year after the diagnosis. x-ray of extremities showed superficial diffuse nodules and plaques. The patient still had elevation of aldolase (19.3 U/L) and a Childhood Myositis Assessment Scale (CMAS) score of 35 out of 52, with a Manual Muscle Testing (MMT8) score of 50 out of 80. So treatment with subcutaneous weekly methotrexate was added, but the areas of calcinosis and ulcerations continued to spread, therefore alendronate was introduced (two years from disease onset), but with no benefit. On the basis of a published report (5), treatment with topical sodium thiosulfate was initiated. Thiosulphate was used initially at a 3% concentration, and subsequently increased to 10%, applied to the calcifications of the upper and lower extremities daily under occlusive dressing. For progressive clinical improvement, daily corticosteroid therapy was slowly tapered and subsequently stopped six months after the start of treatment with thiosulfate. Hydroxychloroquine and alendronate were also discontinued at the same time.

Nine months later, the clinical signs and symptoms improved, aldolase was in the normal range (7 U/L) and the Childhood Myositis Assessment Scale (CMAS) score was 50 out of 52, with a Manual Muscle Testing (MMT8) score of 79 out of 80. Moreover, a significant improvement of calcinosis and ulcerations was noted, as well as a lack of progression. Clinical photography, with the family consent, were taken before and after thiosulfate treatment (Fig. 1).

Calcinosis is one of the severe complications of JDM, and still occurs in up to 40% of patients, sometimes even within 6 months of disease onset. The pathogenesis of calcinosis is not well known, but it seems to be associated with inflammation. Proinflammatory cytokine polymorphism of TNF- α and IL-1 have been suggested as risk factors for the development of calcinosis (1). The depi-

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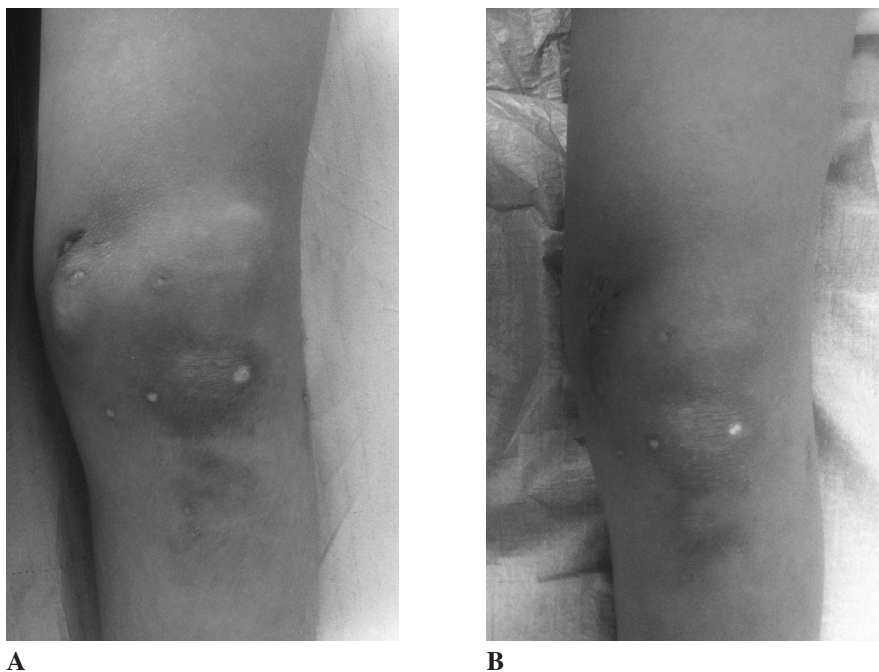


Fig. 1. **1A:** Nodules of calcinosis and skin ulceration on the right knee, before starting treatment with topical sodium thiosulfate.
1B: After 9 months of treatment with topic sodium thiosulfate, an improvement of calcinosis and ulcerations is shown.

tion of calcium, mostly around the joints and in the fascial planes, may cause more long-term disability than myositis itself. Earlier diagnosis and aggressive treatment to achieve rapid and complete control of inflammation, may minimise this complication (1). Several agents have been used for its treatment, such as calcium channel blockers, probenecid, colchicine, thalidomide, tumour necrosis factors inhibitors, bisphosphonates, and intra-lesional corticosteroids (6, 7). None of these however has shown to be consistently effective and no controlled trial exist.

Sodium thiosulfate is a potent antioxidant and vasodilator that also chelates

and dissolves calcium deposits (8-10). Topical use has been described for ulcerations associated with lupus calcinosis and uremic calciphylaxis (9). However, to our knowledge the use of this agent for treatment of calcinosis associated to dermatomyositis has been reported only once in literature (5).

We hypothesise that sodium thiosulfate may have had a role in improving calcinosis in our patient, although we cannot exclude that improvement of disease activity could also have played a role. A controlled study in order to determinate the safety and efficacy of this treatment in JDM-related calcinosis is currently ongoing.

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