

Successful Probenecid Treatment for Disabling Calcinosis Cutis in a Patient with Juvenile Dermatomyositis

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Abstract

Calcinosis Cutis (CC) is a common condition in juvenile dermatomyositis (JDM), it is disabling, severe and usually refractory to several therapies. A 14-year-old girl suffering JDM developed disabling CC which failed to oral steroids, methotrexate, diltiazem, alendronate, aluminium hydroxide and colchicine. Radiographs showed severe CC in different areas of the skeleton. Probenecid was used to reduce CC, resulting in a dramatic improvement and a calcification discharge by axillas and elbows. We suggest that probenecid may be useful in refractory CC associated to JDM.

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Introduction

Juvenile dermatomyositis (JDM) is a rare, inflammatory vasculopathic disease. Skin calcinosis (SC) is a frequently reported complication of juvenile dermatomyositis (JDM), appearing in 10-70% [1]. CC is commonly located on elbows, knees and distal areas, leading to significant weakness, pain, muscle atrophy, skin ulcers and disability [2]. Although spontaneous regression has been reported in several cases, no consistently effective medical therapy is available [3]. We report a 14-year-old girl with JDM and extensive disabling CC who improved after 2 year probenecid therapy.

Case Report

A 14-year-old Caucasian girl presented at our hospital with severe generalized calcinosis plaques. She had initially presented in a paediatric hospital in 2002 with muscle weakness of the limbs, erythema of the eyelids (heliotrope patch), and laboratory studies showed following abnormal values: serum creatinine phosphokinase (CPK) 3611 IU/L (normal range 40-200), aspartate aminotransferase 232 IU/L (AST), alanine aminotransferase 97 IU/L (ALT); she was diagnosed from a JDM and was successfully treated by prednisone (less than 40 mg daily) and methotrexate (MTX) (25 mg weekly). After 2-year treatment, in 2004, she was impaired by extensive subcutaneous calcifications in her arms, axillas, limbs, trunk and buttocks (Figure 1a, 1b, 1c, 1d), leading great disability and restricted range of motion in all mentioned areas. She also had severe flexum contracture in both knees and ankles, and she needs to intensive physiotherapy care. We performed biopsy from an axillar lesion, showing a dermic fibrosis and hydroxyapatite deposits. She continued her immunosuppressive treatments and started diltiazem (240 mg daily) and colchicine (0.5 mg daily) in combination with aluminium hydroxide and alendronate (10 mg daily) for several months, but no improvement was detected. We started treatment with probenecid, at dosage of 1 gr daily, in October 2006. After 2-years treatment, she improved range of motion of all joints affected, and X-Ray studies showed fewer calcification (Figures 2a, 2b). Flexum contractures also improved leading better walking. Lesions from right elbow and both axillas suppurred each calcification (Figure 3). Serum phosphorus and calcium levels were maintained in normal range or slightly higher through follow-up (Table 1). She discontinued immunosuppressive treatments and only maintains 1 gr probenecid and low dose prednisone treatments.

Discussion

CC is commonly observed in JDM, affecting approximately 30-70% of children suffering JDM [4,5]. Pathogenesis of calcification is unclear, though it is thought to develop by release of mitochondrial calcium from damaged muscles into matrix vesicles, which then promotes mineralization [5]. Hydroxyapatite calcium phosphate deposits in the dermis and hypodermis produce CC with normal calcium and phosphorus levels. The calcinosis can progress although underlying disease remains in remission [5]. Early aggressive treatment of inflammatory disease is the best method of prevention calcinosis, with no consistently effective medical therapy being available [3]. Several treatments have been reported to be effective in treating CC: aluminum hydroxide, warfarin, colchicine, biphosphonates, diltiazem, intralesional corticosteroids injection, infliximab, and probenecid [2,6-14]. We present a patient who developed severe and worsening CC despite adequate therapy of her underlying JDM with prednisone and MTX. Treatment with diltiazem, aluminium hydroxide in combination with colchicine and alendronate was unsuccessful. We started probenecid obtaining an amazing beneficial effect, with a decrease of the motor limitation improving her everyday activity, school assistance and self-esteem. We assessed the improvement by radiographs, and the efficacy continued in follow-up, maintaining probenecid therapy with no adverse event. We associate the response to probenecid by its ability to decrease serum phosphorus while leaving serum calcium levels unchanged and an increased renal phosphate excretion. This condition probably leads a decreased calcium deposition, though it is unclear how this mechanism results in fewer calcifications [15,16]. Our patient also showed a discharge of calcifications in axillas and elbows, helping in motion improvement.

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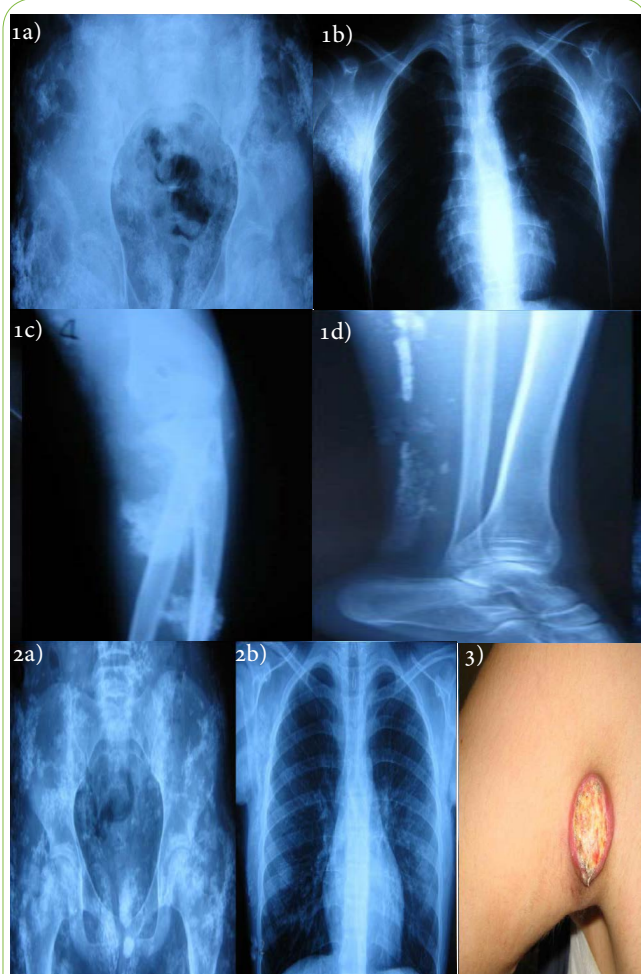


Figure 1. Compilation of patient's body X-rays and arm pictures before (1a, 1b, 1c and 1d) and after (2b, 2c, 3) Probenecid treatment.

	Serum Calcium (mmol/L)	Serum Phosphorus (mmol/L)	Urine Calcium (mmol/L)
Before treatment	2.43	1.71	0.40
After treatment	2.30	1.38	0.50

Table 1. Patient's Serum Calcium, Phosphorus and Urine Calcium before and after Probenecid treatment.

*Normal Range (mmol/L): Serum Calcium 2.15-2.55; Serum Phosphorus 0.87-1.45; Urine Calcium 1.70-5.30

In summary, we present the effectiveness of probenecid for CC in a JDM patient with a dramatic improvement in pain, range motion and radiographs. This suggests a beneficial effect of probenecid as treatment of CC. However, there are no reports of absolute efficacy and randomized controlled trials are difficult to achieve.

Competing Interests

The authors declare that they have no competing interests.

Author Contributions

All the authors substantially contributed to the study conception and design as well as the acquisition and interpretation of the data and drafting the manuscript.

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