

CASE REPORT**A CASE OF 13-YEAR-OLD GIRL WITH PROLIDASE DEFICIENCY****Arshad Khushdil, Fatima Murtaza**

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Prolidase deficiency is a rare autosomal recessive disorder characterized by recurrent and non-healing skin ulcers along with facial dysmorphism and mental retardation. We report a 13-year-old girl who has clinical manifestation of Prolidase deficiency. It is a very rare disorder and no such case has been reported so far from Pakistan.

Keywords: Autosomal recessive disorder; Prolidase deficiency; Facial dysmorphism

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INTRODUCTION

Prolidase deficiency (PD) is a rare autosomal recessive disorder of proline and hydroxyproline metabolism.¹ It presents with a variety of signs and symptoms, the most common being the dermatological manifestations.² About 50% of the patients present with pedal ulcers at presentation which are resistant to treatment and heal with irregular scar formation. It is also associated with various dysmorphic features, recurrent chest infections, mental sub normality, anaemia and organomegaly, most commonly splenomegaly.³

Prolidase enzyme breaks down the iminodipeptides that have proline and hydroxy proline. Due to the deficiency of this enzyme, there is an increased urinary excretion of proline and hydroxy proline. The lack of proline in body leads to poor wound healing and ulcer formation.⁴ We present a 13-year-old girl who presented with classic clinical features of PD.

CASE REPORT

A girl of 13 years' age presented to our OPD, on 3rd February 2016, with complaints of multiple erythematous ulcers on anterior surface of right leg for the last 8 years which were associated with oozing of clear watery fluid. She was asymptomatic until one year of age when she developed an ulcer on the dorsum of the right foot along with oozing of clear watery fluid. The lesion kept on extending despite multiple home-made remedies as well as topical and systemic medicines prescribed by different physicians (Figure-1). She also had crusted erythematous plaques on left forearm and left lower leg just above the lateral malleolus, for the last two years. The lesion finally healed with a depigmented scar. Her parents were consanguineous and two of her other siblings had similar condition. Previously she was labelled as a case of mycetoma and treated with different antifungal and topical medication with no relief of symptoms.

The girl had stable vital signs with a pulse rate of 76 beats per minute, Blood pressure of 110/70

mmHg, and respiratory rate of 16 /minute. Her weight was 43 kilograms and height of 120 cm. Both were below the third centile for age and gender. She also had multiple chronic recurrent deep cutaneous ulcers bilaterally on lower legs having ragged margins, floor covered by a yellowish exudate later drying to form adherent yellowish crusts, not fixed to underlying tissue (Figure-1). There was no lymphadenopathy, or varicosities and normal peripheral pulses. Other dermatological manifestations included dry crusted lesions on face, multiple atrophic macules and linear telangiectases on malar regions of face, multiple small atrophic hyperpigmented macules on extensors of extremities and buttocks, matt like telangiectases on knees and lower legs and dry fissured palms and soles. Photosensitivity was not reported.

Other manifestations were facial dysmorphism (saddle nose, hypertelorism, mal-aligned teeth, high arched palate (Figure-2) but no simian crease, mild mental sub-normality, frequent chest, ear and wound infections, partial deafness and short stature. There was also massive splenomegaly extending up to the umbilicus. Rest of the systemic examination was unremarkable.

Her complete blood count (CBC) showed microcytic, hypochromic anaemia with Hb of 7.5 g/dl, normal platelet and white cell count. Her renal function and liver function tests were within normal limits as was her chest x-ray. Her abdomen ultra sound revealed splenomegaly measuring 32.2 cm along with mild hepatomegaly.

On the basis of her facial dysmorphic features, typical ulcers especially on lower limbs, partial deafness, recurrent infections, short stature, microcytic anaemia, and splenomegaly, she was diagnosed as a case of Prolidase deficiency. The definitive diagnosis of PD requires demonstration of decreased prolidase activity in erythrocytes, leukocytes and skin fibroblasts as well as increased urinary excretion of proline and hydroxyproline iminodipeptides. But these facilities are not yet available in Pakistan.



Figure-1: Ulcers on leg



Figure-2: Facial dysmorphism

DISCUSSION

The first case of PD was described by Goodmen, *et al*, in 1968 in a male patient who had characteristic recurrent non-healing ulcers on lower legs and mental retardation.⁵ The gene for the PD enzyme is located on chromosome 19⁶. It is a very rare disorder with an overall incidence of 1–2 per 1000,000 individuals. So far only 93 cases have been reported in the English language literature.⁷ Our search of the literature revealed that no such case has been reported so far in Pakistan.

These patients have characteristic facial features such as saddle nose deformity, frontal bossing, dull expression, micrognathia, hypertelorism and mandibular protrusion. Apart from facial dysmorphism, these children have short stature, splenomegaly, joint laxity, high arched palate, erosive cystitis and mental sub normality. But the most striking and most common manifestation is the involvement of skin in the form of irregularly shaped ulcers with prominent granulation tissue most commonly involving the lower legs. These ulcers heal with characteristic scars which are pitting in nature. There may also be telangiectasia, dry crusted lesions on face and

extensor surfaces of lower limbs, dry erythematous fissured palms and soles and purpuric lesions.³ Also, patients with PD have increased incidence of infections due to splenic dysfunction. The splenic dysfunction is caused by the deposition of amyloid in spleen which is seen in patients with PD.⁸

Prolidase enzyme is required for the degradation of iminidipeptides which are the major degradation product of collagen. The decreased prolidase levels lead to increased urinary excretion of dipeptides, that is proline and hydroxyl proline, which in turn causes defective collagen synthesis and wound healing. The diagnosis of PD is confirmed by the demonstration of reduced levels of prolidase in erythrocytes, leukocytes or fibroblasts, and increased urinary levels of proline and hydroxy proline.⁴ There is no effective treatment for PD. Various topical and systemic treatment options have been used for the treatment of skin lesions with poor response.

Various treatment modalities which have been tried so far with variable results include dapsone, diphenylhydantoin, ascorbic acid and manganese, Pulsed corticosteroid, apheresis exchange, topical application of 5% glycine and 5% proline and blood transfusion containing manganese activated prolidase enzyme.^{9,10}

CONCLUSION

Prolidase deficiency is a rare autosomal recessive disorder, difficult to identify and diagnose and even difficult to treat. Formal evaluation of the affected patient by a competent dermatologist and paediatrician is required in order to start early treatment and more importantly, provide genetic counselling to the parents of affected patient, so that recurrence is prevented in the affected family.

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