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Oral Phosphodiesterase Type 5 Inhibitors in Recurrent Priapism Complicating Thalassemia Intermedia: A Case Report

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Abstract

Recurrent priapism is a rare, serious and difficult to treat complication of some hematological disorders, for which no standard therapy exists. This study reports a case of a 42-year-old man with thalassemia intermedia complicated by recurrent episodes of priapism. To prevent priapism recurrences, a trial of PDE5is use was initiated. One day after initiation of a PDE5i (25 mg sildenafil repeated every 8 hours), priapism was improved. For 3 weeks, the patient reported improvement, without experiencing any episodes of priapism and a normal physiologic erectile function. Four weeks after treatment he experienced priapism reoccurrence and doubling of the Sildenafil was not effective. Gonadotropin-releasing hormone agonist initiated and one week after initiatin of new drug he improved. He was free of priapism episodes for more than 2 years afterward. PDE5 deregulation seems to be an underling pathologic mechanism of recurrent priapism at least in thalassemia intermedia patients. It appears that PDE5is may have a role in the management of such patients and further testing in clinical trials is needed.

Keywords

PDE5is, Reccurent Priapism, Thalassemia Intermedia, PDE5is for Priapism, Gonadotropin-Releasing Hormone Agonist for Priapism

1. Introduction

Priapism is an abnormal persistent erection of the penis. It is an undesired prolonged erection unrelated to sexual stimulation and unrelieved by ejaculation [1].

Stuttering or recurrent priapism is characterised by spontaneous and prolonged erections, lasting up to 3 hours,

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which usually ends with spontaneous penile detumescence [2]. Recurrent priapism is encountered in patients with sickle cell disease [3]-[5]. A few case reports of recurrent priapism occurring in thalassemia intermedia especially after splenectomy [6] [7], hemoglobin-E beta thalassemia [8], hereditary spherocytosis [9] and glucose-6-phosphate dehydrogenase (G6PD) deficiency [10] [11] have been documented in the literature.

Recurrent priapism is a rare but serious and difficult to treat condition. The pathophysiology of this type of priapism is not fully elucidated [12] [13]. A mechanism based on dysregulation of Nitric oxide and phosphodiesterase type 5 in the corporal smooth muscle has been proposed [2] [14]-[16]. Yet no standard therapy exists for the prevention of recurrent ischemic priapism [17] [18].

2. Case Report

A 42-year-old male patient with thalassemia intermedia was admitted with recurrent episodes of priapism. He underwent splenectomy at age 23, for enlarged spleen and increased red blood cell transfusion demand, since then he had received transfusions no more than once every three months. He has received deferoxamine infusions regularly. He is married and has three children. He had been facing frequent episodes of priapism on a daily manner for 6 years which mandated multiple decompressive procedures. During the last two years, he had experienced one or two episodes of priapism each day, and lost his social acts and was bedridden. These episodes occurred after midnight every night and sometimes in the afternoon, and were unrelated to sexual arousal or activity. He was a cigarette smoker and had chronic bronchitis.

On physical examination, he had pallor, icterus, diffuse wheezing. The penis was circumcised with multiple scars of decompressive punctures.

His hemoglobin was 10.5 g/dl, he matocrit 34%, MCV 65 fl, platelets 274 × 10^9/L, and WBC 6.9 × 10^9/L. Peripheral smear showed poikilocytosis, hypochromia, microcytosis and nucleated RBCs without any sickle cells. Hemoglobin electrophoresis showed Hb A, A_2 and F to be 94%, 5.6% and 0.4% respectively. His serum ferrittin level was 1750 ng/ml.

His clinical picture, blood count, peripheralsmear and electrophoresis were consistent with thalassemia intermedia.

He was treated with sildenafil, a PDE5is, 25 mg every 8 hours. The day after initiation of sildenafil priapism did not occur and on the third event free day the patient was discharged. For 3 weeks, the patient reported improvement, without experiencing any episodes of priapism and a normal physiologic erectile function. Four weeks after treatment he experiences priapism reoccurrence and doubling of the Sildenafil was not effective. Gonadotropin-releasing hormone agonist initiated and one week after initiatin of new drug he improved. He was free of priapism episodes for more than 2 years afterward, albeit with the loss of libido and erectile function.

3. Discussion

Recurrent priapism is a very uncommon, serious and difficult to treat complication of some hematological disorders, for which no standard therapy exists.

Episodes of recurrent priapism are treated by home intracavernous self-injections of the alpha-adrenergic agonists [19] [20]. This treatment needs patient admission for verifying drug effectiveness, dose adjustments and patient training on the self-injection procedure.

A few medications are reported to be effective in prevention of recurrences, including phosphodiesterase type 5 inhibitors (PDE5is) [4] [14], gonadotropin-releasing hormone agonists [21], antiandrogens [22] [23], ketoconazole plus prednisone [18], oral gabapentin [24] and baclofen [25]. Most reports are based on small trials or case reports. Gonadotropin-releasing hormone agonists, antiandrogens, and ketoconazole plus prednisone, as hormonal manipulations, have been successful in preventing episodes of priapism, but may be associated with the loss of libido and erectile function as seen in this case.

Gabapentin and baclofen have been used successfully to prevent episodes of priapism, but have no clear correlation with its pathophysiology.

Nitric oxide serves a fundamental role in the erectile response by mediating relaxation of smooth muscle. PDE5 inhibitors inhibit breakdown of cGMP and potentiate nitric oxide-mediated penile smooth muscle relaxation for erectile function. A regulatory defect in the nitric oxide pathway has been proposed to account for some patients with priapism, particularly those with sickle cell disease [2] [10] [12] [15]. Successful use of PDE5is in preventing episodes of recurrent priapism has been reported, in sickle cell disease-associated, idiopathic and

thalassemia intermedia-associated priapism.

This case of thalassemia intermedia-associated recurrent priapism, treated with PDE5is, supports the findings of two previous reports on the effectiveness of PDE5is in recurrent priapism. However, PDE5is didn't prevent episodes for long term.

These observations may show that PDE5 deregulations have a pathogenic role in recurrent priapism. Although it is suggested that PDE5is therapy may be a useful preventative strategy for recurrent priapism, additional evaluation is needed. Gonadotropin-releasing hormone agonist was preventative in this case as reported before that.

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