Recurrent priapism in Sickle Cell Trait with Protein S deficiency

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Abstract

We report the case of a young Omani man, a regular blood donor, who presented twice in two months, with painful penile erection lasting more than 12 hours. The patient is known to have sickle cell trait [HbS 34.6%]. Although the first episode of penile erection settled with aspiration of blood and local injection of epinephrine, on the second occasion necessitated cavernosal glandular shunting. A subsequent investigation revealed a mild protein S deficiency. Although priapism is known to occur in sickle cell disease, it is unusual in sickle cell trait. Association of mild protein S deficiency with erythrocytosis could have precipitated the onset of priapism.

Introduction

Priapism is defined as prolonged and persistent erection of the penis without sexual stimulation. It is seen in a number of conditions that cause disturbance of blood flow to penis such as in ischaemic vessel disease, elevated white blood cells (WBC), polycythemia, essential thrombocythaemia and sickle cell disease.[1,2] Priapism can also be caused by haematologic malignancies associated with hypercoagulation, metastatic disease involving the corpora cavernosa with thrombosis of the venous outflow from the penis, or fat embolism, or rarely from intracavernous injections of papaverine and phentolamine used for the treatment of impotence.[3-5] Rarely, it is also seen in patients receiving drugs like oral anticoagulants, LMWH, cocaine and sildenafil.[6-9] Although sickle cell disease is a recognized cause of priapism, sickle cell trait [SCT] is not known to cause it per se.[10] Incidentally, while searching for an underlying cause the patient was also found to have protein S deficiency.

Case report

A 28 year old healthy Omani male presented with a history of penile erection of 12 hours duration. He denied history of any unusual sexual activity, perineal trauma or straddle injury or drug abuse like sildenafil or cocaine prior to the onset of the episode. Physical examination was unremarkable except for the tender penile erection. His initial investigations showed a haemoglobin of 15.2 g/dl with a haematocrit of 0.46 L/L, red blood cell count was 5.32 $x10^{12}$/l, WBC was 9.91$x10^{9}$/l, with a normal differential, and platelet count was 256$x10^{9}$/l. Sickle cell screening test was positive and HPLC showed HbS level of 34.6%, with a HbA of 55%, HbA2 of 3.9%, and HbF of 0.3% suggestive of SCT. Routine biochemical investigations were normal. Penile aspiration was done by removing 20ml of blood from the corpus cavernosum,

followed by irrigation with 20mcg of epinephrine diluted in 5 ml of normal saline. This resulted in complete relief of priapism with a gradual relaxation.. After two months the patient presented again with priapism of more than 12 hours duration. Penile aspiration, followed by injection of epinephrine did not provide any relief. Venesection was performed. However, all these interventions did not resolve priapism, and a surgical intervention with the cavernosal glanular shunting became necessary. The patient was also started on low molecular weight heparin, empirically, to prevent the possibility of venous thrombosis. Priapism settled gradually. The patient had a relatively high haemoglobin (15.4 g/dl) hence investigations were carried out for an underlying cause. His leukocyte alkaline phosphatase score was raised at 245(35-100), serum ferritin 152 ng/ml, serum erythropoietin was elevated at 35.5 IU/L (10.2-25.2), thyroid functions were normal, lipid profile was normal with Serum triglycerides 37.3 mg/dl, Serum LDL 146.7 mg/dl (70-165), Serum HDL 32.8 mg/dl (31-63), total Serum cholesterol 196.9 mg/dl, blood sugar 109 mg/dl, immunoglobulin levels including IgM, IgG, and IgA were all normal with no monoclonal band. Ultrasound of abdomen and x-ray of chest was normal. Ultrasound of penis, after penile aspiration showed collapsed veins with no doppler flow [low flow veno-occlusive type]. Thrombophilia screen showed type 1 protein S deficiency. The functional protein S level was of 42 IU/dl (RR 77-143 u/dl), antigenic protein S was also low at 43 IU/dl (RR 70-140), with free protein S of 47 iu/dl (RR 70-140). A repeat study along with family screening was also carried out to confirm the protein S deficiency. The rest of his thrombophilia work up including protein C, antithrombin III, activated protein C resistance and factor V leiden were normal. Upon discharge the patient was lost to followup.

Comment

Priapism is seen in about 10-20 % cases of sickle cell patients at some time in their life, however, it is extremely rare in sickle cell trait, but it has been reported in haemoglobin C trait.[6,10,11] Similarly, although thrombophilic risk factors like protein C deficiency, factor V leiden, Bechet's disease have been documented to be associated with priapism,[12-14] an extensive literature search failed to show any reported association between protein S deficiency and priapism, as was seen in our patient.

It is also interesting to note that patient's haemoglobin was relatively high. Furthermore, he also had a high LAP score, high HCT, and elevated serum erythropoietin [EPO]. All these features are suggestive of a possible underlying uncharacterized myeloproliferative or myelodysplastic condition which could have contributed to a state of hyperviscosity leading to penile vessel occlusion and priapism. Therefore, we believe that the basis of priapism in our patient is most probably multifactorial; especially since priapism is a well known complication of patients with various myeloproliferative disorders with leukocytosis, polycythaemia and thrombocytosis.[1,5] Furthermore, erythropoitin-induced recurrent priapism has also been reported in a patient of end stage renal disease that responded to reducing the dose of erythropoietin.[15]

Conclusion

The incidental discovery of sickle cell trait and protein S deficiency is interesting; however, there is no information to suggest that these two relatively common factors contributed to the development of recurrent priapism. Infact, it is always prudent to actually look for all the possible underlying factors particularly when the priapism is prolonged and recurrent. This is an unfortunate scenario, but often it has been seen that once priapism develops it often recurs.

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