CASE REPORT

Clozapine Induced Priapism: Case Series

Thangam N, Farah Radhiah H, Sashitharan D, Abdul Kadir AK

**Hospital Permai, Jalan Persiaran Kempas Baru,
81200 Johor Bahru, Malaysia**

Abstract

Clozapine is effective in treatment resistant schizophrenia. Priaprism is a rare side effect of Clozapine. It is a urological emergency and can lead to permanent damage to the penis. We present two cases two cases of clozapine induced priapism. Both patients were started on Clozapine in view of treatment resistant. For the first patient, priapism was noted after 2 years on Clozapine and treated conservatively. Clozapine was rechallenged in this patient but in a lower dosage and was augmented with amisulpride. He did not develop priaprism until date. In the second case, patient developed priaprism after 7 months on clozapine and required urological intervention. He redeveloped recurrent episode of priaprism as clozapine was restarted on the previous dose. In conclusion, priaprism is not related to dosage or duration of treatment of Clozapine. Thus, a careful risk-benefit assessment need to done as there is always a risk of priapism to recur when clozapine rechallenged.

Keywords: Clozapine, Priapism, Urologist

Introduction

Clozapine is an atypical antipsychotic whose therapeutic effects were mediated by dopaminergic and serotonergic activity. It is effective for treatment resistant schizophrenia [1]. It has been shown to reduce the suicidality in schizophrenia [2-3] and is also useful in aggression. One of its rare side effects is priapism. An early case of priapism caused by clozapine was reported in 1992 [1]. Priapism is defined as sustained and persistent erection of the penis without any sexual desire or stimulation [5]. It is a urological emergency and can lead to permanent damage to the penis resulting in impotence, penile necrosis and urinary retention if left unattended. Priapism can be divided into a nonischemic type (high flow; arterial) which can be treated conservatively and an ischemic type (low flow; venoocclusive) which may become a urological emergency that requires immediate intervention [6]. Drug-induced priapism usually cause ischemic priapism accounting for 15% to 41% of all cases and antipsychotics-induced priapism is commonest. Clozapine has also been cited as to cause priapism apart from trazodone, chlorpromazine, and thioridazine [7]. This case series is on clozapine-induced priapism.

Case Scenario 1

This 34 years old male had Schizophrenia since 2007. He had been admitted in our setting from 2011 and developed priaprism after two years on clozapine. He had

previously been treated with adequate doses of risperidone, olanzapine and amisulpride but without much improvement. He was then started on clozapine November 2012. Clozapine was started as per protocol and was slowly tapered up to 350mg per day. He wasn't on any other medication. Patient awoke from sleep one day with a painful penile erection that started at 6am that day. He alleged that the penile erection occurred spontaneously and denies sexual activity that day. There was neither fever nor urethral discharge. He was still able to pass urine in the morning. He said that this was the second episode. The first episode occurred a few months earlier, lasted for six hours and spontaneously resolved. He denied taking any other traditional medication. His vitals were stable and the total white count was normal. He was given pain killer to control his pain and ice pack compression was done. Clozapine therapy was withheld and he was seen by the urologist who suggested changing the antipsychotic and conservative management. A shared decision between the patient and the psychiatrist was to continue clozapine therapy in view of previous treatment resistance. He was restarted on clozapine 100mg twice daily and was slowly titrated up to a total dose of 300mg due to persistant psychotic symptoms. Further augmentation with Amisulpride was needed to stabilize his condition. However, no recurrent episode of priapism was reported by the patient upon restarting the clozapine.

Case Scenario 2

This is a 27 years old male treated for Schizophrenia with Mild Intellectual Disability who was admitted in our setting from December 2016 for aggressive behaviour toward mother. He has been on follow up in another hospital from 2009. He had history of priaprism with Clozapine, IM Haloperidol and IM Paliperidone. Patient was started with Clozapine since January 2017 as patient did not show any improvement with sublingual Asenapine. Clozapine was optimized up to 325mg daily. In August 2017, patient developed spontaneous painful penile erection that lasted for hours. He was not on any other medication and denied sexual activity on that day. He was then referred to urologist and was diagnosed to have venous low flow priapism. Bedside aspiration was done and subcutaneous Lucrin was given. He was sent back to our setting and Clozapine was continued. Patient had recurrent episode of priaprism after 4 days. He was again referred to urology and treated conservative as it resolved spontaneously after few hours. Thereafter, Clozapine was withheld and no antipsychotic was started as patient is manageable in ward.

Discussion

Occurrence of priapism is thought to be related to alpha-adrenergic blockage mediated by the alpha receptors in the corpora cavernosa of the penis [8]. Clozapine is also an adrenergic antagonist. This adrenergic blocking action is seen in other drugs such as guanethidine, prazosin and trazodone which also noted to cause priapism. Corpora cavernosa is richly innervated by adrenergic fibers. These fibers maintain the penis in the detumescent state by means of vasoconstriction. Alpha Adrenergic blockade causes priapism by favoring erection, which is parasympathetically mediated, and by inhibiting the sympathetically mediated detumescence. This theory is proven by intracorporeal injections of relatively nonspecific a-adrenergic blockers such as phenoxybenzamine and phentolamine [9]. It has also been suggested that priapism may be caused by the central nervous system effects of psychotropic drugs by prolonged stimulation of the psychic centers [10]. This theory explains the delay in onset of priaprism in this patient.

Unfortunately, no correlation is found between dosage or duration of treatment and priapism in most cases of drug-induced priapism [11]. Priapism may be seen as an embarrassing condition by this patient as he admitted having a previous episode which he did not inform staff in the ward. Patients may find it hard to discuss about this openly in ward rounds and might require asking specifically about priapism. Decision making to rechallenge with clozapine was tough as there is a risk of priapism to recur. In such cases, a careful risk-benefit assessment involving the patient and significant others need to be done. Discontinuation of clozapine could lead to relapse and there will be limitation of antipsychotic choice in view of refractory schizophrenia. Patient should be informed regarding other options of antipsychotic medication and possibility of a relapse. Patient should be well informed on the possibility on recurrence of priapism and if it occurs to inform the staff or the clinician as soon as possible. Amisulpride and sulpride can be used for augmentation as it has no alpha-1 receptor affinity. In a nutshell, priaprism is a one of the rare but dangerous complications of antipsychotics which is a urological emergency and needing prompt intervention.

References

[1] Voruganti L, Cortese L, Oyewumi L, Cernovsky Z, Zirul S, et al. Comparative evaluation of conventional and novel antipsychotic drugs with reference to their subjective tolerability, side-effect profile and impact on quality of life. Schizophrenia research. 2000 Jun; 43(2):135-145.

[2] Baruch Spivak, Evgeny Shabash, Brian Sheitman, Abraham Weizman, and Roberto Mester. The Effects of Clozapine Versus Haloperidol on Measures of Impulsive Aggression and Suicidality in Chronic Schizophrenia Patients: An Open, Nonrandomized, 6-Month Study. J Clin Psychiatry. 2003;64(7):755-760.

[3] Meltzer HY, Alphs L, Green AI, Altamura AC, Anand R et al. Clozapine treatment for suicidality in schizophrenia: International Suicide Prevention Trial (InterSePT). Arch Gen Psychiatry. 2003 Jan;60(1):82–91.

[4] Seftelel AD, Saenz de Tejada I, Szetela B, Cole J, Goldstein I. Clozapine-associated priapism: a case report. J Urol. 1992 Jan;147:146–148.

[5] Keoghane SR, Sullivan ME, Miller MAW. The aetiology, pathogenesis and management of priapism. Br J Urol Int. 2002 June 24;90:149–154.

[6] Bivalacqua TJ and Burnett AL. Priapism: new concepts in the pathophysiology and new treatment strategies. Current Urology Reports. 2006 Dec; 7(6):497–502.

[7] Thompson JW Jr, Ware MR, Blashfield RK. Psychotropic medication and priapism: a comprehensive review. J Clin Psychiatry 1990; 51:430-433.

[8] Sood S, James W, Bailon M. Priapism associated with atypical antipsychotic medications: a review. Int Clin Psychopharmacol. 2008 Jan; 23(1): 9–17.

[9] Segraves RT. Effects of psychotropic drugs on human

erection and ejaculation. Arch. Gen. Psychiat. 1989; 46:275.

[10] Hinman F Jr. Priapism:reasons for failure of therapy. J. Urol. 1960 April, 83:420.

[11] Thompson JW Jr, Ware MR, and Blashfield RK. Psychotropic medication and priapism: a comprehensive review. Journal of Clinical Psychiatry. 1990 Oct; 51(10): 430–433.

Corresponding Author
Thangam Nagarethinam
Hospital Permai,
Jalan Persiaran Kempas Baru,
81200 Johor Bahru,
Malaysia

Email: than916@gmail.com