Clinical Image – Andrology
Grand J Urol 2023;3(3):121-3
DOI: 10.5505/GJU.2023.22932

The Synergistic Effect of Trazodone on the Development of Priapism in the Background of Chronic Myeloid Leukemia

Trazodonun Kronik Miyeloid Lösemi Zemininde Priapizm Gelişimi Üzerindeki Sinerjistik Etkisi

Sebnem Izmir Guner[1], Deniz Noyan Ozlu[2], Ekrem Guner[2]

[1]Department of Hematology and Bone Marrow Transplantation Unit, Gelisim University, Memorial Sisli Hospital, Istanbul, Türkiye
[2]Department of Urology, University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital, Istanbul, Türkiye

Cite as: Izmir Guner S, Ozlu DN, Guner E. The synergistic effect of trazodone on the development of priapism in the background of chronic myeloid leukemia. Grand J Urol 2023;3(3):121-3

Submission date: 29 May 2023 **Acceptance date:** 12 July 2023 **Online first:** 17 July 2023 **Publication date:** 20 September 2023

Corresponding Author: Deniz Noyan Ozlu / University of Health Sciences, Dr. Sadi Konuk Training and Research Hospital, Department of Urology, Istanbul, Türkiye
noyanozlu@hotmail.com / ORCID ID: 0000-0003-2435-5482

A 50-year-old male patient was admitted to our emergency department with the complaint of prolonged erection lasting for about three hours without sexual stimulation. As understood from the patient's anamnesis and medical file, he applied to the emergency department with the complaints of fever, lassitude, and fatigability in 2015. His hemogram parameters on admission were: WBC:18.2 x10^9/L, Hgb: 12.9 g/dl, Htc: 39%, PLT: 379 x10^3 K/µL. Besides, his lactate dehydrogenase (LDH) and uric acid values were elevated were found to be high, and he was referred to the hematology clinic with a preliminary diagnosis of leukemia. In the physical examination, any remarkable finding other than splenomegaly was not detected. Microscopic examination of his peripheral blood smear revealed the presence of platelet deformities, megakaryocyte fragments, normocytic normochromic erythrocytes, all cells of myeloid series, markedly increased number of basophils and eosinophils, myelocytes, metamyelocytes, rods and fragmented neutrophils.

It was learned from his medical documents that the patient received the diagnosis of "CML in chronic phase" based on the histopathologic examination reports of the bone marrow aspiration and biopsy specimens obtained for definitive diagnosis, Karyotype analysis revealed the presence of Philadelphia (Ph*) chromosome, and BCR/ABL chimeric gene was detected using PCR and FISH techniques. The patient diagnosed with CML received initial treatment with single daily oral doses of a first-generation tyrosine kinase inhibitor (imatinib 400 mg cap.) and allopurinol (300 mg tb) and he was called for outpatient control. The patient, who claimed that severe muscle and bone pain developed during the imatinib treatment stopped taking the drug by his own decision, so hematology physician started to give him second generation tyrosine kinase inhibitors in turn (nilotinib and dasatinib). However, it was observed that these drugs also caused severe pancytopenia, and treatment with single daily oral doses of 400 mg imatinib was started again. Still, it was noted that the patient used the drug irregularly, stopped using the drug from time to time and did not routinely attend the hematology outpatient clinics for control.

The patient stated that he had been prescribed trazodone HCl (50 mg/d PO) in another center due to the anxiety he had experienced and had taken the first dose the previous evening. The patient said that he had never experienced a spontaneously prolonged erection before and thought that the cause of the problem developed was related to trazodone tablet he had used for the first time the previous evening. From the anamnesis of the patient, it was learned that he did not use any drugs containing phosphodiesterase-5 (PDE-5) inhibitors. The results of the hemogram test performed when the patient applied to our emergency department were as follows; WBC: 22.2 x10^9/L, Hgb: 10.9 g/dl, Htc: 30%, and PLT: 579 x10^3 K/µL. The patient was admitted to the urology clinic for examination and treatment because of the sustained rigid erection. As the first intervention performed in the urology clinic, an 18G butterfly needle was inserted laterally into both penile corpora cavernosa of the patient to aspirate cavernosal blood. When the erection persisted despite aspiration, intracavernosal irrigation with 0.90% w/v saline was performed, but when detumescence could not be achieved, intracavernosal injection of 2 ml 1/100,000 adrenaline was performed. After the procedure, detumescence was ensured, a CobanTM self-adherent bandage was wrapped around the penis to prevent development of hematoma. The patient was

ORCID ID: **S. Izmir Guner** 0000-0002-6326-9424 **E. Guner** 0000-0002-4770-7535

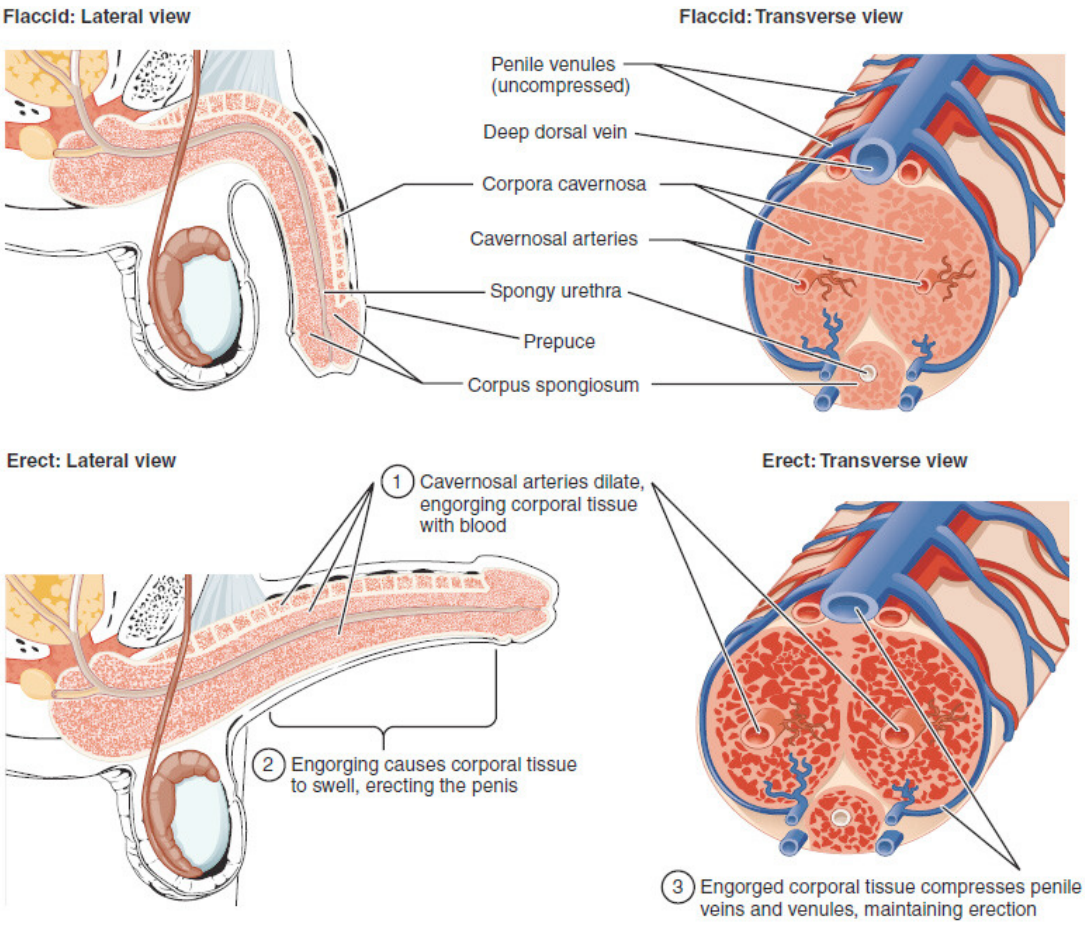

Figure 1. Top: Flask penis, Bottom: Erect penis
Corporeal relaxation exerts external pressure on the emissary veins emerging from the tunica albuginea, causing blood to remain in the penis resulting in an erection. https://storymd.com/journal/mpq5pdku6j-penis/page/elqozasy75pq-penis

monitorized for 4 hours, and then discharged. Priapism did not occur again during the follow-up period.

Chronic Myeloid Leukemia (CML) is a stem cell disease manifested by abnormal clonal proliferation of myeloid precursor cells and accounts for 15% of adult leukemias. Its incidence is 1-2/100,000. It is more common in men (male/female: 1.3/1) and its incidence increases between the ages of 40-60. CML was the first disease in humans to be associated with a specific chromosomal abnormality. In more than 90% of CML cases, the Philadelphia (Ph*) chromosome is detected by cytogenetic analysis [1,2].

Symptoms associated with anemia (such as weakness, fatigue, effort intolerance, decreased functional capacity), splenomegaly (abdominal swelling and pain, rapid satiety due to pressure of enlarged spleen on the stomach) hypermetabolic state (fever, anorexia, weight loss, gout), platelet dysfunction (hemorrhage, ecchymosis, hematoma, thromboembolic events, retinal hemorrhage), hyperleukocytosis and hyperviscosity-related findings (tinnitus, stupor, visual impairment, dyspnea, priapism and cerebrovacular events), thrombocytosis, hypereosinophilia, increase in basophil counts, anemia, elevated LDH and uric acid levels can be seen in CML. Physical examination reveals the presence of splenomegaly in 50-90%, and hepatomegaly in 10-20% of CML patients [1,2].

Priapism is an uncontrolled, prolonged, and sustained erection developing without sexual stimulation and cannot be terminated by ejaculation, **(Figure 1)**. This is a true urological emergency and early intervention is crucial for functional recovery. It has ischemic, non-ischemic and intermittent subtypes. Although often idiopathic priapism is seen, many etiologic factors of priapism are known including hematological diseases (ie. sickle cell anemia, thalassemia, leukemia, multiple myeloma), toxins (ie. scorpion, spider, malaria), metabolic diseases (ie. Fabry disease, amyloidosis), neurogenic diseases (ie. brain tumors, cerebrovascular diseases, spinal cord injury), metastatic or local invasion of tumors (ie. prostate, urethra, testis, lung) and drugs (PDE-5 inhibitors, vasoactive erectile agents such as papaverine, alpha adrenergic receptor agonists, heparin, warfarin, antidepressants, antipsychotics, antihypertensives, testosterone, alcohol, and cocaine) [3].

Imatinib mesylate is the first selective tyrosine kinase inhibitor (TKI) to target the BCR-ABL protein. While nilotinib and dasatinib are second generation tyrosine kinase inhibitors used in the treatment of imatinib-resistant CML. Muscle cramps, joint, muscle or bone pain, which are common imatinib-related side effects, may also occur during imatinib treatment or after its discontinuation [4].

Trazodone HCl is an antidepressant used in the treatment of

symptoms caused by anxiety and depression such as anxiety, appetite disorder, insomnia, and attention deficit. Serotonin reuptake inhibitors (SSRIs) belong to the drug group and its most basic feature is that their effects start to improve symptoms within a short period of about a week.

In addition to common side effects such as blurred vision, headache, dizziness, and severe fatigue, long-term painful erection (not associated with sexual activity) may also occur in men when using trazodone HCl [5]. Although the relevant mechanism is not fully understood, its high affinity for the α1 and α2 receptors that trazodone antagonizes is blamed in the pathophysiology [6]. This antagonism causes an increase in blood flow due to arteriolar dilation followed by a decrease in venous flow and obstruction of the emissary veins. In addition, α1 blockade may trigger nitric oxide release in nerves innervating arterioles and corpora cavernosa [7]. This whole process results in an erection.

CML is one of the etiologies of priapism and there are multiple relevant case reports in the literature [8,9]. Herein, it has been accepted that priapism develops due to stasis associated with leukocyte aggregation in the corpora cavernosa and penile dorsal vein due to hyperleukocytosis. Another contributing factor to venous occlusion is the mechanical effect of pressure from the abdominal veins draining the spleen. In addition, infiltration into the sacral nerves or central nervous system by leukemia cells is thought to contribute to the process [9].

In our case, remission of the disease could not be achieved because the patient did not regularly use tyrosine kinase inhibitor (TKI) drugs that regulate the leukocyte level of the patient. Despite hyperleukocytosis and hyperviscosity in the bloodstream, which are considered to be the causes of priapism in CML, the patient did not develop priapism. However, priapism, which cannot develop on the basis of CML alone, has been predicted to develop due to the synergistic effect of antidepressant agent trazodone HCL in the pathogenesis.

Keywords: trazodone, chronic myeloid leukemia, priapism, adrenergic effect, alpha adrenergic receptor
Ethics Committee Approval: N / A.
Informed Consent: An informed consent was obtained from the patient.
Publication: The results of the study were not published in full or in part in form of abstracts.
Peer-review: Externally and internally peer-reviewed.
Authorship Contributions: Any contribution was not made by any individual not listed as an author. Concept – S.I.G.; Design – S.I.G.; Supervision – S.I.G., E.G.; Resources – D.N.O.; Materials – D.N.O.; Data Collection and/or Processing – S.I.G., D.N.O.; Analysis and/or Interpretation – S.I.G., D.N.O.; Literature Search – D.N.O.; Writing – S.I.G.; Critical Review – S.I.G., E.G.
Conflict of Interest: The authors declare that they have no conflict of interest.
Financial Disclosure: The authors declare that this study received no financial support.

References

[1] Sawyers CL. Chronic myeloid leukemia. N Engl J Med. 1999;340(17):1330-40. https://doi.org/10.1056/NEJM199904293401706.

[2] Faderl S, Talpaz M, Estrov Z, O'Brien S, Kurzrock R, Kantarjian HM. The biology of chronic myeloid leukemia. N Engl J Med. 1999;341(3):164-72. https://doi.org/10.1056/NEJM199907153410306.

[3] Salonia A, Eardley I, Giuliano F, Hatzichristou D, Moncada I, Vardi Y, et al. European Association of Urology. European Association of Urology guidelines on priapism. Eur Urol. 2014;65(2):480-9. https://doi.org/10.1016/j.eururo.2013.11.008.

[4] Masatomo M. Therapeutic Drug Monitoring of Imatinib, Nilotinib, and Dasatinib for Patients with Chronic Myeloid Leukemia. Biol Pharm Bull. 2015;38(5):645-54. https://doi.org/10.1248/bpb.b15-00103.

[5] Khouzam HR. A review of trazodone use in psychiatric and medical conditions. Postgrad Med 2017;129(1):140-8. https://doi.org/10.1080/00325481.2017.1249265.

[6] Andersohn F, Schmedt N, Weinmann S, Willich SN, Garbe E. Priapism associated with antipsychotics: role of a1 adrenoceptor affinity. J Clin Psychopharmacol. 2010;30(1):68-71. https://doi.org/10.1097/JCP.0b013e3181c8273d.

[7] Deirmenjian JM, Erhart SM, Wirshing DA, Spellberg BJ, Wishing WC. Olanzapine-induced reversible priapism: a case report. J Clin Psychopharmacol. 1998;18(4):351-3. https://doi.org/10.1097/00004714-199808000-00023.

[8] Gaye O, Thiam NM, Cassell A, Gueye SM, Sow Y, Fall B, et al. Unusual Presentation of Priapism Associated with Acute and Chronic Myeloid Leukemia in Two Patients: Emergency Management. Case Rep Urol. 2020;2020:4982432. https://doi.org/10.1155/2020/4982432.

[9] Minckler MR, Conser E, Figueroa JJ, Scott AJ, Gaither J, Amini R. The semantics of priapism and the first sign of chronic myeloid leukemia. Case Rep Emerg Med. 2017;2017:2656203. https://doi.org/10.1155/2017/2656203.2656203.