Letter to Editor

MEDICINE PALLIATIVE CARE

DOI: 10.47582/jompac.1462353

*J Med Palliat Care*. 2024;5(2):147-148

# Entecavir induced gynecomastia-triggering factor or coincidence?

Alpaslan Tanoğlu[1] Murat Yeniçeri[2]

[1]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Bahçeşehir University, İstanbul, Turkiye
[2]Department of Internal Medicine, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkiye

**Cite this article as**: Tanoğlu A, Yeniçeri M. Entecavir induced gynecomastia-triggering factor or coincidence? *J Med Palliat Care*. 2024;5(2):147-148.

**Received**: 31.03.2024 ◆ **Accepted**: 25.04.2024 ◆ **Published**: 30.04.2024

**Dear Editor,**

Hepatitis B is still a viral infection agent that constitutes an important health problem all over the world. Despite widespread vaccination and innovations in treatment modalities, it still maintains its effectiveness. It is very important to diagnose this viral infection on time, to include the patient in the follow-up protocol, to determine the severity of the disease and then to plan the optimal treatment steps.[1-4] Entecavir is an important nucleoside analogue that plays a pivotal role in the treatment of HBV.[5] In this case report, it was aimed to present a case report regarding bilateral gynecomastia and mastodonia while receiving entecavir treatment.

A 52-year-old male patient who was followed up for chronic HBV was admitted to the hospital with complaint of painful enlargement in both breasts. He stated that his current complaints started about 15-20 days ago and that he had never encountered such a situation before. The patient had a known history of chronic HBV infection for 2 years and had been using 0.5 mg/day entecavir tablet therapy for HBV infection for the last 5 months. The patient stated that he did not use any medication other than entecavir treatment. He also declared that he did not use alcohol, cigarettes or other herbal medicines. None of the family members had such a disease or complaint. In physicial examination, his general condition was good, he was conscious and cooperative, and also he was overweight. Physical examination revealed no abnormal findings. In blood tests, serum aspartate aminotransferase was 45 IU/L and alanine aminotransferase levels was 50 IU/L, respectively. Serum direct bilirubin level was within normal range and total bilirubin level was 1.3 mg/dL. His creatinine level was 1.2 mg/dL and other routine biochemical tests were within normal range and HBV-DNA level was also negative. Ultrasonography imaginary revealed minimal splenomegaly with chronic liver disease appearance. On upper gastrointestinal endoscopy examination, esophageal varices were not noticed. Mammography and breast ultrasonography were performed and gynecomastia was confirmed. Follicle-stimulating hormone, luteinizing hormone, testosterone, TSH levels were within normal range.

According to patient's clinical picture, physical examination, biochemical tests, ultrasonography and endoscopic evaluation entecavir-induced gynecomastia was considered to be possible and entecavir treatment was stopped. After stopping entecavir, it was first considered to switch to tenofovir treatment, but this was not done due to the creatinine level being at the upper limit and the GFR value. After 2 weeks, entecavir treatment was restarted because the mastodinia was resolved and the clinical condition was stable. No recurrence of mastodynia was observed and gynecomastia did not progress.

The etiology of gynecomastia is multifactorial, however, in most cases, no demonstrable cause can be identified.[6] In fact, gynecomastia can occur due to physiological, pathological or pharmacological reasons. As a result, regardless of the situation that causes gynecomastia, the underlying pathophysiological mechanism of gynecomastia is increased estrogen levels, decrease in androgen levels, defect or insensitivity of androgen receptors.[6,7] Thus, gynecomastia develops as the ratio of hormonal levels changes. It is estimated that approximately 10-25% of all clinically detected gynecomastia cases are caused by various medications.[6] Entecavir is a nucleoside analog used in the treatment of chronic hepatitis B infection and reduces viral replication. It began to be widely used all over the world after it was approved by the US Food and Drug Administration in 2005.[8] The case of gynecomastia due to entecavir use has been reported very rarely in the literature. In the literature, the development of gynecomastia was first reported in a 55-year-old male patient using entecavir by Bayramıçlı et al.[9]

**Corresponding Author**: Murat Yeniçeri, 4256.gatf@gmail.com

As a result, patients treated with various agents during hepatitis B treatment should be closely monitored for treatment response and, of course, treatment side effects. Although the pathophysiological cause needs to be clarified, entecavir-induced gynecomastia may develop in patients. In this case, close monitoring of the patient and changing the treatment if the clinical situation requires it may be an appropriate approach.

## ETHICAL DECLARRATIONS

**Referee Evaluation Process**
Externally peer-reviewed.

**Conflict of Interest Statement**
The authors have no conflicts of interest to declare.

**Financial Disclosure**
The authors declared that this study has received no financial support.

**Author Contributions**
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## REFERENCES

1. Karagoz E, Selek MB, Tanoglu A, Hatipoglu M, Ulçay A, Turhan V. Comparison of the elecsys HBsAg II assay and the architect assay for quantification of hepatitis B surface antigen in patients with chronic hepatitis B. *Infez Med.* 2016;24(4):287-292.
2. Karagöz E, Tanoğlu A. Importance of serum hepatitis B surface antigen and hepatitis e antigen quantification among patients with chronic hepatitis B. *Turk J Gastroenterol.* 2015;26:357.
3. Nikolopoulou GB, Tzoutzas I, Tsakris A, Maltezou HC. Hepatitis B in healthcare personnel: an update on the global landscape. *Viruses.* 2023;15(12):2454. doi: 10.3390/v15122454
4. Karagoz E, Ulcay A, Tanoglu A, et al. Clinical usefulness of mean platelet volume and red blood cell distribution width to platelet ratio for predicting the severity of hepatic fibrosis in chronic hepatitis B virus patients. *Eur J Gastroenterol Hepatol.* 2014;26(12):1320-1324.
5. Koklu S, Gulsen MT, Tuna Y, et al. Differences in nephrotoxicity risk and renal effects among anti-viral therapies against hepatitis B. *Aliment Pharmacol Ther.* 2015;41(3):310-319.
6. Deepinder F, Braunstein GD. Drug-induced gynecomastia: an evidence-based review. *Expert Opin Drug Saf.* 2012;11(5):779-795. doi: 10.1517/14740338.2012.712109
7. Berger O, Landau Z, Talisman R. Gynecomastia: a systematic review of pharmacological treatments. *Front Pediatr.* 2022;10:978311. doi: 10.3389/fped.2022.978311
8. Henriquez-Camacho C, Hijas-Gomez AI, Risco Risco C, Ruiz Lapuente MA, Escudero-Sanchez R, Cuerda VM. Lamivudine and entecavir for acute hepatitis B: a systematic review and meta-analysis. *Viruses.* 2023;15(11):2241. doi: 10.3390/v15112241
9. Bayramıçlı OU, Ahishali E, Dabak R, Ak Ö, Dolapçioğlu C. A case of gynecomastia due to entecavir. *Turk J Gastroenterol.* 2010;21(3):313-316. doi: 10.4318/tjg.2010.0108