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CASE STUDY: ART INDUCED HEPATITIS

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ABSTRACT

HIV infection is a sexually transmitted disease caused by the Human Immunodeficiency Virus, which targets the infection fighting CD4 cells, weakening the immune system and rendering it vulnerable to disease. HIV infection is treated with antiretroviral medicines (ARV). ARV medicines do not cure HIV, but they do enhance quality of life and prolong life. Anti Retroviral Therapy (ART) is the use of ARV medications to treat HIV. It includes at least three ARV drugs from various classes. ARV, like many other medicines, has mild to severe side effects. Acute pancreatitis, hypersensitivity reactions, lactic acidosis, Stevens-Johnson syndrome, hepatomegaly, and lipodystrophy are all severe adverse effects. It is difficult to determine how each medicine contributes to the development of hepatotoxicity in an ART regimen. A 47 year old male patient was admitted to a general medicine department with chief complaints of intermittent high grade fever with chills and rigours accompanied by nocturnal sweats, two episodes of non-bilious vomiting, and a persistent cough with sputum dating back two months. The past history of the patient was found to be HIV-positive 1 month ago and is on antiretroviral therapy (ART) Dolutegravir 50mg, Lamivudine 300mg, Tenofovir Disoprovil Fumarate 300mg, OD PO H/S. The patient also had a prior history of tuberculosis approximately 2 years ago and completed a 6-month ATT course. The patient chews tobacco as well as smokes. A full examination and investigation were conducted and ART-induced Hepatitis with AFI was diagnosed and treated. This Case study creates awareness among healthcare personnel about the diseases connected with the ART regimen, which is the primary stay of therapy in HIV+ patients. HIV patients should be routinely monitored and counselled for the possibility of opportunistic infections, making sure they don't miss doses.

KEYWORDS: *HIV, ART, Drug induced hepatitis, ART induced hepatitis, ARV, Antiretroviral drugs.*

INTRODUCTION

Human immunodeficiency virus (HIV) is the virus that causes HIV infection. HIV targets and destroys the immune system's infection-fighting CD4 cells (CD4 T lymphocytes), weakening defence against many diseases and several types of cancer. As CD4 cells decrease, the body's ability to fight infections and certain cancers is compromised. Infected people gradually become immune deficient as the virus destroys and affects the function of immune cells. Without therapy, HIV can gradually damage the immune system, and HIV infection progresses to AIDS, which can take several years to develop depending on the individual.[1][2]

HIV is a sexually transmitted disease. It can be disseminated via HIV-positive individual's bodily fluids. Blood, sperm, pre-seminal fluid, vaginal fluids, rectal fluids, and breast milk are examples of bodily fluids. Only contact with HIV-infected bodily fluids can result in HIV transmission. HIV is primarily transmitted through: having anal or vaginal intercourse with someone who has HIV without using a condom or taking HIV prevention or treatment medications. Sharing HIV-infected injection drug equipment (works), such as needles or syringes. During pregnancy, or breastfeeding, it can also be passed from mother to child. The symptoms may last for a few days to several weeks. Aside from night sweats, muscle aches, sore throats, fatigue, and swollen lymph nodes. HIV infection can sometimes seem like a symptomless condition in the early stages (referred to as acute HIV infection). The HIV virus multiplies rapidly in this earliest stage of infection. After the initial stage of infection, HIV continues to replicates but at very low levels. When HIV has progressed to AIDS, the disease presents more severe symptoms, including opportunistic infections and a badly damaged immune system. Some people may advance to AIDS sooner with HIV infection if they do not receive HIV medicines.[1][2][3]

The use of ARV medications to treat HIV infection is known as antiretroviral therapy (ART). ART consists of the use of a combination of at least three ARV drugs from different classes to inhibit the replication of HIV and reduce viraemia to undetectable levels leads to the restoration of immune response, reflected by an increase in the CD4 count. Increase in CD4 count leads to slowing of the disease progression, reduced frequency of OIs, improvement in the quality of life and increased longevity. Although ART cannot cure HIV, HIV medications can help persons with the virus live longer, healthier lives. HIV transmission is also reduced

with ART. One of the primary goals of ART is to lower viraemia to undetectable levels. An undetectable viral load indicates that the level of HIV in the blood is undetectable. The risk of transmitting HIV to a HIV-negative partner through sex is effectively zero for people with HIV who maintain an undetectable viral load.[4][7]

ARVs, like many drugs, have side effects. The majority of the adverse effects are mild and managed, but some are severe enough to warrant discontinuing medication and switching to another regimen. Headache, nausea, fatigue, diarrhoea, abdominal discomfort, fever, rash, insomnia, and mayalgia are examples of mild side effects. Acute pancreatitis, hypersensitivity responses, lactic acidosis, Stevens-Johnson syndrome, hepatomegaly, and lipodystrophy are some of the most serious adverse effects linked with ARVs. It is difficult to determine the contribution of each medicine to the development of hepatotoxicity in an ART regimen. Hepatotoxicity may be caused by a variety of pathogenic processes, including direct drug toxicity, immunological reconstitution in the presence of HCV and/or HBV co-infections, hypersensitivity reactions with liver involvement, and mitochondrial toxicity. The treatment of liver toxicity is mostly determined by its clinical impact, severity, and pathogenic mechanism. These patients should have their AST/ALT levels checked more frequently.[4][5] Hepatitis is an inflammation of the liver. It usually caused by a viral infection, however there are other causes includes autoimmune hepatitis as well as hepatitis by medications, narcotics, poisons, and alcohol. Symptoms include Fatigue, flu-like symptoms, dark urine, pale stool, abdominal pain, loss of appetite, unexplained weight loss, and yellow skin and eyes which may be signs of jaundice. Chronic liver disease, cirrhosis, and liver failure can occur if your liver stops functioning correctly. Hepatitis complications include bleeding disorders, ascites, portal hypertension, renal failure, and hepatic encephalopathy, cause fatigue, memory loss, and impaired mental abilities due to the build up of toxins, such as ammonia, that influence brain function, hepatocellular carcinoma, a kind of liver cancer, and death. Liver toxicity is more common in people with chronic HCV and/or HBV co-infections, as well as in alcoholics. In individuals co-infected with HCV/HBV, complex immunological alterations that modify the response to hepatitis virus antigens may be involved in the rise of transaminase levels after suppression of HIV replication by ART Regimen.[5][6]

CASE REPORT

A 47-year-old male patient was admitted to the general medicine department with the chief complaints as fever, vomiting, and headache for 2 months. The patient's present illness

history is intermittent high grade fever with chills and rigours accompanied by nocturnal sweats, two episodes of non-bilious vomiting, and a persistent cough with sputum dating back two months. The past history of the patient was found to be HIV-positive 1 month ago and is on antiretroviral therapy (ART) Dolutegravir 50mg, Lamivudine 300mg, Tenofovir Disoprovil Fumarate 300mg, OD PO H/S, the symptoms did not subside after diagnosis and start of treatment. The patient also had a prior history of tuberculosis approximately 2 years ago completed a 6-month ATT course. The patient is a smoker with tobacco chewer.

On general examination, the patient was in an altered mental state, drowsy unresponsive to commands, on physical examination the patient had BP 100/70 mmHg, PR 100bpm, Temperature 99.5^{o}F, Icterus +, Stiff neck and decreased planter reflexes,. On systemic examination CVS: S1S2 +, RS: BAE+. On Laboratory examination LFT revealed a considerably higher than normal level of AST, ALT, and ALP0 at 373.09 U/L, 140.36 U/L, and 809.70 U/L, respectively. The CBP impression is normocytic, normochromic anaemia, mild thrombocytopenia with relative neutrophils, and. The CD4 count observed as an absolute CD4 count is 77 cells/mm3 (normal range is 381-156 cells/mm3), CD4 count present 13 cells/mm3 (normal range is 25-49 cells/mm3). USG Abdomen showing grade III fatty liver disease with hepatomegaly. With above all mentioned examination patient was diagnosed as ART-induced Hepatitis with Acute Febrile Illness. And was treated as follows.

Treatment Chart:-

S. No	Generic Name	Dose	ROA	Freq	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10
1	Acyclovir	500 mg	IV	TID	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
2	Ceftriaxone	2g	IV	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
3	Vancomycin	500mg	IV	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
4	Ciprofloxacin	500mg	PO	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
5	Fluconazole	550mg	PO	OD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
6	Pantoprazole	40mg	IV	OD	✓	✓	✓	✓						
7	Ondenstron	4mg	IV	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
8	Dexamethasome	6mg	IV	TID	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
9	Acetaminophen	500mg	PO	TID					✓	✓	✓	✓	✓	✓
11	Ranitidine	150mg	IV	OD					✓	✓	✓	✓	✓	✓
12	Iron Folic Acid	200mg	PO	BD					✓	✓	✓	✓	✓	✓
15	25% Dextrose	25%	IV	BD	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

On 4th day night during hospital stay, the patient had 3 episodes of high grade fever accompanied by chills and rigours which was treated accordingly, and symptoms were slowly subsiding from 5th day onwards. LFT and CBP was performed and it was obsorved to be

decrease in the levels of AST,ALT and ALP0 and increase in haemoglobin and platelet count to normal range, symptoms were subsided and patient was feeling better so, he was discharged.

DISCUSSION

The hepatitis mentioned above has a direct association to the ART treatment. The adverse reaction is dose-related and can be classified as a Type A adverse reaction. According to the Naranjo causality assessment of the adverse drug reaction, it might be called probable or likely adverse drug reaction. Many instances of hepatitis caused by antiretroviral medications have an aetiology that has been identified in many subjects and described in studies.

CONCLUSION

The above study was written to raise awareness among healthcare personnel about the diseases connected with the ART regimen, which is the primary stay of therapy in HIV+ patients. Using liver function tests as a routine monitoring tool for HIV patients as well as counselling them about the possibility of opportunistic infections, making sure they don't miss doses, and having regular checkups is recommended.

Abbreviations

- ALT – Alanine Transaminase
- ALP0 – Alkaline Phosphatase
- AST – Aspartate Transaminase
- ART – Anti retroviral Therapy
- ATT- Anti Tubercular Treatment
- BAE – Bronchial Artery Embolisation
- BD – Twice Daily
- CBP – Complete Blood Picture
- CVS – Cardio Vascular System
- HBV – Hepatitis B Virus
- HCV - Hepatitis C Virus
- HIV – Human Immunodeficiency Virus
- IV – Intravenous
- LFT – Liver Function Test
- PO – By Mouth

- PR – Pulse Rate
- OD – Once Daily
- OI - Opportunistic Infections
- RS – Respiratory System
- ROA - Route of Administration
- TID – Three times Daily
- USG – Ultrasound

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

REFERENCES

1. https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-and-aids-basics.
2. https://www.who.int/news-room/fact-sheets/detail/hiv-aids.
3. https://www.cdc.gov/hiv/basics/index.html.
4. http://naco.gov.in/sites/default/files/National_Guidelines_for_HIV_Care_and_Treatment_2021.pdf.
5. Tripathi K D. Antiviral drugs, 5th edition. Essentials of Medical Pharmacology, New Delhi; Jaypee, 2004; p 725 -734.
6. Tripathi K D. 3rd edition. Clinical Pharmacology, New Delhi; Elsevier, p 390.
7. Anti infectives, 6th Edition. National Formulary of India 2021, Ghaziabad; Indian Pharmacopeia Commission, p 120.