Case Report

Amoxicillin/Clavulanic Acid Induced Hyperbilirubinemia in a Patient with Melanoma: A Rare Case Report

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ABSTRACT

Amoxicillin/Clavulanate is a synthetic Penicillin that is widely used today, particularly to treat respiratory and cutaneous infections. It is a generally well-tolerated oral antibiotic. However, in some cases, Amoxicillin/Clavulanate can cause side effects, primarily cutaneous, gastrointestinal, hepatic, and hematologic. Amoxicillin/Clavulanate has been linked to hundreds of cases of clinically obvious Acute Liver Injury, and this combination is now the most common cause of drug-induced liver disease in the majority of large case series. The onset of injury can range from a few days to up to 8 weeks after the start of therapy. Hyperbilirubinemia is seen in Drug-induced Cholestatic Liver Injury, but direct inhibition of transporter proteins that facilitate bilirubin transport also results in Hyperbilirubinemia. We present a case of Hyperbilirubinemia following Amoxicillin/Clavulanate administration.

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INTRODUCTION

Hyperbilirubinemia is a condition in which bilirubin levels in the blood rise, causing yellow discoloration of the eyes and skin. A high bilirubin level almost always indicates the presence of an underlying illness. A thorough history and physical examination, followed by a biliary tree and liver imaging examination, is the best way to assess a patient with jaundice[1]. Amoxicillin/Clavulanate is a drug that can cause hepatitis and subsequent systemic dysfunction in physicians. While recovery is usually complete following drug withdrawal, in patients with hyperbilirubinemia or other unusual symptoms, it may be worthwhile to consider initiating systemic steroids earlier in the hopes of avoiding a progressive systemic response[2].

If Amoxicillin/Clavulanic acid is prescribed, Transaminase, Alkaline phosphatase and Bilirubin tests should be obtained within the first two weeks and after four to five weeks after beginning of treatment to recognize early enough undesired hepatic side effects[3]. The quantity of serum bilirubin represents a complicated metabolic and anatomic process that includes haemoglobin breakdown from senescent erythrocytes, hepatic uptake at the sinusoidal membrane, and active release of both inorganic and organic components that make up bile at the canalicular membrane. The presence of anomalies in the post sinusoidal sequence due to intra- or extrahepatic effects is indicated by an increase in the Direct bilirubin fraction[4]. Amoxicillin alone, on the other hand, is safe and does not potentially trigger recurrence of liver injury unless the penicillin, rather than the clavulanate, is to blame for the liver injury[5]. Since antibiotics are known to be overused in today's society, physicians and clinical pharmacists should be cautious while prescribing antibiotics to cancer patients[6].

CASE HISTORY

A 76-year-old male with a known case of Melanoma, Hypertension, and Coronary artery disease was admitted to a tertiary care hospital with complaints of Headache, Vomiting for the past 7 days, and black stools for the past 2 days. The patient has been administered Amoxicillin/Clavulanate since his admission. From day 2 onwards, the patient had abnormal Bilirubin levels (Total Bilirubin = 2.37 mg/dl, Direct Bilirubin = 0.89 mg/dl, and Indirect Bilirubin = 1.49 mg/dl). His bilirubin levels were normal on the day of admission. In view of the abnormal level of Bilirubin, the drug was stopped on day 3 and the levels went back to normal.

We have analysed to establish the relationship between the drug and the observed ADR through causality assessment. The Naranjo adverse drug reaction causality assessment yielded 'probable' on suspected drug ADR with a score of 7 and severity of reaction was found to be 'mild' in nature.

Table 1: Bilirubin Level Variations Before and After Amoxicillin + Clavulanate Administration

Days	Total Bilirubin (mg/dl)	Direct Bilirubin (mg/dl)	Indirect Bilirubin (mg/dl)
Day 1	0.96	0.21	0.75
Day 2	2.37	0.89	1.49
Day 3	1.33	0.42	0.91
Day 4	1.11	0.34	0.77

Drug-Induced Hyperbilirubinemia is a rare side-effect of Amoxicillin and Clavulanic acid. Our study demonstrated similar findings to a case report published in the Journal of Clinical and Translational Hepatology in 2019, Amoxicillin-Clavulanate-Induced Granulomatous Hepatitis[7]. Melanoma of the liver, whether primary or metastatic, is an extremely rare cause of acute liver failure. When the Naranjo adverse reaction probability scale was used to determine the relationship between Hyperbilirubinemia and Amoxicillin/Clavulanate, it was found to be 7. The cause of Amoxicillin/Clavulanate hepatotoxicity is unknown, but it is most likely immune-allergic. This report demonstrates the significance of Clinical pharmacists in tertiary care hospitals.

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