Case Report

Gastroenterology

Cytolytic Hepatitis: A Rare Complication Of Oral Contraceptives

CHAUDHARY AKASH, KANKANALA VISHNU V, KUMAR AJIT, JOSHI NAYANA, CHANDRA NAVAL

ABSTRACT

Drugs form one of the most frequent and important reversible causes of cholestatic hepatitis. Oral contraceptive pills usually cause bland cholestasis. Hepatic cytolysis is rarely reported as a complication of OC pills.

We report here a case of a young female with background history of intra-hepatic cholestasis of pregnancy , who presented to us with features suggestive of acute viral hepatitis with cholestasis and was later diagnosed to have oral contraceptive pill induced hepatic cytolysis.

Key Words: Cholestatic hepatitis, OC pills,Hepatic Cytolysis, Cholestasis of Pregnancy.

INTRODUCTION

Cholestasis can be defined as clinical and biochemical syndrome caused by impaired bile flow often associated with clinical manifestations, such as jaundice, itching and biochemical disturbances. Drugs form one of the most frequent and important reversible causes of cholestatic hepatitis. Combination oral contraceptive steroids are (rarely) associated with cholestasis that resembles intrahepatic cholestasis of pregnancy. The incidence of cholestasis due to oral contraceptive steroids is approximately 1:10,000 women exposed in Western Europe, but as high as 1:4000 women exposed in Chile and Scandinavia [1].

We report here a case of a young female who presented to us with features suggestive of acute viral hepatitis with cholestasis and was later diagnosed to have oral contraceptive pill induced cholestatic hepatitis with background history of intra-hepatic cholestasis of pregnancy.

CASE SUMMARY

A 30 year old woman presented with a clinical picture of progressive jaundice of 1 month duration along with severe generalized pruritus. She gave history of cholestatic jaundice during pregnancy, 7 years prior, which improved after delivery, with a benign course. She also gave history of consuming oral contraceptive pill (Levonorgestrel 0.25 mg /Ethinylestradiol 0.05 mg) for polymenorrhoea and menorrhagia 2 months prior to the onset of jaundice for a duration of 3 months. On examination she was deeply icteric with scratch marks all over the body. Mild hepatosplenomegaly was noted. Initial laboratory investigation revealed a total serum bilirubin of 22mg/dl mainly direct fraction. The serum alkaline phosphatase level was 1020 U/L while serum ALT level was 849 U/L and serum AST level was 799 U/L. (ALT levels were observed to be higher than AST). Prothrombin time was 12.4sec.

A provisional diagnosis of cholestatic viral hepatitis Vs drug induced hepatitis was considered. She denied any consumption of alcohol or over-the counter acetaminophen. She had never received blood transfusions and denied taking any medications, including herbal and folk remedies. There was no recent travel history. Results of viral serologies for hepatitis including hepatitis A, B, C, and E viruses; cytomegalovirus; Epstein-Barr virus; HIV; and herpes simplex virus were all negative. Tests for auto antibodies (anti-nuclear, anti-mitochondrial, anti-smooth muscle, anti liver kidney microsomal anti-bodies) were also negative. Alpha1 anti-trypsin and ceruloplasmin values were within normal limits. Results of hepatobiliary imaging with ultrasonography and MRCP were normal. Liver biopsy showed prominent spotty necrosis and focal confluent necrosis. Portal and mild periportal lymphomononuclear inflammation. Intra hepatic and sinusoidal cholestasis was seen [Table/Fig 1 and 2].

She was started on UDCA and other liver supportives and followed up at regular intervals. Follow-up liver function test showed similar values of serum bilirubin with gradually improving values of transaminases and alkaline phosphatase. On 3 months of followup after her first visit there was significant improvement in her serum bilirubin levels which normalized in the next 2 months [Table/Fig 3].

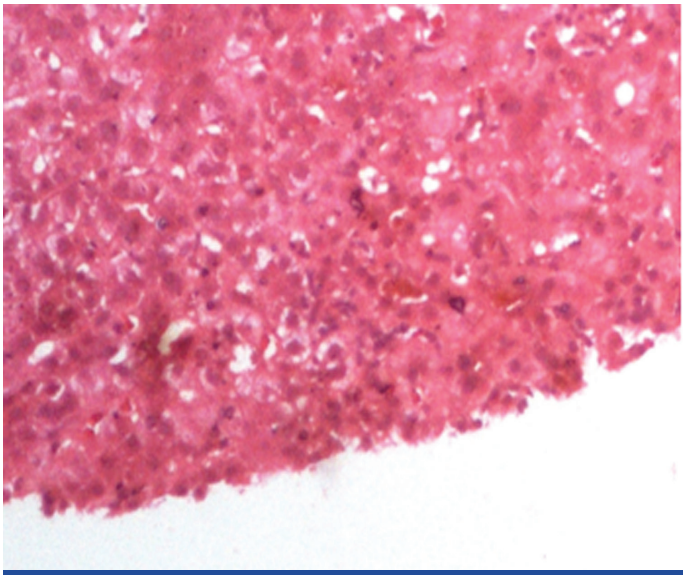
DISCUSSION

Drugs are important and often unrecognized cause of acute cholestasis. The clinical presentation and laboratory picture of acute cholestasis resembles that of obstructive hepatobiliary disorders and acute viral hepatitis [2].

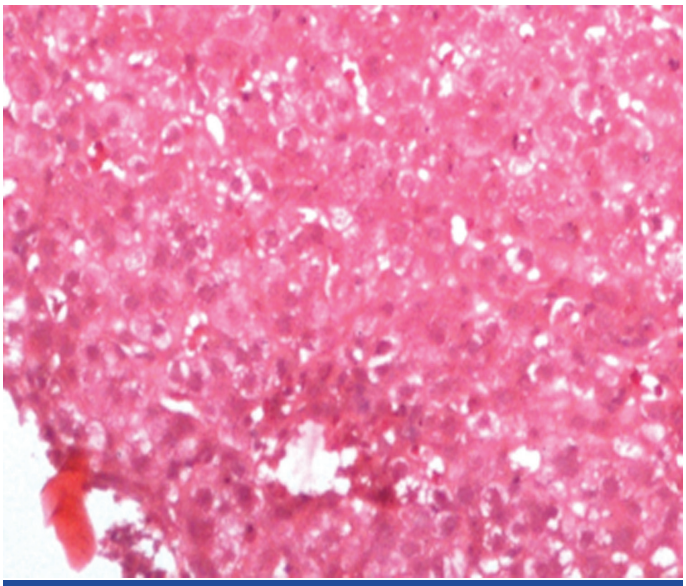
The pathogenesis (immuno-allergic or toxic) of contraceptive-induced hepatotoxicity is unclear. Estrogens have long been known to cause intrahepatic cholestasis in susceptible women during pregnancy, after administration of oral contraceptives, or during postmenopausal hormone replacement therapy. Estrogen receptor alpha-mediated repression of hepatic transporters and alterations of bile acid biosynthesis may contribute to development of the estrogen-induced hepatotoxicity [3].

Studies in rats suggest that canalicular bile transporters, particularly multidrug resistant protein 2 (MRP2), responsible for biliary secretion of several organic anions including bilirubin glucuronides may be implicated in estrogen induced cholestasis [4]. By lowering bile canalicular Na-K-ATPase activity, ethinyl estradiol decreases bile transport independent of bile flow.

In most cases of OC induced cholestasis, a pre-existent liver ailment is involved. In many cases, patients with pregnancy, cholestasis develops during OC use. Woman whose first degree relatives have



[Table/Fig-1]: Intra-hepatic & sinusoidal cholestasis



[Table/Fig-2]: Confluent necrosis

experienced cholestatic symptoms during pregnancy, induced possibly by oral contraceptives usage, may be at increased risk and should be closely monitored while taking birth control pills.

	6/1/11	21/2/11	9/3/11	4/5/11	9/6/11
T.Bil	22.7	26	21	10.7	1.7
D.Bil	18.45	21	17	8.9	1.2
ALT	849	27	63	67	11
AST	799	36	42	48	27
SAP	1020	689	674	544	280
T.Prot	7.1	6.8	6.9	7.2	7.8
Alb	4	3.7	3.4	4.2	4.1

[Table/Fig-3]: Serial liver function tests of the patient

A review of the literature has disclosed only two published reports of hepatic cytolysis with the association of levonorgestrel and an estrogen [5], [6].

CONCLUSION

OC pills are an important, often unrecognized cause of intra-hepatic cholestasis. The disease course is usually benign with "recovery as a rule". Cytolytic hepatitis has been infrequently reported with only two reports in World literature to the best of our knowledge. We wish to highlight the point, that physicians should be cautious while prescribing OC pills to patients with history of intra-hepatic cholestasis of pregnancy and be especially vigilant while prescribing the same to first degree relatives of patients with similar background and with history of OC pill induced hepatitis.

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