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Case Report

Ursodeoxycholic acid induced skin eruption: a case report

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ABSTRACT

This case report discusses a rare adverse reaction associated with ursodeoxycholic acid (UDCA), highlighting its potential impact on patient management and treatment outcomes. UDCA, commonly used for gallstone dissolution and liver disease, occasionally induces skin eruptions, though mechanisms remain unclear. A 23-year-old male with a history of jaundice and fatty liver presented with a right inguinal hernia. He was prescribed UDCA (300 mg), among other medications, post-surgical intervention. Twelve hours later, he developed sharply demarcated, dusky red plaques on his hands, suggestive of a type IV delayed hypersensitivity reaction. The Naranjo score indicated a probable association between UDCA and the skin eruption. Discontinuation of UDCA led to gradual resolution of symptoms. This case underscores the importance of recognizing and managing rare adverse reactions to UDCA, such as dermatological manifestations. While typically non-life-threatening, these reactions can necessitate treatment discontinuation, potentially compromising therapeutic efficacy. Vigilant monitoring and further research are essential to elucidate underlying mechanisms and optimize patient care strategies.

Keywords: Ursodeoxycholic acid, Skin eruption, Gall stones, Liver disease, Rash

INTRODUCTION

Ursodiol is in a class of medications called gallstone dissolution agents. Gallbladder is a small, pear-shaped organ on the right side of our abdomen, just beneath the liver.[1,2] The gallbladder holds a digestive fluid called bile that's released into your small intestine. Gallstones are hardened deposits of digestive fluid that can form in gallbladder.

Ursodiol is most commonly used to treat gallstones, this drug decreases production of bile acids, which may in theory help lower elevated levels of liver enzymes in people with liver disease.[3,4] Ursodeoxycholic acid (UDCA: 3α,7β-dihydroxy-5β-cholanic acid) is also used for the treatment of cholestatic liver diseases. It works by decreasing the production of cholesterol by dissolving the cholesterol in bile to prevent stone formation and by decreasing toxic levels of bile acids that accumulate in primary biliary cirrhosis. It plays very predominant role in the management of fatty liver because the other methods of removal of gall stone involves only surgery.[5-7]

The surgery includes endoscopic retrograde cholangio-pancreatography (ERCP), laparoscopic cholecystectomy – 'keyhole' surgery.[7,8] Common ADR of ursodeoxycholic acid constipation, diarrhoea, dyspepsia, nausea, dizziness, headache, upper respiratory tract infection >10%.[9,10] Single or multiple round, sharply demarcated and dusky red plaques appeared soon after drug exposure. Itching by ursodeoxycholic acid has been noted by 2% of person who receive this drug according to the data of this pharmaceutical company. This ADR prevents the patient from continuing the drug which may lead less effective option in the treatment/prevention of gall stone. This leads to the complication like slower recovery. Understanding and trying to rule out the risk factors present in the 2% population can help identify strategies to prevent the skin eruption.[11-13]

CASE REPORT

A 23-year-old male patient admitted at general surgery ward with complaints of swelling over right groin area in the last 6 years of age associated with mild pain on and off. The size of the swelling was gradually measured till 13 years of age after which swelling remained same. Patient was suffering from swelling, pain on and off by long standing and playing. Swelling reduces by itself completely during patient sleeps (lying for long time). The patient was allergic to analgesic, consume mixed diet, no history of smoking and alcohol. The patient was diagnosed with jaundice 2 months back and treated with native medications. His family history shows the patient mother has type II diabetes mellites, systemic hypertension and hypothyroidism, sister has hypothyroidism, his maternal uncle had hernia and operated for the same. The patient personal history shows normal bowel habits, bladder habits, normal sleep pattern and no history of addiction. From the ultrasound the impression shows presence of grade I fatty liver, splenomegaly and right inguinal scrotal hernia. At present the patient was diagnosed with right sided indirect inguinal hernia and hyperbilirubinemia.

During hospitalization the patient was treated with injection (inj.) Pan 40 mg 1-0-0, inj. Tramadol 50 mg 1-0-1, inj. Emeset 4mg 1-0-1, inj. Phenergan 12.5 mg IM 0-0-1, inj. Fortwin 30 mg IM 0-0-1, tablet (t.) Udiliv 300 mg 1-0-1, and t. Nac 600 mg 1-0-1 and surgery done for open hernia repair. In the course of treatment, single or multiple round, sharply delineated, dusky red plaques have appeared on the hands, originating from the elbow and spreading towards the fingers. The lab parameters were checked.

The medication T. Udiliv - 300 mg was suspected to be the cause of the event, which was confirmed by the Naranjo score, indicating a probable association. Following the withdrawal of the medication, the eruption gradually subsided, leaving behind small patches and scars. The patient's recovery progressed slowly, with complete resolution observed during the follow-up appointment one week later.

Udiliv start date was 11 April 2024 and reaction start date was 12 April 2024.

Description of the reaction

During the inspection mild redness with tiny bumps over a small area to peeling of the cutaneous skin eruption was observed. It was suspected to be ursodeoxycholic acid induced skin eruption and the drug was withdrawn.

Follow up

The patient came for the review on 25 January 2024 the status of the skin condition was found to be healed and resolved.

Table 1: Lab investigations.

Parameters	Observed values
Total bilirubin (mg/dl)	3.4
Direct bilirubin (mg/dl)	1.1
Indirect bilirubin (mg/dl)	2.3
SGPT (U/l)	146
SGOT (U/l)	80
Alkaline phosphatase (U/l)	65
Globulin (g/dl)	3.2
Albumin (g/dl)	4.9
GGT (U/l)	55
Creatinine (mg/dl)	0.748
Sodium (mEq/l)	139
Potassium (mEq/l)	4.60
Chloride (mEq/l)	105
Bicarbonate (mEq/l)	26.1
Glucose random (mg/dl)	103
Total RBC count ($\times10^6$/ul)	4.66
Hemoglobin (g/dl)	14.7
Haematocrit (PCV %)	41.3
MCV (fL)	88.7
MCH (pg)	31.5
MCHC (g/dl)	35.5
RDW (%)	63.9
WBC count ($\times10^3$/ul)	12.0
Neutrophil (%)	62.6
Lymphocyte (%)	29.8
Monocyte (%)	4.8
Eosinophil (%)	1.5
Basophil (%)	1.3
Absolute neutrophil count ($\times10^3$/ul)	7.5
Absolute lymphocyte count ($\times10^3$/ul)	3.6
Absolute monocyte count ($\times10^3$/ul)	0.6
Absolute eosinophil count ($\times10^3$/ul)	0.2
Absolute basophil count ($\times10^3$/ul)	0.2
Platelet count ($\times10^3$/ul)	275
MPV (fL)	8.4
PCT (%)	0.231
PDW (%)	18.1

Table 2: Following the occurrence of the event.

Lab investigations	Observed values
Total bilirubin (mg/dl)	3.4
Direct bilirubin (mg/dl)	1.1
Indirect bilirubin (mg/dl)	2.3
SGPT (U/l)	146
SGOT (U/l)	80
Alkaline phosphatase (U/l)	65
Globulin (g/dl)	2.7
Albumin (g/dl)	4.7

WBCs: Total count is increased, differential count is within normal limits

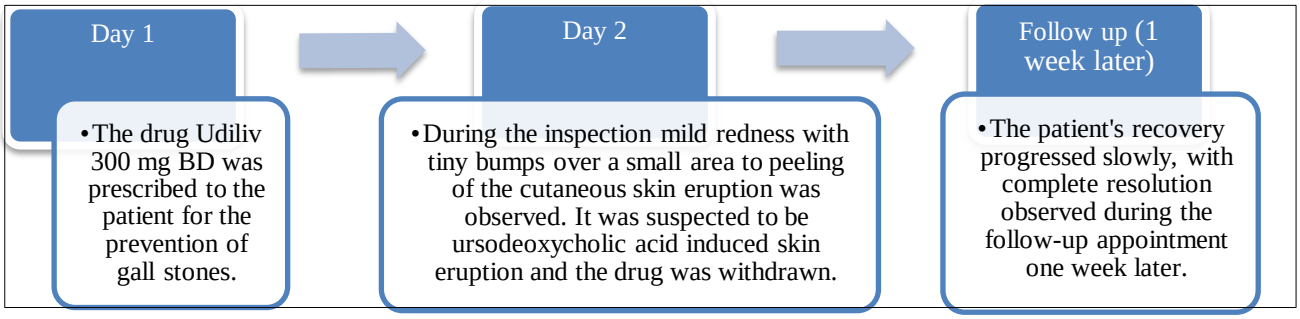

Figure 1: Timeline 1.

On examination patient blood pressure was 120/80 mm Hg, pulse rate 72/min, respiratory rate 17/min. The general examination found conscious, oriented, afebrile.

DISCUSSION

A fatty liver suggests an excessive quantity of fat, particularly cholesterol. Bile acids, which are chemicals synthesised from cholesterol in the liver, are impacted when hepatic cholesterol levels rise. It promotes increased cholesterol precipitation in bile, which results in cholesterol gallstones, the most frequent kind of gallstones. Gallstones (also known as cholelithiasis) are one of the most common biliary illnesses.[14,15] The stones are formed mostly by the precipitation of calcium salts or cholesterol in bile. The most frequent kind of gallstone is known as "cholesterol gallstones," and they are generally chalk white or greenish-yellow due to the presence of undissolved cholesterol as the major component .The surgical procedures used to treat gall stones include laparoscopic cholecystectomy, open cholecystectomy, and open cholecystectomy.[16-18]

Ursodeoxycholic acid plays an important role in the prevention and treatment of gall stones caused fatty liver. Ursodiol is used to dissolve gallstones in persons who do not want or cannot have surgery to remove gallstones. Oral dissolution therapy ursodiol (Actigall) and chenodiol (Chenix) are medications that contain bile acids that help dissolve gallstones. These medications work best for breaking up tiny cholesterol stones. The condition is completely recoverable on proper treatment. Ursodeoxycholic acids induced skin eruption is rare condition and occur only in 2% of the population. Being the drug with high utilisation the common adverse effects of ursodeoxycholic acid includes Bladder pain, bloody or cloudy urine, burning, or painful urination, dizziness, fast heartbeat, frequent urge to urinate, indigestion, lower back or side pain, severe nausea, skin rash or itching over the entire body, stomach pain, vomiting and weakness.[16-18]

Skin eruptions and dermatological issues caused by ursodeoxycholic acid have been rarely reported. The exact mechanism by which UDCA triggers these reactions remains unclear, but it's thought to involve immune-mediated pathways or hypersensitivity reactions. These reactions can manifest as various types of skin eruptions, including rashes, hives, or more severe conditions such as Stevens-Johnson syndrome or toxic epidermal necrolysis. The observed reaction occurring 12 hours after exposure to the drug suggests a type IV hypersensitivity reaction. This type of reaction is considered delayed hypersensitivity as it typically occurs more than 12 hours after exposure to the allergen, with peak reaction times between 48 and 72 hours. Type IV hypersensitivity reactions are mediated by T cells, which provoke an inflammatory response against either exogenous or endogenous antigens. In certain situations, other cells such as monocytes, eosinophils, and neutrophils may also become involved. While skin eruptions resulting from ursodeoxycholic acid are not usually life-threatening, they can hinder patients from benefiting from the treatment with this medication.[19-21]

CONCLUSION

In conclusion, the presented case sheds light on the infrequent occurrence of skin eruptions associated with UDCA administration. Although the precise pathophysiological mechanism remains elusive, evidence suggests an immune-mediated process, possibly involving type IV delayed hypersensitivity reactions. This hypothesis is supported by the onset of symptoms approximately 12-hours post-exposure, indicative of a delayed T-cell-mediated response.

While skin eruptions induced by UDCA are generally non-life-threatening, their impact on patient compliance and treatment efficacy cannot be understated. The development of adverse cutaneous reactions may necessitate the discontinuation of UDCA therapy, depriving patients of its potential therapeutic benefits. Moreover, the psychological distress and discomfort caused by these eruptions further underscore the significance of vigilant monitoring and prompt intervention.

This case underscores the importance of comprehensive patient evaluation and careful consideration of alternative therapeutic options in the management of adverse drug reactions. Furthermore, it emphasizes the need for continued research efforts to elucidate the underlying

mechanisms of cutaneous adverse reactions to UDCA and identify strategies for risk mitigation and personalized patient care. By enhancing our understanding of these phenomena, clinicians can optimize treatment outcomes and minimize the burden of adverse events on patient well-being.

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REFERENCES

1. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases. 2012.
2. Angulo P. Use of ursodeoxycholic acid in patients with liver disease. Curr Gastroenterol Rep. 2002;4(1):37-44.
3. Thistle JL. Ursodeoxycholic acid treatment of gallstones. Semin Liver Dis. 1983;3(2):146-56.
4. Ward A, Brogden RN, Heel RC, Speight TM, Avery GS. Ursodeoxycholic acid: a review of its pharmacological properties and therapeutic efficacy. Drugs. 1984;27(2):95-131.
5. Abate MA. Medical management of cholesterol gallstones. Drug Intell Clin Pharm. 1986;20(2):106-15.
6. Tangedahl T. Dissolution of gallstones--when and how? Surg Clin North Am. 1979;59(5):797-809.
7. Konikoff FM. Gallstones - approach to medical management. Med Gen Med. 2003;5(4):8.
8. Beuers U, Boyer JL, Paumgartner G. Ursodeoxycholic acid in cholestasis: potential mechanisms of action and therapeutic applications. Hepatology. 1998;28(6):1449-53.
9. Kowdley KV. Ursodeoxycholic acid therapy in hepatobiliary disease. Am J Med. 2000;108(6):481-6.
10. Sharma A, Shanti H, Nageswaran H, Best LMJ, Patel AG. Role of Ursodeoxycholic Acid in the Prevention of Gallstones Formation in Bariatric Patients-a Systematic Review and Meta-Analysis of Randomised Trials. Obes Surg. 2023;33(12):4115-24.
11. Hossain I, Brodie J, O'Brien E, Tedman-Aucoin K, Lawlor D, Murphy R, et al. Ursodeoxycholic acid for prevention of gallstone disease after laparoscopic sleeve gastrectomy: an Atlantic Canada perspective. Surg Endosc. 2023;37(7):5236-40.
12. Cheng K, Ashby D, Smyth RL. Ursodeoxycholic acid for cystic fibrosis-related liver disease. Cochrane Database Syst Rev. 2012;10:CD000222.
13. Huang L, Li S, Chen J, Zhu Y, Lan K, Zeng L, et al. Efficacy and safety of ursodeoxycholic acid in children with cholestasis: A systematic review and meta-analysis. PLoS One. 2023;18(1):e0280691.
14. Radchenko VG, Seliverstov PV, Sitkin SI. New aspects of pharmacological effects of ursodeoxycholic acid. Eksp Klin Gastroenterol. 2014;(8):4-10.
15. Kotb MA. Molecular mechanisms of ursodeoxycholic acid toxicity & side effects: ursodeoxycholic acid freezes regeneration & induces hibernation mode. Int J Mol Sci. 2012;13(7):8882-914.
16. He YQ, Deng JL, Zhou CC, Jiang SG, Zhang F, Tao X, et al. Ursodeoxycholic acid alleviates sepsis-induced lung injury by blocking PANoptosis via STING pathway. Int Immunopharmacol. 2023;125(Pt B):111161.
17. Ellul JP, Groves R, Walters JR, Murphy GM. Lichen planus associated with chenodeoxycholic acid and ursodeoxycholic acid for gallstone dissolution. Dig Dis Sci. 1992;37(4):628-30.
18. Ozkol HU, Calka O, Dulger AC, Bulut G. Ursodeoxycholic acid induced generalized fixed drug eruption. Cutan Ocul Toxicol. 2014;33(3):256-8.
19. Hall L, Halle-Smith J, Evans R, Toogood G, Wiggins T, Markar SR, et al. Ursodeoxycholic acid in the management of symptomatic gallstone disease: systematic review and clinician survey. BJS Open. 2023;7(2):zrac152.
20. Fromm H, Roat JW, Gonzalez V, Sarva RP, Farivar S. Comparative efficacy and side effects of ursodeoxycholic and chenodeoxycholic acids in dissolving gallstones. A double-blind controlled study. Gastroenterology. 1983;85(6):1257-64. PMID: 6354826.
21. Horiuchi Y. Lichenoid eruptions due to ursodeoxycholic acid administration. Gastroenterology. 2002;121(2):501-2.

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