

DRESS Syndrome and Drug induced liver Injury- A product of Antibiotic cocktail

Simin Khan MD¹, Philip Bouchette MD¹, Sudha Pandit MD²

1. Department of Internal Medicine, Louisiana State University Health Science Center, Shreveport, Louisiana

2. Department of Gastroenterology and Hepatology, LSUHSC, Shreveport, Louisiana



INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe cutaneous drug reaction characterized by the presence of a maculopapular rash, fever, lymphadenopathy, eosinophilia, and visceral involvement such as hepatitis, pneumonitis, pericarditis, nephritis, and colitis. The Liver is the most commonly involved organ and the most common cause of death. We present an interesting case of DRESS syndrome with drug induced cholestatic liver injury.

CASE DESCRIPTION

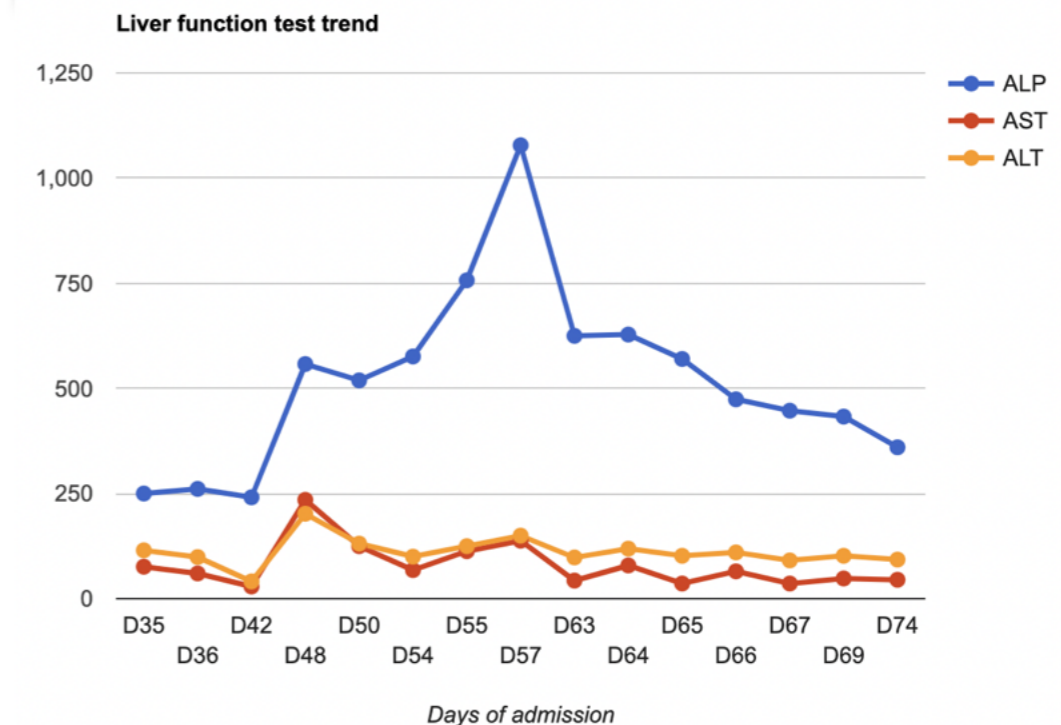
- Patient is a 63-year-old male with PMHx of Coronary artery disease, hypertension, Diabetes mellitus and polysubstance abuse, admitted as a transfer from an outside hospital with right toe gangrene and osteomyelitis status post amputation of the tip.
- Bone cultures of the amputated tip grew *E. coli* and *staphylococcus lugdunensis*. The pathology report from the previous hospital showed clean margins at the resection site with no signs of acute osteomyelitis in the rest of the foot. The patient was then treated with **Ampicillin/Sulbactam** for 1 week at our hospital.
- However, on **day 17**, while the patient was pending placement, he was noted to have wound dehiscence. Xray of the right foot was obtained which showed signs of osteomyelitis and was confirmed by MRI.
- Broad spectrum antibiotics **Vancomycin, cefepime** and **metronidazole** were started.
- Cultures from the right foot grew MRSA.
- Two days later, antibiotics were switched to **Vancomycin** and **Clindamycin** for 3 weeks per ID recommendations.
- On **day 36**, the patient tested positive for flu, **Oseltamivir** was started, and clindamycin was discontinued.



Rash seen on patient's right foot.

- On **day 40**, liver enzymes started increasing in a cholestatic pattern with alkaline phosphatase levels continuously trending up to **240 IU/L**.
- Due to lack of improvement, **Ertapenem** was later added to **vancomycin**.
- On **day 48**, ertapenem and vancomycin were held as elevated liver enzymes and AKI were noticed on lab work.
- Oral **Augmentin** and **doxycycline** were started on **day 48** for MRSA coverage as all other antibiotics were discontinued.
- MRCP was done to further evaluate the cholestatic pattern of elevated liver enzymes which was suggestive of normal common bile duct and pancreatic duct caliber.
- On **day 54**, patient developed a diffuse maculopapular rash that progressed to an erythematous rash with facial edema, eosinophilia, fever, and severe elevation of ALP levels reaching **1159 IU/ L**. CT imaging was suggestive of acute pancreatitis.
- All the antibiotics were stopped at this point.
- Dermatology was consulted and diagnosis of DRESS syndrome was made. Patient was started on prednisone 1 mg/kg which was eventually tapered over 4-6 weeks and the patient's symptoms resolved.

LAB TREND



	D35	D36	D42	D48	D50	D54	D55	D57	D63	D64	D65	D66	D67	D69	D74
T. Bilirubin	0.9	1.1	0.8	3.6	3.8	3.2	3.7	3.8	1.6	1.3	1.7	1.5	1.4	1.3	1.1
INR		1.0		1.1				1.2	1.2			1.1			1.0

DISCUSSION

- The multinational Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) states that DRESS cases must have at least three of the following systemic features: acute skin rash, fever above 38°C, enlarged lymph nodes, internal organ involvement, or hematological abnormalities, including lymphocytosis, lymphocytopenia, eosinophilia or thrombocytopenia; our patient satisfied most of these criteria.
- Liver is the most commonly involved organ (86.1% cases) but only 9.7% cases have liver injury before skin presentation.
- Liver involvement in DRESS may range from a transitory increase in liver enzymes to liver necrosis with fulminant hepatic failure.
- Among the DRESS patients, the frequency of severe cases range from 6% to 22%.
- Our case falls under the **severe** category as per the DILI severity index with elevation of ALT $\geq 5 \times$ upper limit of normal (ULN); ALP $\geq 2 \times$ ULN and total bilirubin $\geq 2 \times$ ULN.
- Patterns of liver injury include cholestatic type (37%) as seen in our case, hepatocellular form (19%), and mixed type (27%).
- The main culprit in this case was assumed to be **Vancomycin** >>> **Doxycycline/Augmentin**.