Clinical Pharmacology & Toxicology Pearl of the Week

~Drug-Induced Liver Injury~

Case

An 88-year-old female is admitted to hospital with a UTI and placed on ceftriaxone 2g IV daily.

Her other medications include acetaminophen, hydromorphone, metoprolol, olanzapine, amlodipine, risperidone, hydrochlorothiazide, pantoprazole, omeprazole, citalopram, and naproxen. There are no changes in dose in any of these medications, and no history of overdose or supratherapeutic use.

Within 3 days of hospitalization, she develops isolated abnormalities in her liver chemistry:

ALP = 296 (N 30-145)

ALT = 87 (N 5-40)

GGT = 204 (N 8-35)

Bili = 5

You are consulted for an opinion on whether this is drug induced liver injury (DILI) from ceftriaxone or acetaminophen. Both drugs have been withheld for now.

Background

- ✓ Drug-Induced Liver Injury (DILI) is a rare complication of more than 1000 prescription, herbal and over-the-counter medications.
- ✓ Two forms of DILI are recognized:
  - Intrinsic – where the drug/herbal is known to cause liver injury in a predictable, dose-dependent manner (e.g., acetaminophen).
  - Idiosyncratic – the drug/herbal causes an unpredictable liver injury, often latent in onset and unrelated to dose (e.g., amoxicillin-clavulanate).
- ✓ It is important to maintain a high degree of suspicion for DILI in patients without a more obvious cause for liver injury.

Diagnosis

- ✓ Diagnosis of DILI involves ruling out other potential causes (e.g. CT, US, MRCP, viral and autoimmune serology), followed by:
  - A thorough review of all medications and supplements & their timeline in association to the liver injury. LiverTox is an excellent resource: LiverTox - NCBI Bookshelf.
  - Calculation of the R-Factor to categorize the type of liver injury (figure 1).
  - Assessment of causality using RUCAM (figure 2).
  - Consideration of a liver biopsy in those with potential for an alternative diagnosis.

Management

- ✓ Management of DILI includes:
  - Early identification & immediate cessation of all potential culprit drugs.
  - Grading of severity as per the DILIN scale.
  - Immediate and ongoing assessment for coagulopathy & encephalopathy as markers of acute liver failure.
  - Following patient's liver chemistry for as long as 6 months after drug cessation to monitor for resolution.
  - Systemic corticosteroids only in select cases if there is clinical evidence of hypersensitivity (e.g. fever, rash).
  - IV NAC in the setting of acute liver failure may help improve transplant-free survival after DILI.
  - Careful consideration of the risks and benefits of rechallenge with potential culprit drugs after the DILI episode has resolved, noting that rechallenge after an idiosyncratic (type B) adverse drug reaction may result in a more severe (and potentially fatal) reaction.

Case resolution

The patient's elevated liver chemistry resolves with cessation of the ceftriaxone. While in hospital, the acetaminophen is restarted with no increase in the patient's liver chemistry. The patient is switched to a different antibiotic class that is less likely to result in DILI and makes a full recovery.

The Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. Clinical Pharmacology consultations are also available through the Netcare e-referral process and through Calgary Zone Specialist Link. Click HERE for more details.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK).

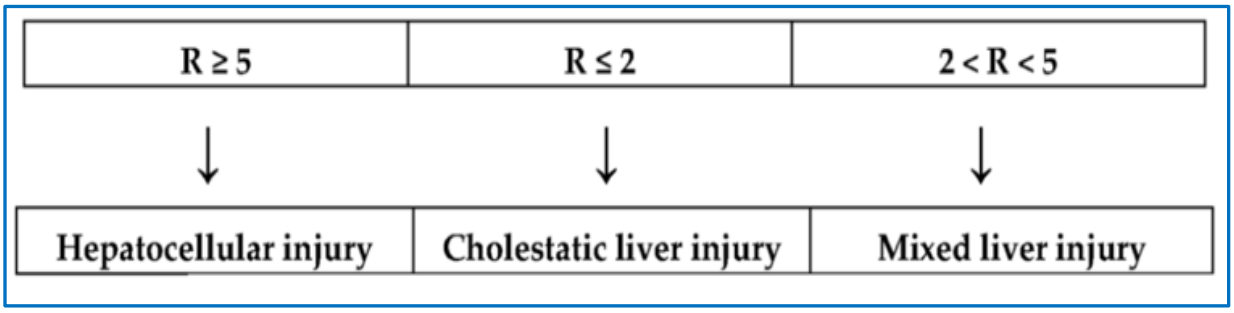

Figure 1: The R-Factor Score

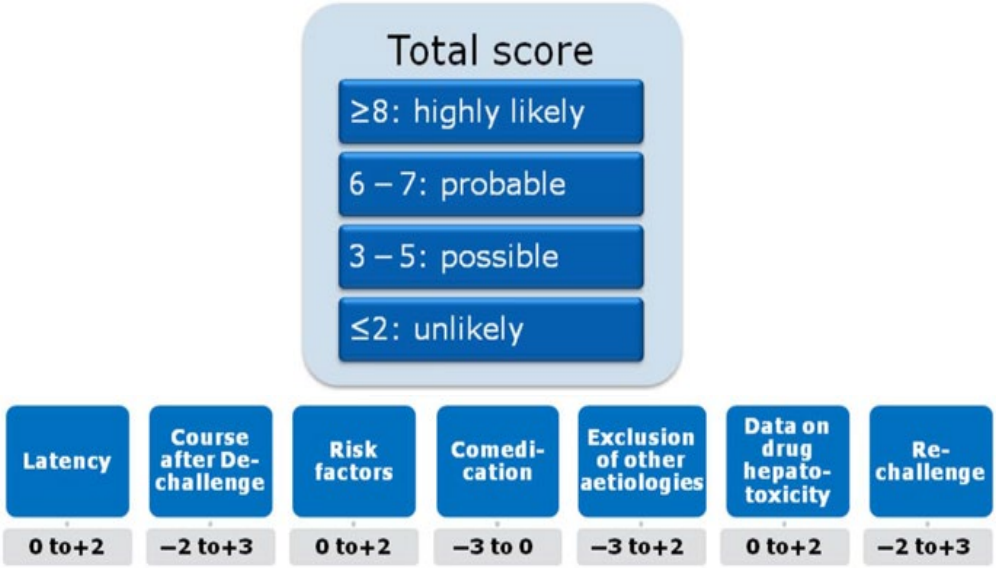

Figure 2: The RUCAM Assessment of Causality