Clinical Pharmacology & Toxicology Pearl of the Week

~ Drug-Induced Thrombocytopenia ~

Drug-Induced Thrombocytopenia (DITP) is a potentially serious complication of many medications with the potential risk of life threatening hemorrhage. There are **two broad categories** of DITP:

1. **Immune-mediated platelet destruction**
   a. Drug-dependent antibodies → Drug stimulates antibody production; drug embeds in platelet glycoproteins and serves as epitope on membrane; Reticuloendothelial sequestration (e.g. Quinine/quinidine)
   b. Drug-independent antibodies Drug stimulates antibody production; antibody production against common platelet epitopes; Reticuloendothelial sequestration in absence of continued drug (e.g. Procainamide, gold)
   c. Immune complex → Immune complex formation with drug and circulating antibodies; complement mediated cascade (e.g. Heparin/HIT)

2. **Non-immune suppression of platelet production**
   a. Direct myelosuppression (e.g. cyclophosphamide)
   b. Alterations in megakaryocyte maturation (e.g. bortezomib)

Establishing a diagnosis

No diagnostic algorithm replaces clinical judgement

1. Clinical Criteria
   a. Thrombocytopenia developed in exposure to a high-risk medication
   b. Extreme platelet nadir (Platelet < 10×10^9). Exception being Heparin-induced Thrombocytopenia (Platelet ~ $20\text{-}50 \times 10^9$)
   c. Time to onset of thrombocytopenia ~ 5-10 days following exposure
   d. Alternative causes of thrombocytopenia are ruled out
2. Laboratory Criteria
   a. Demonstration of platelet specific antibodies (Not widely available)

- Drugs with a strong association to DITP include vancomycin, septra, heparin, carbamazepine, Dilantin, valproate, and quinidine**.** A more extensive drug list may be found at the end of this document.

Management

- Discontinue the offending medication
- Extreme thrombocytopenia (Platelet < 10×10^9) should receive platelet transfusion
- Benefits of IVIg, PLEX and corticosteroid therapy is not clear

Expected clinical course

- **Clinically significant bleeding is common** and proportional to the degree of thrombocytopenia
- Platelet recovery is typically rapid (1-2 days) following drug discontinuation
- **Do NOT re-challenge** the medication. High rates of recurrence are reported

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the Alberta Referral Directory (ARD) by searching "Pharmacology" from the ARD home page. Click HERE for more details about the service.

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). Information about our outpatient Medical Toxicology Clinic can be found in Alberta Referral Directory (ARD) by searching "Toxicology" from the ARD home page.

More CPT Pearls of the Week can be found HERE.

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Table 1. Drugs Commonly Implicated as Triggers of Drug-Induced Thrombocytopenia.*

Drug Category	Drugs Implicated in Five or More Reports	Other Drugs
Heparins	Unfractionated heparin, low-molecular-weight heparin	
Cinchona alkaloids	Quinine, quinidine	
Platelet inhibitors	Abciximab, eptifibatide, tirofiban	
Antirheumatic agents	Gold salts	D-penicillamine
Antimicrobial agents	Linezolid, rifampin, sulfonamides, vancomycin	
Sedatives and anticonvulsant agents	Carbamazepine, phenytoin, valproic acid	Diazepam
Histamine-receptor antagonists	Cimetidine	Ranitidine
Analgesic agents	Acetaminophen, diclofenac, naproxen	Ibuprofen
Diuretic agents	Chlorothiazide	Hydrochlorothiazide
Chemotherapeutic and immunosuppressant agents	Fludarabine, oxaliplatin	Cyclosporine, rituximab

* For a more extensive list, see Aster,[2] Warkentin,[12] and George et al.[13] and the University of Oklahoma Web site (http://moon.ouhsc.edu/jgeorge/DITP.html).

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