The 3D case: A tale of Drugs, Dysfunction & Dyscrasias

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Case Report

Objective:
To report a suspected case of drug-induced thrombotic microangiopathy (DITMA) potentiated by quinapril.

Clinical Features:
Presentation:
A 59 year old Caucasian female presented to a regional hospital with a three day history of nausea, vomiting, abdominal pain and rectal bleeding. Routine blood tests and examinations were performed and reported to be unremarkable (Figure 1). She was discharged home with the provisional diagnosis of mild abdominal pain related to constipation.

Three days later, the patient reported to the same regional hospital complaining of increasing lethargy, nausea, abdominal pain, jaundice movements and an aura accompanied by the feeling of a pending seizure. She reported that her constipation had resolved, and complained of symptoms of diarrhoea. At this time she was noted to have some mild memory impairment & expressive dysphasia. Routine blood tests and examinations were performed and reported to be markedly abnormal (Figure 2). A provisional diagnosis of Thrombotic Thrombocytopenic Purpura (TTP) was made and the patient was transferred to a tertiary hospital for management.

Clinical Progress & Interventions:
Progress:
The patient was admitted to the Intensive Care Unit (ICU), for further investigations and management.

On admission:
- ADANTS-13 test performed - to confirm provisional diagnosis of TTP
- Stool sample cultured - to rule out Shiga Toxin Escherichia Coli (STEC) Haemolytic Uraemic Syndrome (HUS)
- IV Methylprednisolone 1g daily
- Plasmapheresis therapy
- Blood & Platelet Transfusions as necessary

The following day:
- ADANTS-13 test result confirmed normal activity thus NOT consistent with TTP
- Presumptive diagnosis of atypical haemolytic uraemic syndrome (aHUS) is made
- Pharmacist performs medication review and reconciliation and suggests quinapril as possible trigger
- Application for eczulizumab initiated - approval pending
- Copy of current vaccination record
- Confirmed negative STEC result
- Meningococcal vaccine administered and prophylactic antibiotics initiated for Neisseria meningitidis cover as per pharmacist advice
- Patient had a witnessed seizure and was intubated & ventilated for airway protection
- Indicative of neurological involvement and thus continued disease progression

Day 2:
- Immunologist and Haematologist consult acknowledge quinapril may be implicated
- Immunologist documents that quinapril is thought to elicit an immune-mediated response and proposes that eczulizumab treatment will likely improve patient outcome
- Stool sample did NOT detect the presence of Shiga Toxin Escherichia Coli (STEC), thus ruling out typical haemolytic uraemic syndrome

Day 5:
- Eczulizumab treatment course commenced

Response:
- Patient showed significant neurological improvement allowing for extubation
- She was discharged from ICU to a general ward for provision of ongoing supportive care and further eczulizumab treatment
- Pharmacist suggested immunisation against other encapsulated bacteria (Streptococcus pneumoniae, Haemophilus influenzae), as risk of infection with these organisms is increased during eczulizumab therapy owing to blockade of the terminal complement activation
- Recommended immunisations
- Vaccinations given
- Patient showed clinical and biochemical response to eczulizumab treatment and was discharged home after 26 days.
- Patient advised to avoid quinapril in future

Background:
Drug-Induced Thrombotic Microangiopathy (DITMA)

- Many drugs have been reported to cause thrombotic microangiopathies (TMAs), which are often labelled as Thrombotic Thrombocytopenic Purpura (TTP) or Haemolytic Uraemic Syndrome (HUS)
- Where a causal association between a drug and onset of TMA is suspected the term Drug-Induced Thrombotic Microangiopathy (DITMA) may be used
- DITMA is a rare and potentially life-threatening condition characterised by the simultaneous occurrence of:
  - Microangiopathic Haemolytic Anaemia (MAHA)
  - Thrombocytopenia
  - Acute Kidney Injury (may not always be present)
- DITMA can be divided into immune-mediated syndromes and dose-dependent toxicity-mediated syndromes
- There has only been one documented case report of quinapril causing immune-mediated DITMA
- It is proposed that exposure to the drug induces the formation of antibodies. These antibodies react with multiple cellular targets, including platelets, neutrophils and endothelial cells, resulting in microvascular damage and the formation of platelet microthrombi

Presentation:
- Fever
- Abdominal pain
- Seizures
- Confusion

Diagnosis:
- Diagnosis is often difficult and is usually a diagnosis of elimination

Management:
- Discontinuation of suspected drug
- Supportive care
- Plasmapheresis
- Blood/Platelet Transfusions
- Dialysis

Conclusion:
This is a rare and interesting case, which highlights the importance of a proactive clinical pharmacist in detecting unusual drug-induced disorders.

This case also emphasises the role of a pharmacist in providing education and appropriate support care before commencement of rare pharmacological treatments, such as eczulizumab.

References