Vancomycin Induced Red Man Syndrome

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KEYWORDS

CASE HISTORY
34 years female patient reported for having chief complains of-
- Flushing of face
- Hypotension
- Tachycardia
- Headache

Within an hour of rapid iv infusion of inj. Vancomycin 500mg
- On Examination
  - BP – 80mm hg systolic
  - Pulse – 140/min
  - RR – 36/min
  - Patient was conscious but agitating

RELEVANT MEDICAL HISTORY
- Patient came on 09/03/2013 with c/o
  - Fever with chills
  - Burning micturition
  - Vomiting
  - Generalized weakness
  - Malaise

Since 7 days

Patient was admitted for the same on 09/03/2013
- BP – 120/70 mm hg
- Pulse – 84/min

DRUG HISTORY

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>STARTED ON</th>
<th>STOPPED ON</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inj. Artesunate (120mg) iv OD</td>
<td>09/03/2013</td>
<td>continued</td>
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<tr>
<td>Inj. Ceftriaxone (1gm) iv BD</td>
<td>09/03/2013</td>
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<tr>
<td>Inj. Ondensatron (4mg) iv OD</td>
<td>09/03/2013</td>
<td>continued</td>
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<tr>
<td>Inj. Pantoprazole (40mg) iv OD</td>
<td>09/03/2013</td>
<td>continued</td>
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<tr>
<td>Inj. Vancomycin (500mg) iv infusion</td>
<td>10/03/2013</td>
<td>10/03/2013</td>
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</tbody>
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INVESTIGATIONS
- TLC – 12,500/cumm
- Hb – 9.6 mg%
- USG – mild hepatomegaly
- PS for MP - negative
- Other laboratory parameters were within normal limits.

MANAGEMENT
- Inj. Avil 2cc iv stat
- Inj. Hydrocortisone 100mg iv stat
- Inj. Dopamine iv infusion
- Inj. Calcium gluconate iv stat
- I.V. fluids

OUTCOME – “Recovered”
- Pt. improved symptomatically
- Flushing released
- BP – 110/70 mmhg
- Pulse – 80/min

CAUSALITY – “Probable”
- Temporal relationship present
- Dechallenge positive

Vancomycin is a glycopeptide antibiotic discovered in 1956
- Against MRSA
- Acts by inhibiting bacterial cell wall synthesis.
- High systemic toxicity

Side effects
- Infusion-related events- Red man syndrome Hypotension, Nephrotoxicity, Ototoxicity
- Hematopoietic – Reversible neutropenia, Rarely thrombocytopenia, Reversible agranulocytosis
- Phlebitis
- Drug rash with eosinophilia and systemic symptoms (DRESS)

VANCOMYCIN INDUCED RED MAN SYNDROME
- Most common
  - "red-man", "red man’s", "red neck" or "red person’s syndrome"
- Despite the replacement of the old formulation of vancomycin, termed “Mississippi mud” due to impurities, the newer and purer vancomycin product still causes toxicities, including RMS.
- RMS is a form of pseudoallergic drug reaction
- Or
- ADR mimic immunologic drug allergies, BUT in which immunologic mechanisms have not be demonstrated.
- RMS can also be seen with other antibiotics [e.g. Ciprofloxacin, Amphotericin-b, Rifampicin and Teicoplanin] or other drugs which releases histamine.
- The incidence 3.7% - 47% in infected patients
- 5–13% of patients when the infusion is given over less than 1 hour
- Flushing, erythema, and pruritus (Upper body, neck, and face)
- Pains and muscle spasms in the back and chest
- Dyspnea and hypotension
- Sensations of burning and itching
- Agitation
- Dizziness
- Headaches
- Chills, fever
- Perioral paresthesia
- Hypotension in isolation has been reported
• RMS is rarely life-threatening, although severe cardiovascu-
lar toxicity and even cardiac arrest have been reported

MECHANISM
• Best classified as _idiopathic infusion reaction_
• Resembles IgE-mediated anaphylaxis
• BUT does not involve drug-specific IgE.
• Studies in animals indicate that vancomycin directly acti-
vates mast cells, resulting in release of vasoactive media-
tors, such as histamine

PREDISPOSING FACTORS
• Mast cells may be more easily activated by vancomycin
  when certain other medications are also present which en-
hances dose or rate-related mast cell degranulation
• Opioids (e.g. Morphine, Meperidine, Codeine)
• Radiocontrast dyes,
• Some smooth muscle relaxants

Relationship To Infusion Rate
• Rapid infusion rate is the most common cause of RMS
• The infusion rate of 33 mg/min (1 gram over 30 minutes)
  causes RMS symptoms in most subjects
• Whereas slower rates of 10 mg/min (corresponding to 1
  gram over 1.67 hours) or less rarely cause symptoms
• Vancomycin should be infused over a minimum of 100
  minutes or at a rate no higher than 10 mg/min, whichever
  results in a slower infusion.

Prevention Of Initial Reactions
• Empiric premedication to prevent RMS is not usually nec-
  essary for the first time at standard rates of infusion (≤10
  mg/min).
• Advise even slower rates of infusion for patients who are
  also receiving opioids or other medications that predispose
to mast cell activation.
• Commonly employed if more rapid infusions of vancomy-
cin are required in emergency or presurgical settings.
• Oral premedication with H1 or H2 antihistamines

Diphenhydramine (≤1 mg per kg)
Cimetidine (≤4 mg per kg),

MANAGEMENT
Mild To Moderate Reactions:-
• Interrupt the infusion,
• Diphenhydramine (50 mg orally or intravenously)
• Ranitidine (50 mg intravenously)
• Infusion can then be restarted at one-half the original rate

Severe Reactions:-
• Stop the infusion
• Diphenhydramine (50 mg intravenously)
• Ranitidine (50 mg intravenously)
• IV fluids if hypotension is present
• The infusion can be restarted, and given over four or more
  hours.
• For future doses - repeat premedication with antihista-
  mines before each dose and infusion over four hours.

Recurrent Reactions
• These individuals may have mast cell and/or basophils that
  are easily activated.
• Desensitization can be attempted in such patients if vanco-
  mycin is absolutely required.
• Desensitization induces clinical “tolerance” to an agent
  when IgE-mediated mechanisms are responsible
• The mechanism by which desensitization might work in
  non-IgE mediated reactions is not known.
• We acknowledge the Medicine dept. for their support &
  efforts.

REFERENCES