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Anaphylaxis to Paclitaxel in a Patient with Delayed Hypersensitivity, Treated with Abraxane Desensitization

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DISCLOSURES

- I have no financial disclosures

CASE

- A 38-year-old female with recently diagnosed endometrial cancer presented with fever, diffuse rash and lip swelling 7 days after her first Carboplatin and Taxol doses.
- Rash was raised, erythematous and maculopapular which coalesced into large papules on the back and chest
- No new medications except recent chemotherapy and dexamethasone.

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LABS

CBC with Differential

WHITE BLOOD COUNT	2.47 (L)
RED BLOOD COUNT	5.04
HEMOGLOBIN	12.1
HEMATOCRIT	37.4
PLATELET COUNT	239
MCV	74.2 (L)
MCH	24.0 (L)
MCHC	32.4
RDW	15.5 (H)
NEUTROPHIL #	1.46 (L)
NEUTROPHILS %	59.2
MONOCYTE #	0.29
MONOCYTE %	11.7 (H)
LYMPHOCYTE #	0.40 (L)
LYMPHOCYTE %	16.2 (L)
EOSINOPHIL #	0.25
EOSINOPHIL %	10.1 (H)
BASOPHIL #	0.01
BASOPHIL %	0.4

Complete Metabolic Profile

SODIUM	135 (L)
POTASSIUM	3.6
CHLORIDE	99
CO2 TOTAL	23
UREA NITROGEN (BUN)	16
CREATININE	0.9
GLUCOSE	113 (H)
TOTAL PROTEIN	6.8
ALBUMIN	3.5
CALCIUM	8.9 (L)
BILIRUBIN TOTAL	0.7
ALK PHOSPHATASE	58
AST	15
ALT	26

CASE

- Leading diagnosis was acute generalized exanthematous pustulosis (AGEP).
- Symptoms resolved with 10-day steroid taper.
- Unclear if Taxol or Carboplatin were the culprit agents.

QUESTION

Given this information, would you go forward with desensitization or challenge for this patient?

A. Yes

B. No

CASE

- Given time course, patient's symptoms not consistent with Type I immediate hypersensitivity reaction.
  - As such, desensitization would not be indicated and ideally recommend avoiding both Taxol and Carboplatin.
- On discussion with Gynecology-Oncology team, no alternative chemotherapy regimen available.
- Thus, plan was to challenge patient to each agent separately under close monitoring.
- Three weeks after initial reaction, patient tolerated a Carboplatin challenge ruling out this medication as the culprit.

CASE

- Within 2 minutes of infusion of Paclitaxel at the rate of 2ml/h (first dose of a challenge) she experienced severe generalized urticaria, hypotension, tongue and throat swelling and loss of consciousness.
- This reaction required intubation and was treated with epinephrine drip.
- Due to anaphylaxis to paclitaxel, plus the history of delayed severe rash to Taxol, the decision was made to switch to Abraxane (albumin bound paclitaxel) given through desensitization protocol.

CASE

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BACKGROUND

- Paclitaxel (Taxol) is an anti-microtubule chemotherapy agent used for the treatment of multiple malignancies.
- Adverse reactions, including anaphylaxis, to Taxol chemotherapy are common occurring in up to 40% of patients.[1-3]
- Premedication with antihistamines and corticosteroids has decreased the incidence of adverse reactions to <10%.[4]
- Majority of reactions to Taxol occur after first exposure. [4]

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BACKGROUND

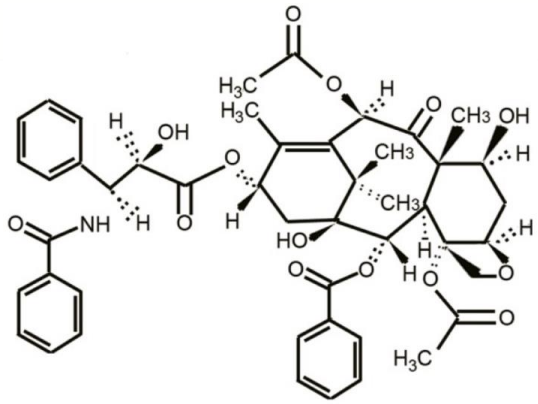
- In patients with Type I immediate hypersensitivity reactions, desensitization to Taxol chemotherapy via a 3-bag protocol has demonstrated safety and efficacy.
- First desensitization can be done inpatient with subsequent desensitizations in the outpatient setting.[4,5]

Solution	Dose in each solution (mg)[a]	Volume	Solution concentration
A	5	100 ml	0.05 mg/ml
B	50	100 ml	0.50 mg/ml
C	500	100 ml	5.00 mg/ml

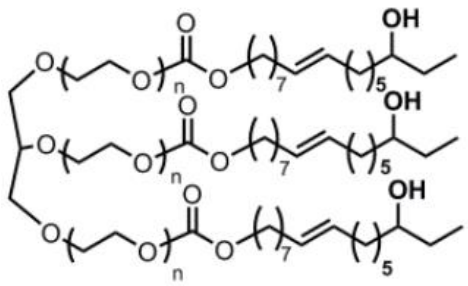
Step	Solution	Rate (ml/h)	Time (min)	Administered dose (mg)	Cumulative dose (mg)
1	A	2	15	0.025	0.025
2	A	5	15	0.063	0.088
3	A	10	15	0.125	0.213
4	A	20	15	0.250	0.463
5	B	5	15	0.625	1.088
6	B	10	15	1.250	2.338
7	B	20	15	2.500	4.838
8	B	40	15	5.000	9.838
9	C	10	15	12.500	22.338
10	C	20	15	25.000	47.338
11	C	40	15	50.000	97.338
12	C	75	64.4	402.663	500.000
		Total time = 3.8 h		Total dose = 500 mg	

BACKGROUND

- The pathophysiology of Taxol hypersensitivity reactions is thought to be multifactorial due to:
  - IgE-mediated or direct mast cell activation by Taxol
  - Complement and/or mast cell activation by solvent Cremophor EL
  - Production of cytokine release, nitric oxide and/or kinin formation



Paclitaxel



Cremophor EL®

BACKGROUND

- Abraxane is a nanoparticle albumin-bound Paclitaxel (Nabpaclitaxel).
- It does not use Cremophor EL as a vehicle and thus has fewer rates of hypersensitivity reactions compared to Taxol.[6]
- However, Abraxane is stable for only 4 hours once mixed and diluting this formulation has a risk of medication dissociation.

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METHODS

- A 14 step one-bag rapid desensitization protocol for Abraxane was created using a single concentration (5mg/mL), since further dilution could not be pharmacologically stable.[4,5]
- As discussed previously, Abraxane is only stable for 4 hours once mixed
- Doses were up-titrated initially by using a specialized low-rate infusion pump
  - Short doses at slowest rate possible (1mL/h) with pauses between doses
  - Progressively decreasing pauses between doses
  - Slowly increasing the rate
  - Total duration of 3 hours and 38 minutes.

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METHODS

Step	Rate (mL/h)	Time (min)	Hold Time (min)	Total Time (min)	Dose Administered (mg)	Cumulative Dose (mg)	Concentration (mg/mL)
1	1	1	9	10	0.08	0.083	5
2	1	2	8	10	0.17	0.25	5
3	1	4	6	10	0.33	0.583	5
4	1	8	2	10	0.67	1.25	5
5	1	10	0	15	1.25	2.5	5
6	2	10	0	15	2.5	5	5
7	4	10	0	15	5	10	5
8	6	10	0	15	7.5	17.5	5
9	8	10	0	15	10	27.5	5
10	12	10	0	15	15	42.5	5
11	15	10	0	15	18.75	61.25	5
12	20	10	0	15	25	86.25	5
13	40	10	0	15	50	136.25	5
14	60	10	0	15	215	351.25	5

RESULTS

- Patient developed urticaria in step 8 which was treated with pausing the infusion, diphenhydramine and methylprednisolone.
- The protocol was then continued with repeating step 8.
- She successfully tolerated the remainder five cycles of the desensitization protocol with localized transient hives in two other cycles.
- She did not have any further severe adverse reactions or delayed symptoms.
- She has since been in remission for 1 year now.

DISCUSSION

- This is a case of a patient with previously delayed reaction to Taxol who upon re-exposure developed an IgE-mediated hypersensitivity reaction.
- Patient's IgE-mediated symptoms during both Taxol and Abraxane shows that she has IgE-mediated allergy to the Taxane and not the Cremophor solvent.
- Furthermore, she had a delayed severe rash with Taxol and not Abraxane suggestive of delayed hypersensitivity to Cremophor.
- We were able to successfully desensitize to paclitaxel using Abraxane through a unique 1-bag method, despite limitations on timing and dilution capabilities.
- Additionally, this case re-emphasizes the possibility of immediate hypersensitivity reactions in patients whose initial reaction was delayed in onset.

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QUESTIONS?