Cyclophosphamide desensitization in a patient with embryonal rhabdomyosarcoma

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INTRODUCTION

Chemotherapy agents have many associated adverse drug reactions including potential anaphylaxis. Oftentimes, an alternative agent cannot be used and desensitization will be required in those with hypersensitivity reactions. Even during desensitization, breakthrough reactions can occur necessitating modification of the original desensitization protocol to prevent future reactions.

CASE REPORT

Patient is a 6 month old male with embryonal rhabdomyosarcoma in the pelvic area who had lip swelling, hives and tachycardia 1.5 hours into his first cyclophosphamide infusion. Given IgE mediated symptoms, a decision was made to perform a cyclophosphamide desensitization adapted from Castells' 12-step protocol for rapid drug desensitization to chemotherapeutic drugs[1]. He was also pretreated with intravenous diphenhydramine, famotidine and dexamethasone.

During his first desensitization, he developed mild facial swelling and flushing 6 hours into desensitization. During his second desensitization, he developed more severe facial swelling and flushing 6 hours into infusion and was unable to complete infusion. Given his continued symptoms despite undergoing desensitization, a decision was made to modify his pretreatment. Prior to third desensitization, oral prednisolone was started 24 hours prior to infusion and a longer acting antihistamine (cetirizine) was added as pre-treatment with the thought that the shorter acting antihistamine may be wearing off at the 6 hour mark. During this desensitization, he developed erythematous cheeks 6.5 hours into infusion but was able to finish his chemotherapy at a lower rate without any further reactions. He then tolerated two further desensitizations under the same protocol.

TABLES

	Concentration (mg/ml)	Dose (mg)	Total Volume (ml)
Solution 1	0.1	0.243	2.430
Solution 2	1	5.063	5.063
Solution 3	10	669.695	66.969

Table 1: Concentration, dose and total volume administered of three solutions

Step	Solution	Rate (ml/h)	Time (min)	Dose (mg)	Volume (ml)	Cumulative dose (mg)
1	1	0.54	15	0.0135	0.135	0.0135
2	1	1.08	15	0.027	0.27	0.0405
3	1	2.7	15	0.0675	0.675	0.108
4	1	5.4	15	0.135	1.35	0.243
5	2	1.35	15	0.3375	0.3375	0.5805
6	2	2.7	15	0.675	0.675	1.2555
7	2	5.4	15	1.35	1.35	2.6055
8	2	10.8	15	2.7	2.7	5.3055
9	3	2.7	15	6.75	0.675	12.0555
10	3	5.4	15	13.5	1.35	25.5555
11	3	10.8	15	27	2.7	52.5555
12	3	21.46	174	622.45	62.25	675

Table 2: Steps of desensitization protocol with rates, time, doses and volumes

DESENSITIZATION PROTOCOL

Three solutions of the cyclophosphamide were prepared: 0.1 mg/ml, 1 mg/ml and 10 mg/ml (Table 1). Steps one through four used the 0.1 mg/ml concentration and administered doses of 0.0135 mg, 0.027 mg, 0.0675 mg and 0.135 mg increasing every 15 minutes. Steps five through eight used the 1 mg/ml concentration and administered doses of 0.3375 mg, 0.675 mg, 1.35 mg and 2.7 mg increasing every 15 minutes. Steps nine through eleven used the 10 mg/ml concentration and administered doses of 6.75 mg, 13.5 mg and 27 mg increasing every 15 minutes. The last step included the same concentration administered over 174 minutes for a dose of 622.45 mg. His full dose was 675 mg (Table 2).

DISCUSSION

Drug desensitization may be required for hypersensitivity reactions but there remains a risk of breakthrough reaction during the desensitization. In this case, an infant continued to react 6 hours into two separate cyclophosphamide desensitizations. It is possible that he may have been reacting once his shorter acting antihistamine wore off or reacting to one of the metabolites of cyclophosphamide. However, we were able to mitigate his reaction for the third and subsequent desensitizations by starting steroids earlier, adding a longer acting antihistamine and decreasing rate of infusion at first sign of reaction.

REFERENCE

Castells, M., Tennant, N., Sloane, D., Ida Hsu, F., Barrett, N., & Hong, D. et al. (2008). Hypersensitivity reactions to chemotherapy: Outcomes and safety of rapid desensitization in 413 cases. *Journal Of Allergy And Clinical Immunology*, *122*(3), 574-580.