Case Report

Cisplatin Desensitization in a Patient with Nasopharyngeal Carcinoma Experiencing Urticarial Allergic to Cisplatin

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Background. Allergic reactions to cisplatin are not uncommon situation with incidence of 5-20%. In general, allergic reactions to cisplatin is a type 1 hypersensitivity with manifestations of itching, redness, papules, urticaria, chest pain, and anaphylactic symptoms. Desensitization methods are needed for patients who have no alternative medication.
Case Report. A 59-year-old woman with nasopharyngeal carcinoma experienced urticaria because of cisplatin in her first-cycle of chemotherapy. In second cycle chemotherapy desensitization program was applied using a 12-step Castell protocol. We measured vital signs and symptoms every 15 minutes. Administration of cisplatin was completed in 2 hours and the patient tolerated whole program very well.
Discussion. Risk factors of hypersensitivity to cisplatin includes age <70 years, previous allergy history, history of carboplatin use with dose >650 mg, mutation of BRACA1/2 gene, and administration of combined regimens with taxane groups or liposomal inhibitor. Desensitization uses 3 solutions with 12 steps. Solution 1 is 100 times the dilution of the target dose. Solution 2 is 10 times the dilution of the target dose and solution 3 use the appropriate target dose. Each solution is administered for 15 minutes using an infusion pump. Strict monitoring of vital signs and patient symptoms are done every 15 minutes during the program.
Conclusion. Doctors should be aware of allergies to cisplatin. Currently the allergic reaction to cisplatin can be overcome using desensitization method when no alternative drug is not available.

Keyword: *Cisplatin, allergy, desensitization*

Background

Cisplatin is a chemotherapy drug derived from platinum. It is first introduced in 1980. This drug is widely used in cases of cancer in various tissue characteristics. Currently platinum-derived chemotherapy drugs have 3 generations, namely cisplatin, carboplatin and oxaliplatin.[1]

Allergic reactions to the platinum group have been widely observed. However, cases from our local setting have never been comprehensively reported. The use of this drug requires consideration and strategy because the incidence of allergic reactions to platinum compounds is increasingly found. Replacing second-line drugs may not improve the disease, because until now the platinum group showed a remarkable response to particular cancer. The use of platinum derivatives is increasing, so that the incidence of allergic cases against this group also increases. The incidence of allergy

to cisplatin is 5-20%, to carboplatin is 9-27%, and to oxaliplatin is 10-19%.[2] Herewith we reported a successful administration of desensitization program to a patient with nasopharyngeal carcinoma experiencing allergic to cisplatin.

Case

A 59-year-old woman presented to our cancer clinic for second cycle of chemotherapy with docetaxel/cisplatin/5-fluorouracil regimen (TPF). The patient suffered from nasopharyngeal cancer and was planned to receive TPF regimen for 3 cycles with 21-day interval and radiotherapy at the end of chemotherapy program. Dose of docetaxel was 113.25 mg on day 1, cisplatin was 37.75 mg on days 1-4 and 5-flurouracil 1132.5 mg on days 1-5. At the first cycle of chemotherapy the patient experienced complaints of itching accompanied by small bumps and redness. These complaints occurred on the second day of chemotherapy. Upon consultation, suspected drug was cisplatin. Cisplatin was stopped while other drugs continued.

In the second cycle, the patient was planned to receive the same regimen because no drugs were considered as effective as cisplatin for nasopharyngeal cancer cases. Other platinum derivatives such as carboplatin and oxaliplatin also have potential for allergic reactions and according to clinical trials are more often used in cases other than nasopharyngeal cancer. Therefore, desensitization to cisplatin drug was the only program that was worthtrying.

The patient's condition was generally good with stable vital signs. There were no complaints upon hospitalization. The desensitization program followed Castell's 12-step procedure which included 3 solutions. According to the 12-step procedure castell cisplatin desensitization starts at step 5 and ignores steps 1 through step 4 so that only 2 cisplatin solutions are needed (Figure 1). The first solution was dissolved in a 0.9% NaCl 0.9% physiological solution at a dose of 4 mg

Patient Name:
Drug: cisplatin

Solution:	Total Volume	Concentration	Dose
Solution 1	100 mL	0.000 mg/mL	0 mg
Solution 2	100 mL	0.04 mg/mL	4 mg
Solution 3	100 mL	0.38 mg/mL	37.75 mg

Step	Solution#	Rate (mL/hr)	Time (minutes)	Volume infused per step (mL)	Dose administered with this step (mg)	Cumulative Dose (mg)
1	1	2	15	0.5	0.000	0.000
2	1	5	15	1.25	0	0
3	1	10	15	2.5	0	0
4	1	20	15	5	0	0
5	2	5	15	1.25	0.05	0.05
6	2	10	15	2.5	0.1	0.15
7	2	20	15	5	0.2	0.35
8	2	40	15	10	0.4	0.75
9	3	10	15	2.5	0.95	1.7
10	3	20	15	5	1.9	3.6
11	3	40	15	10	3.8	7.4
12	3	80	59.90	79.87	30.35	37.75

Figure 1 Castells 12-step cisplatin desensitization protocol[6]

(concentration 0.04 mg / ml). The second solution was dissolved in 0.9 ml physiological solution NaCl as much as 100 ml at a dose of 37.75 mg (concentration 0.38 mg).

The dosage of the drug is given according to the protocol and monitor of vital signs and complaints was done every 15 minutes. During administration of solution 1 to solution 2, vital signs are stable and no complaints of itching, skin lesions, redness, nausea and vomiting to shortness of breath. In general the administration of cisplatin supposed to last for 1 hour according to the chemotherapy protocol. In this desensitization program the drug administration was finished in 2 hours.

Discussion

Chemotherapy drugs that are commonly reported to have allergic and anaphylactic reactions are platinum, taxan, anthracycline, asparginase and epipodofilotoxin groups. Manifestations include skin rash, cardiovascular symptoms, gastrointestinal symptoms and respiratory symptoms. Cancer incidence rate is increasing and so is the incidence of allergic symptom. The use of platinum group chemotherapy drugs is widely used because their effectiveness to induce curative or remission. The platinum group is drugs with a very small molecule that cannot induce an immunological response except after haptenisation. Mechanism of allergic reaction to cisplatin according to several studies will emerge after several cycles of chemotherapy exposure.[3]

Hypersensitivity reaction to cisplatin is a type 1 allergic reaction mediated by the role of IgE but in some cases reported to be caused by allergic reactions type 2, 3 and 4. Type 1 allergic reactions have clinical manifestations such as itching, redness of the skin, papules or urtikaria, chest pain or even anaphylactic symptoms. The incidence of allergic reactions to cisplatin is 1-14%. Rare reports of severe allergic reactions were also observed. The median value of the appearance of symptoms is after chemotherapy for 6 cycles. The second generation platinum drug, carboplatin, has a higher incidence of 1-44%, while the third generation of this drug, oxaliplatin, has an incidence of 10-25%.[4]

Risk factors of allergic to cisplatin are as follows: age under 70 years, a history of previous allergies, a history of using carboplatin with doses >650 mg, a long period of time after last receiving platinum class drugs, mutations in the BRACA1 / 2 tumor inhibiting gene, receive chemotherapy of combination with taxans or liposomal inhibitors such as docorubicin.[5] There are several factors that can be used as predictor of allergic reactions in the platinum group, the total cumulative dose of chemotherapy with the previous platinum group, high lymphocyte count and low monocyte count.[1]

This patient had no alternative medicine besides cisplatin for achieving effectiveness to kill cancer cells. This stimulated desensitization program. According to the protocol introduced by Castell, desensitization uses 3 solutions with 12 steps. Solution 1 is dilution 100 times the target dose. Solution 2 is a dilution of 10 times the target dose and solution 3 uses the target dose. Each solution was administered for 15 minutes using an infusion pump with the number of drops set according to protocol. Every 15 minutes strict monitoring including vital signs and assessment of patient complaints were carried out.[6] If minor complaints presents, supportive drugs can be given. When severe complaints are observed, desensitization program needs to be terminated.

The implementation of cisplatin desensitization in this patient was successful and no complaints were found. The time needed for all processes were 2 hours and this time span was 1 hour longer than the time that should be used for cisplatin chemotherapy. However, a span of 2 hours remains effective in achieving the chemotherapy target. According to previous observation, the success rate of cisplatin desensitization is 100%.[7] However, desensitization is temporary and only lasts 2-3 times the half-life of the given drug. Therefore, desensitization has to be administered in the next cycle of chemotherapy.[8]

Conclusion

In the situation where allergic stimulating drug cannot be substituted, desensitization is a considerable choice. The desensitization protocol that widely used is the 12 step protocol according to Castells. This protocol has been successfullyapplied in the present case.

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