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Platin desensitizations in thoracic malignancies and risk factors for breakthrough reactions

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Abstract
Although platin desensitization is a safe and effective alternative for patients with hypersensitivity reactions (HSRs), sometimes breakthrough reactions (BTRs) can be encountered. However, data about the risk factors for BTRs are limited. The aim of this study is to define the outcomes of desensitization, the characteristics of BTRs, and to identify the risk factors for BTRs with platins in thoracic malignancies. This is a retrospective report of patients with thoracic malignancies who underwent platin desensitization. Patients' demographics, initial HSR characteristics, skin test results, desensitization outcomes, and BTR characteristics were recorded. Thirty-three lung cancer and 14 malignant pleural mesothelioma (MPM) patients were included in the study. The culprit drug was cisplatin in 29 and was carboplatin in 18 patients. Skin test positivity was 43.5% with cisplatin, 50% with carboplatin, and it was found to be higher if the interval between the initial HSR and skin testing (ST) was >20 days ($p = 0.027$). One hundred and five desensitization courses were performed. Twenty-two patients had 33 BTRs. Skin test positivity was higher in the BTR-positive group ($p = 0.025$). BTRs (18.2%; $n = 6$) were more severe than initial HSR. In the case of epinephrine administration during initial HSR, epinephrine administration during the first BTR was found to be more ($p = 0.036$). The target dose was achieved in 92.4% of desensitization courses. The number of previous platin infusions ≥10 was found to be an independent risk factor for BTR development ($p = 0.036$ OR:17.641, 95% CI: 1.211-256.971). Identification of risk factors for BTR will guide appropriate management and desensitization approaches for platin HSRs.

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Introduction

Repeated courses of chemoterapy with the same or similar agent may cause sensitization and hypersensitivity reaction (HSR) after reexposure.[1,2] HSRs limit the use of these agents because of their potential to cause more severe reaction or even death in the next administration.[3,4] In immediate-type HSRs, rapid drug desensitization can provide tolerance and reuse of the offending agent thus giving patients a chance to be treated with first-line chemotherapeutics.[1,5]

Although chemotherapeutic desensitization has been shown to be safe and effective, sometimes breakthrough reactions (BTRs) can be encountered during the procedure. BTR rates are higher in platins compared to other chemotherapeutics.[6-11] There are some studies reporting the outcomes of desensitizations and the BTRs with platins.[6-15] However, only a few studies have evaluated risk factors for BTRs with platins and reported different risk factors from each other such as the number of previous platin infusions ≥ 10 courses, total IgE level ≥ 100 U/mL, drug skin test positivity, or severe initial HSRs for moderate to severe BTRs.[7,9,13] Further studies are needed to identify patients in the risk group.

The aim of this study was to define the outcomes of desensitizations, list the characteristics of BTRs, and to identify the risk factors for BTR in patients with thoracic malignancies who underwent desensitization with cisplatin or carboplatin.

Materials and Methods

Patients

This is a retrospective observational study of patients who were diagnosed with lung cancer or malignant pleural mesothelioma (MPM) and who underwent desensitization with carboplatin or cisplatin from January 2013 to January 2022 in our Allergy and Clinical Immunology Clinics. The study was approved by the local ethics committee (approval number 2012-KAEK-15/2501). Inclusion criteria were: (1) patients who had symptoms compatible with immediate-type HSR during or within 1 hour after the chemotherapy infusion and (2) desensitizated to the culprit platin. Exclusion criteria were: (1) delayed-type HSR and (2) insufficient medical records.

Baseline data including patients' characteristics (age, gender, diagnosis, concomitant diseases, and drug allergy), culprit platin, number of previous platin infusions, therapy line, the symptoms and severity of initial HSR, administration of epinephrine during initial HSR, the results of skin tests if performed, number of desensitization courses, occurrence of BTRs, the symptoms and severities of BTRs, administration of epinephrine during BTRs, and desensitization completion status are collected from medical records.

Signs and symptoms of HSRs were defined as cutaneous (flushing, pruritus, urticaria, and angioedema), cardiovascular (chest pain, tachycardia, syncope, hypotension, and hypertension), nasal (sneezing and congestion), respiratory (dyspnea, cough, broncospasm, wheezing, and oxygen desaturation), laryngeal (throat tightness, difficulty swallowing, and hoarseness), gastrointestinal (nausea, vomiting, diarrhea, and abdominal pain), neurologic (dizziness, fatigue, and consciousness changes), and other systemic symptoms (discomfortness, sweating, and chills).

The severity of initial HSRs and BTRs was classified according to Brown's classification. The reaction was considered as mild if there was only cutaneous involvement; as moderate if there were symptoms suggesting respiratory, cardiovascular, or gastrointestinal involvement; and as severe if hypoxia, hypotension, or neurologic compromise was considered.[16]

Skin Test (ST)

Skin prick test (SPT) and intradermal test (IDT) were performed with previously defined non-irritant concentrations to determine the sensitization to culprit platin.[17-21] SPT was performed with the undiluted drug as follows: for 10 mg/mL carboplatin, 1 mg/mL cisplatin. After a negative SPT, IDT was performed with 1/100 and 1/10 dilutions respectively for both drugs and with undiluted concentration for cisplatin. In case of a positive response to histamine (10 mg/mL) and negative response to control solution (0.9% saline) SPT was considered positive when the skin reaction was a wheal with a diameter at least 3 mm larger than the negative control and had a surrounding erythema. IDT was considered positive if the initial wheal increased by at least 3 mm in diameter and was surounded by erythema after 20 minutes.

Desensitization protocols

A 3-bag 12-step desensitization protocol described by Brigham and Women's Hospital was implemented.[18] Written informed consent was obtained before each desensitization procedure. Thirty minutes before starting the desensitization, premedication with methylprednisolone 40 mg, H_1-antihistamine (pheniramine 45.5 mg) and H_2-antihistamine (famotidine 20 mg or ranitidine 50 mg) was administered as a routine practice of the oncology team before chemotherapy course. All desensitizations were carried out at outpatient settings under close observation with one-on-one nurse-to-patient care in the allergy unit. If any BTR occured during the protocol, infusion was suspended and the reaction was treated. After the reaction resolved, the protocol was continued starting from the previous step which BTR occured. For subsequent desensitizations additional premedication and/or intermediate steps was added before the step where previous BTR occured.

Statistical analysis

All statistical analyses were performed using the SPSS (statistical package of social sciences) for Windows 16.0 software package. In the evaluation of the data, mean and standard deviation for normally distributed data, median and interquartile range for data that did not show normal distribution, values and percentages for ratios were determined by descriptive statistical method. In univariate

analyses, Chi-square, Fischer, Student's t-test and Mann-Whitney U tests were used, as appropriate. Multivariate analysis was conducted through a binary logistic reggression model and the variables were sellected by backward selection with the elimination of variables at p-value over 0.20. Results was evaluated at 95% confidence interval. All p values lower than 0.05 were considered to be statistically significant.

Results

Patient characteristics

A total of 47 patients; 15 female and 32 male with mean age 58.04 ± 8.46 were included in the study. The diagnosis was lung cancer in 33 and MPM in 14 patients. The pathological diagnosis of all lung cancer patients were non-small cell lung cancer (NSCLC) with subtypes as 40.4% (n = 19) adenocarcinoma (CA), 21.3% (n = 10) squamosis CA, 2.1% (n = 1) adenoskuamoz CA and 6.4% (n = 3) unidentified subtype. 53.2% (n = 25) of the patients had at least one concomitant disease; the most common ones were chronic obstructive pulmonary disease, hypertension and diabetes mellitus. 14.9% (n = 7) of the patients had other drug allergies.

Treatment and initial HSR characteristics

Culprit platin was cisplatin in 61.7% (n = 29) and was carboplatin in 38.3% (n = 18) of the patients. Median number of platin infusions which patients reacted was 8 (range 4–15) and there was no significant difference between the cisplatin and carboplatin treated groups (p = 0.101). 55.3% of the patients (n = 26) had initial HSR during the second line therapy. 85% (n = 40) of the reactions developed during the infusion of the culprit platin, of which 75% (n = 30) developed during the first half of the infusion.

Initial HSRs were mild in 40.4% (n = 19), moderate in 38.3% (n = 18) and severe in 21.3% (n = 10) of the patients. In the treatment of these reactions, epinephrine was administered in 5 patients (10.6%) (4 patients with severe and 1 patient with moderate reaction). Treatment and initial HSR characteristics was shown in Table 1.

Symptoms of the initial HSR according to involved organ systems were evaluated as; cutaneous 87.2% (n = 41), respiratory 38.3% (n = 18), cardiovascular 27.7% (n = 13), gastrointestinal 23.4% (n = 11), neurologic 14.9% (n = 7), laryngeal 10.6% (n = 5), nasal %2.1 (n = 1), other systemic symptoms 25.5% (n = 12).

Results of ST

Skin tests (SPT and IDT) were performed in 40 patients but could not be evaluated due to histamin deficiency in 7 patients. In the remaining 33 patients, skin test positivity with cisplatin was 43.5% (10 of 23), and with carboplatin was 50% (5 of 10). Skin test positivity in all patients was observed with IDTs and 80% (n = 12) of the positivity was with 1/100 dilution. There was no statistical difference between cisplatin and carboplatin skin test reactivity (p = 1.00).

Most of the patients (93.93%, n = 31) had ST before first desensitization course. The median time between the initial HSR and the skin test was 19 (range: 1–60) days. Skin test positivity was found to be higher in patients with this period >20 days (p = 0.027).

Skin test positivity was 40% (6 of 15) in mild reactions, 58% (7 of 12) in moderate reactions, 33% (2 of 6) in severe reactions. There was no statistical difference between the severity of the initial HSR and the positivity of the skin test (p = 0.512).

Desensitization outcomes and BTR characteristics

A total of 105 desensitization courses were performed in 47 patients (58 courses in 29 cisplatin patients, 47 courses

Table 1 Treatment and initial HSR characteristics.

Variables	All patients n = 47 (%)	Cisplatin group n = 29 (% 61.70)	Carboplatin group n = 18 (% 38.30)	P
Median platin infusion, n (range)	8 (4-15)	8 (4-12)	8 (6-15)	0.101
Previous platin infusions ≥ 10 courses, n (%)	13 (27.7)	5 (17.2)	8 (44.4)	0.043
Therapy lines n (%)				
First line	13 (27.7)	4 (13.8)	9 (50.0)	0.020
Second line	26 (55.3)	20 (69.0)	6 (33.3)	
Third line	8 (17.0)	5 (17.2)	3 (16.7)	
Initial HSR timing n (%)				
During infusion	40 (85.1)	25 (86.2)	15 (83.3)	1
Within the first hour after infusion	7 (14.9)	4 (13.8)	3 (16.7)	
Initial HSR grade, n (%)				
Mild	19 (40.4)	11 (38.0)	8 (44.4)	0.463
Moderate	18 (38.3)	13 (44.8)	5 (27.8)	
Severe	10 (21.3)	5 (17.2)	5 (27.8)	
Epinephrine administration during initial HSR, n (%)	5 (10.63)	4 (13.8)	1 (5.6)	0.636

HSR, hypersensitivity reaction.

in 18 carboplatin patients). The median number of desensitization courses was 2 (range: 1–7). A total of 33 BTRs were developed in 46.8% (n = 22) of the patients. Demographic, diagnostic, treatment, and clinical characteristics of BTR-positive and-negative groups are shown in Table 2.

Twelve patients had 16 BTRs with cisplatin and 10 patients had 17 BTRs with carboplatin. No statistical difference was observed in cisplatin and carboplatin BTR rates (p = 0.344). Skin test positivity was statistically significantly higher in the BTR-positive group than the BTR-negative group (66.7% vs 27.8%, p = 0.025). Although the BTR-positive group had more patients who received ≥10 courses of platin infusion than the BTR-negative group (n = 9 vs 4 patients, respectively), it was not statistically significant (p = 0.057).

Cutaneous symptoms were observed in all BTRs (n = 33); other symptoms of the BTRs according to involved organ systems were evaluated as gastrointestinal 24.2% (n = 8), respiratory 18.8% (n = 6), laryngeal 12.1% (n = 4), and cardiovascular 9.1% (n = 3). BTRs were mild in 57.6% (n = 19), moderate in 36.4% (n = 12), and severe in 6.1% (n = 2) patients. When compared with initial HSR severity, most of the BTRs (81.8%, n = 27) were milder than or on similar severity with the initial HSR, whereas 18.2% (n = 6) of the BTRs were more severe than the initial HSR.

Most of the patients had their first BTR during the first desensitization course (72.7%, n = 16), 9.1% (n = 2) during the second course, and 18.2% (n = 4) during the third course. Recurrent BTRs were observed in 46.7% (7 of 15) of patients who developed BTR and continued

Table 2 Demographics, diagnostics, treatment, and clinical characteristics of BTR-positive and -negative patients.

Variables	All patients (n = 47)	BTR-negative group (n = 25)	BTR-positive group (n = 22)	P
Age (mean ± SD)	58.04 ± 8.46	59.72 ± 7.71	56.14 ± 9.03	0.149
Sex, n (%)				
Female	15 (31.9)	7 (28.0)	8 (36.4)	0.539
Male	32 (68.1)	18 (72.0)	14 (63.6)	
Diagnosis, n (%)				
NSCLC	33 (70.2)	17 (68.0)	16 (72.7)	0.724
Malignant pleural mesothelioma	14 (29.8)	8 (32.0)	6 (27.3)	
NSCLC subtypes, n (%)				
Adeno carcinoma	19 (57.6)	10 (58.8)	9 (56.3)	0.716
Squamosis carcinoma	10 (30.3)	5 (29.4)	5 (31.3)	
Adenosquamosis carcinoma	1 (3.0)	1 (5.9)	0	
Undefined	3 (9.1)	1 (5.9)	2 (12.5)	
Presence of concomittant disease, n (%)	25 (53.2)	16 (64.0)	9 (40.9)	0.113
Culprit platin, n (%)				
Cisplatin	29 (61.7)	17 (68.0)	12 (54.5)	0.344
Carboplatin	18 (38.3)	8 (32.0)	10 (45.5)	
Number of platin infusions (mean ± SD)	8.26 ± 2.35	7.80 ± 2.02	8.77 ± 2.63	0.160
Previous platin infusions ≥10 courses, n (%)	13 (27.7)	4 (80.0)	9 (40.9)	0.057
Therapy lines, n (%)				
First line	13 (27.7)	7 (28.0)	6 (27.3)	0.980
Second line	26 (55.3)	14 (56.0)	12 (54.5)	
Third line	8 (17.0)	4 (16.0)	4 (18.2)	
Skin test results, n (%)				
Positive	15 (31.91)	5 (20.0)	10 (45.5)	0.025
Negative	18 (38.29)	13 (52.0)	5 (22.7)	
Initial HSR grade, n (%)				
Mild	19 (40.4)	10 (40.0)	9 (40.9)	0.561
Moderate	18 (38.3)	11 (44.0)	7 (31.8)	
Severe	10 (21.3)	4 (16.0)	6 (27.3)	
Initial HSR clinical symptoms n (%)				
Cutaneous	41 (87.2)	22 (88.0)	19 (86.4)	1.00
Respiratory	18 (38.3)	10 (40.0)	8 (36.4)	0.798
Cardiovascular	13 (27.7)	7 (28.0)	6 (27.3)	0.956
Gastrointestinal	11 (23.4)	5 (20.0)	6 (27.3)	0.557
Neurologic	7 (14.9)	3 (12.0)	4 (18.2)	0.690
Laryngeal	5 (10.6)	3 (12.0)	2 (9.1)	1.00
Other systemic	12 (25.5)	6 (24.0)	6 (27.3)	0.797
Nasal	1 (2.1)	1 (2.1)		
Epinephrine administration during initial HSR, n (%)	5 (10.6)	2 (8.0)	3 (13.6)	0.654

BTR, breakthrough reaction; NSCLC, non-small cell lung cancer; HSR, hypersensitivity reaction.

Table 3 Comparision of the initial HSR and first BTR clinical symptoms in the BTR-positive group.

Clinical symptoms, n (%)	Initial HSR	First BTR	P
Cutaneous	19 (86.4)	22 (100)	
Respiratory	8 (36.4)	5 (22.7)	0.309
Cardiovascular	6 (27.3)	5 (22.7)	0.100
Gastrointestinal	6 (27.3)	3 (13.6)	1.00
Neurologic	4 (18.2)		
Laryngeal	2 (9.1)	3 (13.6)	0.260
Other systemic	6 (27.3)		

HSR, hypersensitivity reaction; BTR, breakthrough reaction.

Table 4 Comparision of the initial HSR and first BTR severities in the BTR-positive group.

		First BTR Grade			
Reaction severity		Mild, n (%)	Moderate, n (%)	Severe, n (%)	P
Initial HSR Grade	**Mild, n (%)**	5 (22.7)	3 (13.6)	1 (4.5)	0.577
	Moderate, n (%)	3 (13.6)	4 (18.2)		
	Severe, n (%)	4 (18.2)	1 (4.5)	1 (4.5)	

HSR, hypersensitivity reaction; BTR, breakthrough reaction.

to be desensitized in subsequent courses; two BTRs were observed in three patients, and three BTRs were observed in four patients.

When initial HSR and first BTR were compared in patients who developed BTR, no statistically significant difference was observed in terms of clinical symptoms (Table 3) and severity of reactions ($p = 0.577$) (Table 4). There was also no statistical difference between first BTR severities among the patients with positive or negative skin tests ($p = 0.402$).

All but one BTR occured during bag 3 and one BTR occured 15 minutes after the end of the desensitization procedure. Most of the BTRs (63.6%; 21 of 33) occured at the last step of the protocol.

In the treatment of BTRs, epinephrine was administered in nine patients (27.3%); two of them had severe BTRs and seven of them had moderate BTRs. Epinephrine administration in the treatment of first BTR was found to be significantly higher in patients who were administered epinephrine during the initial HSR ($p = 0.036$).

The target dose could be achieved in 97 of 105 (92.4%) desensitization courses. The characteristics of the remaining eight patients were as follows: one patient did not want to continue the procedure, two patients were in the last course of their therapy and the primary physician decided not to continue the procedure, one of them had severe BTR, three patients had a second BTR during the continuation of the procedure, one of them required two repeated doses of epinephrine, two patients required epinephrine administration for BTR and we decided not to continue procedure, and one of them had severe BTR.

Potential risk factors for BTR

Patients with ($n = 22$) and without ($n = 25$) BTRs further analyzed to determine the potential risk factors for BTR. The variables with a "p-value" less than 0.20 in the univariate analysis were included in the multivariate analysis and logistic regression analysis was performed in the model established with age, concomitant disease, previous platin infusions ≥ 10 courses, and skin test positivity. Previous platin infusions ≥ 10 courses were found to have increased the risk for BTR development ($p = 0.036$ OR: 17.641, 95% CI: 1.211–256.971)

Discussion

In this study, we retrospectively reported the characteristics of initial HSRs, the outcomes of desensitizations, and the characteristics and risk factors for the development of BTRs with cisplatin and carboplatin in patients with lung cancer and MPM. During the study period, a total of 105 desensitizations were performed in 47 patients. Thirty-three BTRs were observed in 46.8% ($n = 22$) of the patients. In most of the patients (72.7%, $n = 16$), the first BTR was observed in the first desensitization course. There was no statistical difference in the frequency or the severity of BTRs between cisplatin and carboplatin. Skin test positivity with cisplatin and carboplatin was 43.5 and 50%, respectively. Skin test positivity was not found to be associated with initial HSR severity but BTR development was statistically significantly higher in patients with positive skin tests. As a result of multivariate analysis, previous platinum infusions ≥10 courses were found to be an independent risk factor for BTR development.

To the best of our knowledge, our study has the largest lung cancer and MPM patient population among studies evaluating platin desensitization outcomes in the literature. Thirty-three lung cancer and 14 MPM diagnosed patients were included in the study. Although platins are first-line treatment options in both NSCLC and SCLC (small cell lung cancer), all of the patients with lung cancer included in this study over a 9-year period were diagnosed as NSCLC. In a study that included 142 patients who developed platin-induced HSR over a 5-year period, three patients with SCLC and two patients with NSCLC were reported.[22] Although no difference was found in terms of BTR development between NSCLC subtypes in our study, it can be more clearly evaluated whether the development of HSR with platins in SCLC is more rare than in NSCLC in future studies with larger patient populations.

HSRs to platins are usually IgE-mediated and require previous exposure before immunological sensitization; therefore, the incidence of HSRs increases with multiple exposure.[18,23,24] A study investigating the clinical features of HSR to carboplatin in 205 patients reported that the incidence of HSRs was increased from 1 to 27% in patients who received seven or more courses.[25] In our study, initial HSRs occurred at median 8 (range: 4–15) infusion of culprit platin, similar to some previous studies.[10,15,25,26]

ST is the most widely used diagnostic tool in the evaluation of platin HSRs. In this study, skin test positivity with cisplatin and carboplatin was 43.5 and 50%,

respectively, and there was no statistical difference between them. In different studies, skin test positivity was reported to be between 34.8 and 98% with carboplatin and between 0 and 90.9% with cisplatin.[8,10–12,18–20,22,26] One of the reasons for reporting such different results may be the time interval between the initial HSR and ST. Performing ST in the early period after initial HSR may have a risk of false negative results due to anergy. It is recommended to perform skin tests at least 2 weeks after the initial HSR and to repeat ST after a negative result if it is performed during the first 4–6 weeks following the initial HSR.[24,27–29] The skin test reactivity in our study was relatively low compared to some other studies. This is probably due to the short interval between the initial HSR and ST. This period was median 19 (range: 1–60) days. In most of the patients (93.9%, 31 of 33), skin tests were performed before the first desensitization course and no repeat skin tests were performed due to the retrospective nature of the study. We consider that the statistically significant increase in the positivity rate in those with time interval between the IR and skin tests >20 days supports our belief. If skin tests performed in the early period were negative, repeat ST may be considered to increase the sensitivity of skin test.

In this study, no correlations were found between the initial HSR severity and the skin test positivity compatible with some previous studies.[8,10,13,15] However BTR development was statistically significantly higher in patients with positive skin tests (66.7% vs 27.8%, p = 0.025).

During the study period, a total of 105 desensitizations were performed in 47 patients. Around 46.8% (22 of 47) of the patients had 33 BTRs. There was no statistical difference in the frequency or severity of BTRs between cisplatin and carboplatin. In previous studies, 33–59% of the patients were reported to have BTR during platin desensitization.[6–8,10,12–15,24]

Most of the patients (72.7%, n = 16) had their first BTR during the first desensitization course. Although the majority of BTRs (57.6%) were mild, 18.2% of the patients had more severe BTRs than the initial HSR. Initial HSR was mild in one of two patients with severe BTR. Epinephrine administration in BTRs was found to be statistically significantly higher in those who were treated with epinephrine in the initial HSR (p = 0.036). Our data showed that the desensitization procedure is generally successful and safe, but not completely risk-free, and that more severe reactions than the intial HSR can be seen in a small number of patients. Therefore, it is important to administer desensitization under appropriate conditions and by experienced allergists.

Risk factors for BTRs during platin desensitizations have been identified in only a few studies.[7,9,13] Caiado et al. reported the outcomes of 1471 desensitizations in 272 patients with different antineoplastics and monoclonal antibodies. One hundred and thirty six of the patients were desensitized to platins (80 oxaliplatin, 49 carboplatin, 7 cisplatin) and had 112 BTRs during 689 desensitizations. A subgroup of platin patients (127 of 136) was further analyzed to investigate risk factors for BTRs and two idependent predictors were identified with multivariate analysis; previous platin infusions ≥ 10 courses (OR:4.11, 95% CI:1.17–14.52) and total IgE level ≥ 100 U/mL (OR:8.24, 95% CI:2.06–30.02).[7] Kim et al. reported 1143 desensitizations with one bag protocol performed in 228 patients. Six hundred and fifty one of the desensitizations were performed with platins in 123 patients (57 oxaliplatin, 49 carboplatin, and 17 cisplatin). BTR rate was 34% for platins. They reported that severe initial HSRs were a significant risk factor of moderate to severe BTRs, especially in platins (OR: 1.556, 95% CI:1.05–2.28), and that the use of steroid was statistically significant in reducing the occurrence rate of moderate to severe BTRs and this preventative effect was more pronounced for platins (OR: 0.504, 95% CI:0.311–0.818). They also reported that the BTR rate was decreased in patients who went through several desensitization cycles (OR:0.944, 95% CI: 0.899–0.992).[9] In another study, Gorgulu Akın et al. reported 232 platin desensitizations in 72 patients (38 carboplatin, 21 oxaliplatin, and 13 cisplatin) with 56 BTRs in 33 patients. They reported that the drug skin test positivity increased the risk of BTRs (OR:5.058, %95 CI:1.371–18.665).[13]

Patients with diagnosis of lung cancer or MPM were included in this study. Since it was not used in the treatment of thoracic malignancies, there was no oxaliplatin-treated patient in our study. In our study, in agreement with Caiado's report, previous platin infusions ≥10 courses were found to be an independent risk factor for BTRs (OR:17.641, 95% CI: 1.211–256.971). Although skin test positivity was statistically significantly higher in the BTR-positive group (66.7% vs 27.8%, p = 0.025) in univariate analysis, it could not be defined as a risk factor in multivariate analyses.

Conclusion

In conclusion, further studies are needed to evaluate whether the development of HSRs with platins is more frequent in NSCLC patients than SCLC patients. Since skin test positivity was found to be higher in patients who were tested >20 days after initial HSR, repeat ST may be considered after negative skin test results performed in the early period after the initial HSR. The desensitization procedure is not completely risk-free. BTRs during platin desensitizations seem to be at a substantial level. Although most of the BTRs are mild, severe BTRs can also be seen. BTRs may be more severe than initial HSRs in a small number of patients. Epinephrine administration during BTRs was found to be higher in patients who were administered epinephrine during the initial HSRs. In this study, previous platin infusions ≥ 10 courses were defined as an independent risk factor for BTR development. Defining additional risk factors for BTR and identification of patients in the risk group will guide the management of platin HSRs and the determination of appropriate desensitization approaches.

Conflict of interest

The authors declare no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

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