Premedication with 20 mg dexamethasone effectively prevents relapse of extensive skin rash associated with gemcitabine monotherapy

Gemcitabine treatment is commonly associated with skin rash, with a reported incidence of 7%–30% [1–3]; however, there exists only one prior report describing the management of gemcitabine-associated rash in the English-language literature [1]. When an extensive skin rash develops, both the patient and physician may experience anxiety about continuing gemcitabine treatment. For patients with a toxic drug-induced rash, continued administration of that drug may exacerbate the rash and put the patient at the risk of a more severe toxic event, such as toxic epidermal necrosis (TEN). From April 2008 to April 2009, we treated 107 patients with gemcitabine monotherapy and experienced four

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Tumor type</th>
<th>Location of rash</th>
<th>Diagnosis of dermatologist</th>
<th>Previous dexamethasone dose (mg)</th>
<th>Previous gemcitabine dose (mg/m²)</th>
<th>Dose at rechallenge (mg/m²)</th>
<th>Interval before gemcitabine rechallenge (days)</th>
<th>Antihistamine used when extensive skin rash occurred</th>
<th>Antihistamine used when extensive skin rash occurred</th>
<th>Dose at rechallenge (mg/m²)</th>
<th>Antihistamine used when extensive skin rash occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>61</td>
<td>Female</td>
<td>Pancreatic</td>
<td>Trunk, upper and lower extremities</td>
<td>Maculopapular pruritic eruption</td>
<td>8</td>
<td>800</td>
<td>600</td>
<td>7</td>
<td>Yes</td>
<td>No</td>
<td>600</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>65</td>
<td>Female</td>
<td>Pancreatic</td>
<td>Upper and lower extremities</td>
<td>No referral</td>
<td>8</td>
<td>1000</td>
<td>800</td>
<td>14</td>
<td>Yes</td>
<td>No</td>
<td>1000</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>Male</td>
<td>Liposarcoma</td>
<td>Trunk, upper and lower extremities</td>
<td>Maculopapular pruritic eruption</td>
<td>4</td>
<td>1000</td>
<td>1000</td>
<td>14</td>
<td>No</td>
<td>Yes</td>
<td>1000</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>72</td>
<td>Male</td>
<td>Pancreatic</td>
<td>Trunk, upper and lower extremities</td>
<td>No referral</td>
<td>8</td>
<td>1000</td>
<td>1000</td>
<td>14</td>
<td>No</td>
<td>No</td>
<td>1000</td>
<td>No</td>
</tr>
</tbody>
</table>

Indicates the dexamethasone dose used as premedication just before the gemcitabine administration that was last associated with extensive skin rash.

Indicates the interval between the previous gemcitabine administration associated with extensive skin rash and gemcitabine rechallenge.

Dose Reduction due to grade 3 neutropenia.
consecutive patients with extensive skin rash associated with gemcitabine. Pretreatment with 4–8 mg i.v. dexamethasone with or without an antihistamine was not sufficient to prevent gemcitabine-induced skin rash. However, when 20 mg dexamethasone was given i.v. before gemcitabine rechallenge, there was no relapse in any case (Table 1). Below, we describe one representative case (patient 4 in Table 1).

**case 1**

A 72-year-old man with advanced pancreatic cancer was undergoing gemcitabine monotherapy at a local hospital. After the first administration of gemcitabine, he developed extensive skin rash, so gemcitabine was discontinued in light of the risk of severe toxic events. The patient was thereafter treated with oral fluorouracil (S-1). Nine months later, he became refractory to S-1 and was referred to Kyoto University Hospital for further treatment. Given that gemcitabine has been administered only once previously, it was decided to attempt gemcitabine rechallenge. For the first readministration of gemcitabine (1000 mg/m²), the patient was premedicated with 8 mg of dexamethasone i.v., but he again experienced extensive skin rash on his trunk and extremities. After recovery from the skin rash, a second readministration was attempted, with 20 mg dexamethasone premedication. The patient developed neither a skin rash nor a toxic reaction. Gemcitabine treatment (on days 1, 8 and 15 of each 28-day cycle) was continued uneventfully thereafter with 20 mg dexamethasone premedication before each gemcitabine administration.

Given the incidence of gemcitabine-associated skin rash, we assume that there have been many cases in which gemcitabine has been discontinued because of this adverse event. However, exclusion of gemcitabine leaves few effective chemotherapy options, especially for patients with pancreatic and biliary tract cancer. Obviously, this is most disadvantageous for the patient. To the best of our knowledge, there has only been one reported case of TEN associated with gemcitabine monotherapy [4]. In that case, the patient developed TEN after the first gemcitabine administration and the genital area was also affected. In our four cases, the mucosal lesions were intact. Since TEN usually involves the mucosal area, it is possible to distinguish between TEN and a simple extensive skin rash. The mechanism underlying the development of gemcitabine-associated rash is poorly understood; however, it seems to be different from that for toxic skin rash [1]. Furthermore, the risk of TEN associated with gemcitabine rechallenge is very low. Therefore, in special cases with no therapeutic alternatives, premedication with 20 mg dexamethasone can be considered.

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**references**


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