Abstract

The case report describes a woman who has an acute psychosis episode during the second course of trimethoprim/sulfamethoxazole therapy, after having an allogeneic hematopoietic stem cell transplant that favored a dose-related effect of this adverse effect.

Key words: Trimethoprim/sulfamethoxazole, Psychosis, Stem cell transplant

Introduction

Trimethoprim/sulfamethoxazole (TMP/SMX), a coformulation in a ratio of 1 to 5, that is the drug of choice for prophylaxis and treating Pneumocystis jiroveci(i) pneumonia in immunocompromised patients and allogeneic hematopoietic stem cell transplant (HSCT) recipients. The adverse effect of TMP/SMX therapy is uncommon and consists mainly of skin rash, while acute psychosis has been noted as a rare complication of the drug in case reports.

We describe a woman having an acute psychosis episode after undergoing an HSCT during her second course of TMP/SMX therapy at a higher dosage. The patient received a third, reduced-dosage TMP/SMX therapy, without psychosis 6 months later, which might favor a dose-related effect of this rare complication.

A 42-year-old woman was diagnosed with acute myeloid leukemia with t(8;21)(q22;q22)/RUNX1-RUNX1T1 in February 2011. Complete remission was achieved after the initial chemotherapies, but the disease returned 1 year later. She was scheduled for an allogeneic HSCT after salvage treatment. A survey before her HSCT showed normal heart, lung, renal, and liver functions, with no known allergies. A psychiatric survey also showed good status for an HSCT without a history of psychiatric problems. Prophylactic antibiotics, consisting of levofloxacin (1 tablet daily by mouth) and TMP/SMX (2 tablets 2 times a day by mouth) were prescribed for 2 weeks before the transplant without any adverse effects. And unrelated allogeneic HSCT was performed, and engraftment of the stem cells was confirmed 11 days later by a bold marrow examination, with recovery of white cell counts and platelet counts gradually later.

Unfortunately, dyspnea and desaturation occurred 13 days after the transplant. Imaging studies revealed bilateral pulmonary infiltrates with effusions. Considering that she had acute respiratory distress syndrome, and possibly a Pneumocystis jiroveci(i) pneumonia infection, the intravenous form of TMP/SMX was prescribed 320 mg every 8 hours (15 mg/kg of TMP daily). The infection was controlled 3 days later, but the patient had restless, hand tremors, and sleep disturbances 5 days after the TMP/SMX was prescribed.

Biochemistry showed no special abnormalities. Results of a brain computed tomography scan and cerebrospinal fluid after a lumbar puncture were unremarkable. After withdrawal of any other medications and with supportive care, these
is an individual’s difference, or whether there is a hypothesis that the psychotic reaction happened only > 18 mg/kg/day. Our case agrees with the second course, and with a higher dosage, the dosage was increased from < 12 mg/kg/day to 30 mg/kg/d, and no adverse effects were found in other courses. We question whether this increased from 0% to 23.5% when the trimethoprim and sulfamethoxazole was prescribed again in a reduced oral dosage, and she had no psychoses.

Trimethoprim/sulfamethoxazole is a well-tolerated antibiotic, widely used to treat many common infections, such as cystitis or bronchitis. Undesired side effects of the central nervous system rarely have been identified, and only few case reports have been noted (Table 1).2-7 Because the psychosis did not improve after discontinuation of the other medications, and it recovered only after we withdrew the TMP/SMX, we suggest that the TMP/SMX induced this complication. The pathomechanisms of TMP/SMX-related psychosis remain unclear,7,8 and the characteristics of these cases vary in age, disease status, medication route, dosage, and time of onset. We question whether this is an individual’s difference, or whether there is a dose-related effect to the psychosis.

In a retrospective study, Lee and associates8 demonstrated that the incidence of psychosis increased from 0% to 23.5% when the trimethoprim dosage was increased from < 12 mg/kg/day to > 18 mg/kg/day. Our case agrees with the hypothesis that the psychotic reaction happened only with the second course, and with a higher dosage, and no adverse effects were found in other courses of treatment. However, the psychosis could occur in patients with a standard dosage of TMP/SMX,4 or even a reduced dosage,7 which raises the question that it is the individual that leads to this adverse effect. Therefore, drug and/or metabolite level monitoring should be performed to clarify things. Withdrawal of the drug reverses this adverse effect and fortunately, most symptoms resolve completely after discontinuation of the drug (Table 1).

In conclusion, this case suggests that TMP/SMX-related acute psychosis could happen after an HSCT, and this may be dose-dependent with the patient. Neither risk factors nor biomarkers can predict this complication; therefore, we should remain alert the possibility of TMP/SMX-related psychosis in patients under treatment. Further studies about the drug level are required to draw a clearer conclusion about dosage and side effects.

References


Table 1. Characteristics of Patients With TMP/SMX-Related Psychosis

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Disease</th>
<th>Route</th>
<th>Dosage</th>
<th>Onset of Symptoms</th>
<th>Outcome After Discontinuing Medication</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>55</td>
<td>UTI</td>
<td>iv</td>
<td>240 mg q 8 h</td>
<td>Day 2</td>
<td>Resolved in &lt; 24 h</td>
<td>Mermel et al²</td>
</tr>
<tr>
<td>Male</td>
<td>88</td>
<td>UTI</td>
<td>po</td>
<td>160 mg bid</td>
<td>Day 2</td>
<td>Resolved in &lt; 24 h</td>
<td>McCue et al³</td>
</tr>
<tr>
<td>Female</td>
<td>74</td>
<td>UTI</td>
<td>iv</td>
<td>160 mg bid</td>
<td>Day 11</td>
<td>Resolved in &gt; 3 d</td>
<td>Gregor et al⁷</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
<td>UTI</td>
<td>po</td>
<td>160 mg bid</td>
<td>Day 2</td>
<td>Resolved in &gt; 3 d</td>
<td>Saidinejad et al²</td>
</tr>
<tr>
<td>Female</td>
<td>46</td>
<td>UTI</td>
<td>po</td>
<td>30 mg/kg/d</td>
<td>Day 2</td>
<td>Resolved in &gt; 24 h</td>
<td>Weiss et al⁸</td>
</tr>
<tr>
<td>Male</td>
<td>52</td>
<td>Renal transplant</td>
<td>iv</td>
<td>120 mg/kg/d</td>
<td>Day 2</td>
<td>Resolved in &gt; 24 h</td>
<td>Walker et al⁹</td>
</tr>
<tr>
<td>Female</td>
<td>69</td>
<td>Renal transplant</td>
<td>po</td>
<td>120 mg/kg/d</td>
<td>Day 3</td>
<td>Resolved in &lt; 24 h</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>72</td>
<td>Renal transplant</td>
<td>iv</td>
<td>120 mg/kg/d</td>
<td>Day 10</td>
<td>Resolved in &lt; 24 h</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: iv, intravenous; po, by mouth; UTI, urinary tract infection