ERTAPENEM ASSOCIATED WITH GENERALIZED TONIC-CLONIC SEIZURE IN A PATIENT WITH CHRONIC KIDNEY DISEASE

Shih-Chang Lin¹, Chih-Cheng Lai², Shih-Tze Chung²

Abstract

Seizures have been associated with meropenem and imipenem, but ertapenem induced seizure was scarce. Here we describe one patient with chronic kidney disease developed seizure after treating with ertapenem for five doses and reviewed previous reports in the English literature. The abnormalities of center nervous system (CNS) and renal function were the most common underlying diseases among these patients. In conclusion, ertapenem should be considered as one of possible etiologies of seizure during its administration, especially in elder patients with CNS disorder or renal insufficiency.

Key words: Ertapenem, Seizure, Carbapenem

Ertapenem is a 1-ß-methyl carbapenem and has excellent activity against many gram-positive and gram-negative aerobic, facultative, and anaerobic bacteria. In the following clinical entities: intra-abdominal infection, skin and soft tissue infection, community acquired infection, acute pelvic infection and complicated urinary tract infection, ertapenem is comparable with other antimicrobials that are used routinely in the treatment of the infections. As a member of carbapenem, ertapenem associated seizure are rarely reported. Here we describe one patient with chronic kidney disease developed seizure after treating with ertapenem for five doses.

A 87-year-old female with a history of hypertension, peptic ulcer disease and chronic kidney disease resided at a long-term care facility for half a year. She had no history of seizure or neurologic disease. On January 7, 2009, she presented with sudden onset of fever, dysuria and frequency. There was no cough, sputum, vomiting, abdominal pain and diarrhea. Her vital signs were temperature of 39°C, pulse rate of 110/min, respiratory rate of 22/min, and blood pressure of 115/63 mm Hg. Physical examinations were unremarkable except mild suprapubic tenderness. The white blood count was 1.82 x 10⁹/l with neutrophil predominance (77.1%), and urinary analysis showed pyuria and bactiuria. Antibiotic treatment with oral cephalexain was given for urinary tract infection after collection of urine culture. Three days later, culture of urine grew extended-spectrum-ß-lactamase (ESBL)- producing Escherichia coli, but blood culture did not yield any bacteria. The antibiotics were shifted to intravenous ertapenem (1000 mg every day). However, after five days of therapy, she developed generalized tonic-clonic seizures (GTCS).
Laboratory examination showed the level of urea and creatinine were 47mg/dl and 1.24 mg/dl, respectively and the estimated creatinine clearance was 30.2 ml/min. Other biochemical studies included the sodium, potassium, calcium, magnesium, glucose, and ammonia were within normal limit. Because of concern of possible ertapenem associated seizure, the antibiotic was switched to meropenem for two more days to complete the course. After the adjustment, no more seizure attack was noted on the follow-up.

Ertapenem is a long-acting carbapenem antibiotic that has a broad antibacterial spectrum against both Gram-positive and Gram-negative bacteria, including Enterobacteriaceae, Streptococcus pneumoniae and most species of anaerobic bacteria. It is also useful for the treatment of ESBL-producing organisms, such as demonstrated in our cases. The indication of ertapenem includes intra-abdominal infections, skin/soft-tissue infections, community-acquired pneumonia, pelvic infections and urinary tract infections. Furthermore, ertapenem was highly effective in patients with a range of disease severity within each indication, including elderly patients and patients with severe infections.

Seizures have been associated with meropenem and imipenem, and the risk factors of neurotoxicity associated with carbapenems included renal insuficiency, low body weight, advanced age and history of central nervous system abnormality. Ertapenem was generally well tolerated in elderly and the adverse effects were usually of mild-to-moderate severity, infrequently resulting in discontinuation of the drug. Seizures in patients treated with etapenem were scarce and the Medline search found only further nine reported cases. The clinical characteristics of all of these patients as well as the present case are summarized in Table 1. All of the ten patients were older than 40 years and eight of them were male. The abnormalities of center nervous system and renal function were the most common underlying diseases. Among eight patients with available of history about type of seizure, all of them presented with GTCS. Most of these patients had seizure attack during the forth to seventh day of ertapenem. No matter ertapenem was discontinued or modified, the outcome was favorable.

In conclusion, ertapenem, similar to imipenem, should be considered as one of possible etiologies of seizure during its administration, especially in elder patients with CNS disorder or renal insufficiency.

Conflict of interest
All authors disclosed no conflict of interest.
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The IRB approval was not required for this case report.

References

Table 1. Summary of ten reported cases of ertapenem associated with seizure

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Comorbidity</th>
<th>Previous seizure</th>
<th>Type of seizure</th>
<th>Day of ertapenem therapy until seizure</th>
<th>Discontinue of ertapenem</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 [3]</td>
<td>2006</td>
<td>71</td>
<td>M</td>
<td>DM, hypertension, ischemia heart disease, old CVA</td>
<td>NA</td>
<td>NA</td>
<td>5</td>
<td>NA</td>
<td>No recurrence</td>
</tr>
<tr>
<td>4 [4]</td>
<td>2007</td>
<td>41</td>
<td>M</td>
<td>CNS disorder</td>
<td>Yes</td>
<td>GTCS</td>
<td>7</td>
<td>Yes</td>
<td>No recurrence</td>
</tr>
<tr>
<td>5 [5]</td>
<td>2008</td>
<td>54</td>
<td>M</td>
<td>Traumatic head injury, ventriculitis, brain abscess</td>
<td>NA</td>
<td>GTCS</td>
<td>9</td>
<td>Yes</td>
<td>No recurrence</td>
</tr>
<tr>
<td>6 [5]</td>
<td>2008</td>
<td>51</td>
<td>M</td>
<td>Squamous cell carcinoma of ethmoid sinus</td>
<td>NA</td>
<td>GTCS</td>
<td>8</td>
<td>Yes</td>
<td>No recurrence</td>
</tr>
<tr>
<td>7 [6]</td>
<td>2008</td>
<td>40</td>
<td>F</td>
<td>Recent SAH, renal insufficiency</td>
<td>No</td>
<td>GTCS</td>
<td>7</td>
<td>Yes</td>
<td>Discharged</td>
</tr>
<tr>
<td>8 [6]</td>
<td>2008</td>
<td>86</td>
<td>M</td>
<td>Brain calcification, renal insufficiency</td>
<td>Yes</td>
<td>GTCS</td>
<td>6</td>
<td>No</td>
<td>No related death</td>
</tr>
<tr>
<td>10 [PR]</td>
<td>2009</td>
<td>87</td>
<td>F</td>
<td>Chronic kidney disease, HTN</td>
<td>No</td>
<td>GTCS</td>
<td>5</td>
<td>Yes</td>
<td>No recurrence</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; CNS, central nervous system; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end stage renal disease; GTCS, generalized tonic-clonic seizure; NA, not applicable; PR, present report
Ertapenem 誘發癲癇在慢性腎病患者

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摘要

儘管癲癇與 meropenem 和 imipenem 的相關已有不少文獻報告過，但是 ertapenem 導致癲癇的案例是罕見的。這裡我們在描述一名有慢性腎病的病人在經 ertapenem 五天的治療下發生癲癇並同時回顧的早先報告的英文文獻。我們發現中樞神經系統和腎功能的異常是在這些患者之中的最常見的的疾病。總而言之，臨床醫師應該考慮 ertapenem 作爲其中可能導致癲癇的其中原因之一，尤其是在使用在有中樞神經系統疾病或腎功能不全的病患身上。

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