Pregabalin Induced Confusional State with Paranoid Delusions

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CASE DESCRIPTION

A 70-year-old woman presented to an acute inpatient rehabilitation facility on postoperative day three, after undergoing left total knee arthroplasty. Her past medical history included severe osteoarthritis, hypertension, and diabetes mellitus type 2 and was negative for any psychiatric illness. The patient took metformin, celecoxib, and oxycodone/acetaminophen prior to undergoing surgical intervention. After surgery, pregabalin, 50 milligrams twice a day, was added to her previous oral analgesic regimen of celecoxib and oxycodone/acetaminophen. However, on the night of admission postoperative day two (POD #2), she developed mild paranoia. Her husband and nursing staff reassured her the entire night. In the morning, she apologized for acting strangely and participated in all therapy sessions. All medications that could cause psychiatric disturbance or delirium, including oxycodone/acetaminophen and pregabalin, were discontinued. That night, however, her paranoia returned and she remained emotionally labile and delusional despite reassurance and delirium intervention. During the night, she pulled the fire alarm in order to have the police and fire department come to protect her.

The following morning, she was oriented to person, place, time, and situation, but had a fixed delusion and paranoia that she was unsafe. She participated in her therapy sessions, but remained apprehensive of place, time, date, had organized speech, she recognized family members, and could recall all events. The only abnormality was the baseline mental status and was discharged home.

That night, she attempted to escape from the hospital and became combative. She was then readmitted to the acute care hospital under the psychiatric service. General blood exams excluded infection or metabolic derangement. While it is unknown if ketamine was used during surgery and in PACU. The patient began exhibiting symptoms of hypothermia, meningitis, encephalitis, cerebral infection, PNA, UTI and its analgesic properties in various clinical scenarios as there are reports of pregabalin causing delirium, psychosis, and other neuropsychiatric sequelae, especially in the context of accelerated dose titration [27, 28]. Even at lower doses we must weigh the risk and benefit to patients.

Discussion

As the population ages, there has been greater concern for maintaining and improving quality of life through medical intervention. Many are having elective joint replacements to decrease pain, increase mobility, and improve their quality of life. However, as the number of joint replacements performed increases, the risk of complications has decreased, but not disappeared. One such complication or areas of concern is pain during the perioperative period as it has been established that pain control after surgery is important for quality of life, participation in physical therapy, and other health-related benefits [13]. Given the need for better pain control, novel and multimodal treatment regimen have been developed, utilizing synergistic agents and affecting multiple pain pathways in order to minimize opioid use and limit opioid-related side effects [48]. One agent that has become more popular in multimodal pain regimens and perioperative period is pregabalin [924]. Some literature supports the use of pregabalin in this setting and has shown a reduction in both pain and narcotic consumption [22]. Additionally, the side effect profile has been relatively insignificant making it a good addition to the pain medication regimen [25,26]. However, there must be diligence in further researching the effectiveness of the this medication and its analogues in various clinical scenarios as there are reports of pregabalin causing delirium, psychosis, and other neuropsychiatric sequelae, especially in the context of accelerated dose titration [27, 28]. Even at lower doses we must weigh the risk and benefit to patients.

**Table 1:** Possible causes of postoperative psychiatric disturbance [29]

<table>
<thead>
<tr>
<th>Structural lesions</th>
<th>CVA, HTN, primary and met tumors, closed trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic cause</td>
<td>hypoxia, hypoglycemia, renal failure, liver failure, vitamin deficiency, acidbase or electrolyte abnormality</td>
</tr>
<tr>
<td>Hypoperfusion</td>
<td>shock, CHF, cardiac arrhythmia, anemia</td>
</tr>
<tr>
<td>Infectious causes</td>
<td>hyperthermia, meningitis, encephalitis, cerebral infection, PNA, UTI</td>
</tr>
<tr>
<td>Drugs</td>
<td>benzodiazepines, barbiturates, etomidate, atropine</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>sleep deprivation, urinary retention, fecal impaction, sensory disturbance</td>
</tr>
</tbody>
</table>

The documented half-life for pregabalin is 6 hours and we expect to elimination to be completed after 35 half-lives. As pregabalin is renally excreted, elimination is dependent on renal function [22]. While the patient described above had normal BUN/Cr values and assumed normal renal function, there was history of diabetes mellitus, relative dehydration, and post-operative blood loss anemia which all may have
contributed to the altered metabolism of pregabalin as manifested by a prolonged period of psychiatric disturbance.

In this case report we describe delirium and fixed paranoid delusion in an older patient with few medical comorbidities after TKA and while on a low dose of pregabalin. While pregabalin may be effective at treating perioperative neuropathic pain, physicians must be aware that even at low doses patients may experience significant psychiatric disturbance.

Conclusion

In summary, the present report suggests that an acute confusional state and paranoid delusions be considered a possible adverse reaction for pregabalin. Even at low doses in certain clinical scenarios, this medication may have the potential to cause significant distress to patients, their families, as well as health care providers. Discontinuation of the medication at the first sign of an adverse reaction will likely result in symptom resolution.

References