Unexpected outcome (positive or negative) including adverse drug reactions

Topiramate-induced psychosis: the picture at 12 months

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Summary

A 19-year-old white British man, not previously known to psychiatric services, presented with acute onset of florid psychotic symptoms. His symptoms included auditory hallucinations, misidentification of family members, thought interference and delusions of control. His level of distress was high and did not respond to verbal or medical de-escalation; therefore, he required nursing in seclusion. It was noted that he recently had an increase of his anti-epileptic medication to 100 mg topiramate twice per day. Topiramate was thought to be the cause of his psychosis and, consequently, was changed to phenytoin. Since discontinuation of the topiramate, his psychotic symptoms settled within 4 days and he was discharged shortly afterwards. He was monitored by the Early Intervention services. At 15-months post-discharge, there was no recurrence of any symptoms despite not receiving antipsychotic medication. To our knowledge, this is the first report that describes the progress of a patient past the initial psychotic episode. Therefore, we believe this is an important finding to report.

BACKGROUND

This case supports other similar reports regarding topiramate-induced psychosis and offers additional evidence of the absence of psychosis following discontinuation of the medication. To our knowledge, there have been no reports that describe the progress of a patient past the initial psychotic episode.

With the trend of topiramate being prescribed for a wider spectrum of disorders, including conditions that have a susceptibility to psychosis, it is important for physicians and psychiatrists alike to be aware that it may trigger a psychotic episode.

CASE PRESENTATION

In February 2009, a 19-year-old man with a history of epilepsy, diabetes and mild mental retardation secondary to a hypoxic brain injury at birth was arrested by the police following destructive actions towards his family property and uncharacteristic hostility.

On assessment in the Accident and Emergency department, it appeared that he was experiencing auditory and visual hallucinations, thought interference, delusions of control and misidentification of family members. The auditory hallucinations were commanding in nature and he believed that his father was somehow inside him and was controlling him. He misidentified his grandmother as his girlfriend and stated that he could see people possessing other people's bodies.

He was detained under section 2 of the Mental Health Act for further assessment of his mental health. He was transferred to a Psychiatric Intensive Care Unit as his level of distress was high and did not respond to verbal or medical de-escalation.

He required nursing in seclusion on multiple occasions. He became extremely hostile very quickly from being reasonable and compliant. During his time in seclusion he appeared to be emotionally labile and was aggressive

towards staff and property. It was noted that he appeared to be responding to unknown stimuli—attempting to grab them and then punching the wall or ceiling. He was unable to give reasons for bizarre behaviour such as drinking his own urine and smearing blood from his wounds onto the walls. A sedative effect was noted of the antipsychotic medication but no change in the intensity of his psychotic symptoms.

During admission, other causes of psychosis were eliminated by investigation. It was noted that he had recently had an adjustment of his anti-epileptic medication from sodium valproate to topiramate in an attempt to control the frequency of his epileptic seizures. At the time of admission he was on 100 mg topiramate twice per day. There appeared to be no change to the frequency of seizures reported by the family.

The introduction of topiramate coincided with the aggressive behaviour noted by his family.

The patient was reported as having a calm and kind disposition but from January 2009, after a few days of taking topiramate, he had become more aggressive and had assaulted two members of the public during an episode of absconding from the medical ward. When assessed by the liaison psychiatry team on 14 January 2009 it was noted that he had odd beliefs of feeling like he was in a video game and 'force fields'.

His presentation was discussed with the neurological treating team and a change to phenytoin was made due to a need for anticonvulsant cover and prompt discontinuation of the topiramate thought to be the cause of his psychosis.

INVESTIGATIONS

The patient was investigated fully for an organic cause of his clinical presentation. Baseline routine blood tests (including full blood count, erythrocyte sedimentation rate, kidney, liver, thyroid functions, serum glucose) were all normal. Urinalysis, microscopy and culture, and drug analysis

were normal. He also underwent CT scan of the head during his stay on the ward, which was also normal.

DIFFERENTIAL DIAGNOSIS

Organic psychotic disorder, acute and transient psychotic disorders, other non-organic psychotic disorders.

TREATMENT

During his stay in hospital, topiramate was discontinued. His psychotic symptoms settled within 4 days and his behaviour improved significantly. He was no longer responding to external stimuli. He was much less agitated and amenable to intervention.

OUTCOME AND FOLLOW-UP

Since discontinuation of topiramate his psychotic symptoms settled. By 24 h he no longer required nursing within the seclusion area. He showed appropriate and co-operative behaviour for a prolonged period. He was escorted off the ward the following days and successfully went on home leave within 5 days. He retained a good amount of insight regarding his experiences and although he was unable to explain them he could describe in detail what he went through and was able to distinguish his delusions and hallucinations from reality. He was discharged from the inpatient setting. He was monitored by the Early Intervention services initially weekly, then fortnightly and subsequently monthly and at 15 months post-discharge he remained symptom-free despite not receiving antipsychotic medication. His seizure frequency remains similar to prior admission and his diabetes remains well-controlled. His family report that he has returned to his previous personality and there have been no further aggressive outbursts.

DISCUSSION

Topiramate has been primarily a treatment for epilepsy and prophylaxis against migraines.¹ Recently there has been an increase in use in bipolar affective disorder,² aggression in borderline personality,³ post-traumatic stress⁴ and weight control secondary to antipsychotic medication⁵ or in eating disorders.⁶

There has been suggestion that topiramate acts both directly and indirectly on the brain causing psychosis,⁷ and that seizure freedom for people who have epilepsy was associated with psychosis.⁸

It can be argued that this patient may have developed psychosis due to a combination of his existing epilepsy, his previous brain injury and the addition of the topiramate. Interestingly, in our case, the frequency of seizures appeared to be consistent throughout and although some literature suggests the use of topiramate to treat aggression in some disorders it appeared to cause the aggression in this case.

Kober and Gabbard⁹ described topiramate-induced psychosis in a case that was not epileptic where topiramate was used for mood stabilisation and weight loss for a patient with obsessive compulsive disorder. Furthermore, Zesiewicz *et al*¹⁰ portrays two cases where the patients have no previous history of mental disorders and are treated for essential tremor. It appears that the precipitating and

maintaining factor in this case has been the use of topiramate as the patient has been free of symptoms of psychosis for over a 15-month period.

Overall, a small number of cases have been reported in neurological journals; however, it is rarely recorded in European psychiatric literature. Despite the case reports and one study indicating that topiramate-induced psychosis may have a prevalence of 1.5%,¹¹ psychosis is not listed as a side effect in the 59th edition of the *British National Formulary*.¹²

The importance of topiramate-induced psychosis needs to be highlighted across the specialties as more disciplines are prescribing for different indications. Clinicians need to be vigilant of the potential of psychosis as the onset is fairly rapid and in severe cases the consequences can cause a high level of distress.

Learning points

- ▶ Detailed history and investigations can suggest the diagnosis and management in unusual clinical situations.
- ▶ In patients presenting with florid psychotic features, physicians/psychiatrists need to consider organic causes.
- ▶ When prescribing topiramate for patients, physicians/psychiatrists should be alerted to the possibility of topiramate-induced psychosis and that clinicians should be vigilant surrounding changes to the patient's mental state.

Competing interests None.

Patient consent Obtained.

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