



Letter to the Editor

## 6-Month follow-up of a case with psychosis triggered by valacyclovir



### To the Editor:

Valacyclovir neurotoxicity, with presentations of mental status change, is a complication increasingly recognized after treatment of herpes infection. Most patients recovered well after discontinuation of the drug, but our case here presented with refractory psychosis triggered by short-term use of valacyclovir.

### Case presentation

An 80 year-old female, had history of well-controlled hypertension and diabetes mellitus. She presented to our psychiatric outpatient clinic in December 2016, with newly onset visual and auditory hallucinations, reference delusions and irritable mood. She received valacyclovir 500 mg/day due to herpes zoster 5 days before having psychosis. Valacyclovir was discontinued while risperidone 0.5 mg/day was prescribed under the impression of valacyclovir neurotoxicity. However, her symptoms persisted 1 week later. Brain computed tomography was done for differential diagnosis, which only revealed generalized atrophic change compatible with her age. Besides, her renal function (eGFR: 71 ml/min/1.73 m<sup>2</sup>) and cognitive function (January 2017 Mini-Mental State Examination MMSE: 23/30, Education: 9 years) were relatively preserved. Risperidone was titrated to 0.75 mg/day and gradual improvements were observed within 1 month. She thus stopped her antipsychotic but prominent psychotic symptoms soon flared up with similar presentations as before. Risperidone was resumed while partial remission of her psychotic symptoms was observed again. Interestingly, there was no further deterioration but even improvement in her cognitive function (March 2017 MMSE 25/30). Moreover, there was no identifiable evidence (i.e. fever, headache, focal neurological deficits or dermatological findings) to support the diagnosis of viral encephalitis, an important differential to be distinguished from valacyclovir neurotoxicity. Her psychosis remained refractory after 6-month follow up, and required low dose antipsychotic for symptom control.

### Discussion

Acyclovir neurotoxicity is a complication increasingly recognized after treatment of herpes infection. Adverse effects include headache, confusion, ataxia, hallucinations, irritability, dysarthria, myoclonus and seizure.<sup>1</sup> Valacyclovir, a prodrug

that rapidly convert into acyclovir, shares similar pharmacology and side effect profiles as its active metabolite.<sup>2</sup> Reviewing the literature, acyclovir neurotoxicity usually develops within 5 days (median onset: 72 h) after administration of the drug, and could cause difficulty in differentiation with herpes zoster encephalitis.<sup>3</sup> Some suggested that visual hallucinations and dysarthria being the unique features of acyclovir neurotoxicity.<sup>4</sup> Besides, absence of fever, headache or focal neurological deficits, lack of lateralization of electroencephalographic findings, normal cerebral spinal fluid and brain image study all favored the diagnosis of acyclovir neurotoxicity.<sup>1</sup> Development of neurotoxicity had been reported under standard oral dose of the drug. Associated risk factors were inappropriate drug dosing, older age, renal dysfunction and diagnosis of cancer.<sup>1</sup>

Patients with acyclovir neurotoxicity generally recovered well within 48–72 h after discontinuation of the drug. Hemodialysis was successfully applied in cases of severe intoxication.<sup>3,4</sup> However, the case we described had refractory psychosis triggered by short-term valacyclovir use under appropriate dose and normal renal function. No other neurological deficits were noticeable while her clinical picture could not be better explained by other neurodegenerative or systematic disorders. For symptomatic treatment of herpes infection, dosage, duration and possible neurotoxicity of valacyclovir should therefore be considered, especially when risk factors are identifiable.

### Conflict of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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