Acute neurotoxicity as a serious adverse event related to rasburicase in a non-Hodgkin’s lymphoma patient

Hyperuricemia and tumour lysis syndrome are well known complications during induction treatment for aggressive non-Hodgkin’s lymphomas (NHLs) [1]. Recently, rasburicase, which converts uric acid into the soluble compound allantoin, has been shown to control hyperuricemia faster and more reliably than allopurinol in adults and paediatric patients with acute leukaemia and lymphoma [2]. Here we report an unusual case of rasburicase neurotoxicity in an NHL patient after rasburicase infusion. The patient, a 35-year-old female, was referred to our unit for consideration of an NHL patient after rasburicase infusion. The patient, a 35-year-old female, was referred to our unit for consideration of a non-Hodgkin’s lymphoma NHL. Pertinent pre-treatment laboratory evaluations included the following: white blood cells, 10.1×10⁹/l; platelet count, 186×10⁹/l; haemoglobin, 10.2 g/dl; blood urea nitrogen, 23 mg/dl (8.2 mmol/l); creatinine 1.1 mg/dl (100 mmol/l); lactate dehydrogenase, 640 IU/l; alkaline phosphatase, 80 U/l; sodium, 140 mmol/l; calcium, 8.5 mg/dl (2.12 mmol/l); potassium, 4.7 mmol/l; and uric acid, 9.1 mg/dl.

As planned, administration of rasburicase was started the day before initiation of chemotherapy at a dose of 0.20 mg/kg. Within the first 2 h after administration, the patient became confused and agitated, she had generalised myoclonus and muscular spasticity. Within the first 2 h after administration, the patient became confused and agitated, she had generalised myoclonus and muscular spasticity characterised by extension of her neck to the left, and protracted deviation of the mouth to the left followed by decorticate positioning of the arms and legs. She became mute. At the time when these symptoms occurred, there were no significant abnormalities in the patient’s serum electrolyte, renal function, calcium level, arterial blood gases or hepatic function to suggest other metabolic causes of the observed symptoms, but uric acid levels decreased to 0.2 mg/dl after rasburicase administration. Results of a brain computed tomography scan with contrast were normal. Twenty-five milligrams of intravenous diphenhydramine were given, which produced an immediate relaxation of all myoclonus and muscular spasticity, but did not change the mutism. Over the next 24 h the patient had several episodes of myoclonus and muscular spasticity, which were resolved by intravenous diphenhydramine. After 36 h, the confusional state and myospasticity disappeared and she was able to speak. The uric acid level was 0.4 mg/dl at this point. Abnormalities not were found on the electroencephalogram. Electrophysiological studies, including nerve conduction, were normal.

The exact mechanism of this unusual toxicity, not commonly seen during treatment with rasburicase, is beyond our understanding. In current oncological practice, most of the characteristic acute pharmacological neurotoxicities reported to date can be referred to acute channelopathies [3, 4]. Na⁺, K⁺-ATPase is an enzyme embedded in the cell membrane that is necessary to maintain neuronal excitability. This enzyme activity is highly susceptible to free radicals, and in this context it has been shown that uric acid has a significant antioxidant activity and a neuroprotective role in both in vitro and in vivo models of cerebral ischaemia [5]. Curiously, in our patient, symptoms of acute neurotoxicity coincided with the drop in uric acid level. Whether uric acid acts on the sodium channels, modifying the action potential, remains to be explored. With increasing clinical use of rasburicase in adult and paediatric patients, a clearer understanding of the real incidence of this toxicity should become apparent.

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References