




# Phenytoin-Induced Red Discoloration of Urine in a Pediatric Neurosurgical Patient: An Unusual Finding

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The use of phenytoin is widespread in neurosurgical patients, especially in space-occupying lesions. It has predominant renal excretion and has been known to cause tubulointerstitial nephritis on chronic use. Despite its common use, there has not been definitive literature on urine discoloration due to phenytoin except for a commentary dated back in 1983 which refuted the finding of urine discoloration by phenytoin use.<sup>1</sup> Hence, we intend to highlight a case where there was episode of red discoloration of urine in a pediatric patient posted for excision of the cerebellar tumor under general anesthesia.

A 9-year-old female, weighing 30 kg, presented to the neurosurgical department with complaints of headache and vomiting for 1 month. On examination, her Glasgow Coma Scale was E4V5M6 with no neurological deficit, left side cerebellar signs were positive, including dysdiadochokinesia and finger nose test. Contrast-enhanced magnetic resonance imaging revealed a 3 × 3.5 × 4 cm lesion in the left cerebellar hemisphere with mild hydrocephalus (►Fig. 1). She was started on tablet levetiracetam 300 mg twice daily, syrup glycerol three tablespoons four times a day, and tablet acetazolamide 250 mg twice daily. She was posted for tumor resection by mid-line suboccipital craniotomy in the prone position. The blood investigations were within normal limits on the day of surgery; after confirming the nil per oral status, the patient was wheeled into the operating room. All the standard monitors, as per ASA (American Society of Anesthesiologists) recommendations, were attached. General anesthesia was induced as per the institute protocol. The patient was positioned prone, and surgery was started. The tumor excision was done. After the hemostasis was achieved, the neurosurgeon advised giving the loading dose of phenytoin given hydrocephalus. As per the advice, 450 mg phenytoin was put in 100 mL of 0.9% normal saline and infusion was

started. After about 5 minutes, we noticed hypotension, which responded to a bolus of intravenous crystalloid administration. After about 10 minutes, we observed red discoloration of urine in the urinary catheter tubing (►Fig. 2). Since phenytoin was the only additional drug administered in temporal association, it was stopped immediately. About 200 mL of 0.9% normal saline was given. After about 15 minutes, again, the color of the urine normalized. There was no similar episode of urine discoloration further. The patient was extubated and shifted to the neurosurgical intensive care unit.

Drug reaction with eosinophilia and systemic symptom (DRESS) syndrome, including a severe skin eruption, fever, hematologic abnormalities (eosinophilia or atypical lymphocytes), and internal organ involvement, usually 2 to 6 weeks after the initiation of drug therapy is a severe adverse drug reaction.<sup>2</sup> The anticonvulsants, including phenytoin and sulfonamide drugs, are most commonly associated with DRESS. The use of antiepileptic drugs (phenytoin, valproic acid, carbamazepine) has also been associated with tubulointerstitial nephritis.<sup>3</sup> Park et al reported a case of acute glomerulonephritis and drug-induced antineutrophil cytoplasmic antibody-associated vasculitis in a 65-year-old male patient with phenytoin use.<sup>4</sup>

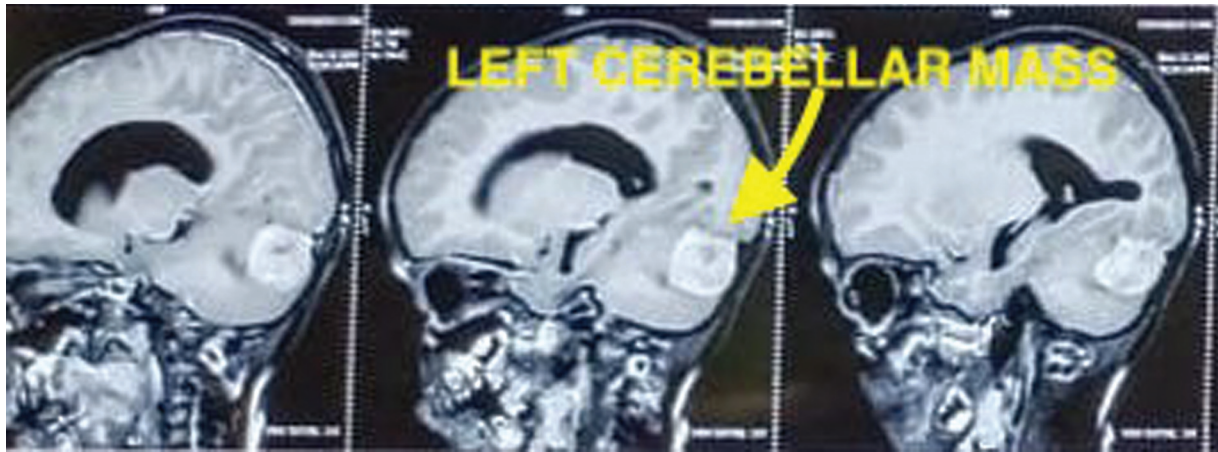
But this usually occurs after around 1 month of phenytoin use. However, the association of phenytoin with urine discoloration has not been aptly studied. There was a finding written in text of urology in 1978 stating that in the presence of urinary acid pH, phenytoin can result in red urine.<sup>5</sup> Derby and Ward did a detailed investigation on that urology text and followed all the sources from which this finding was reported.<sup>1</sup> On investigating Parke-Davis product information they did not find any reliable source of such finding. They found out some references where pink, red, and brown discoloration of urine

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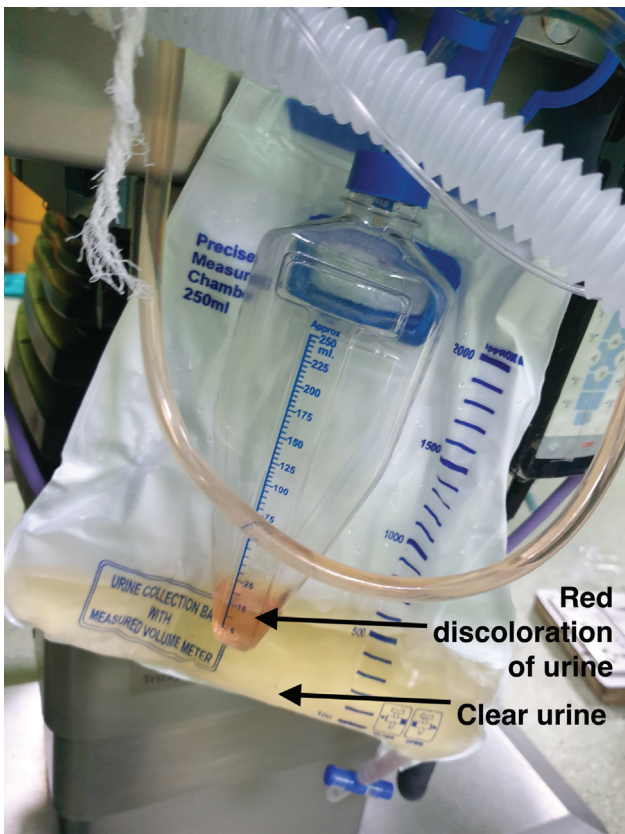
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**Fig. 1** T1 sagittal magnetic resonance imaging (MRI) scan showing left cerebellar space-occupying lesion (arrow).



**Fig. 2** Red color of the urine in urinary catheter tubing, which occurred in temporal association with the administration of phenytoin.

were listed owing to phenytoin use.<sup>6-8</sup> They continued their investigation to trace the source and found out that the source of reference was from a medical text by Shirkey.<sup>9</sup> They contacted him and were surprised to find out that he did not have

any knowledge of such finding been mentioned. Based on their extensive investigation, they refuted the finding of urine discoloration by phenytoin. With this case report, we intend to mention the fact that phenytoin can cause red discoloration of urine as evidenced by us and this could occur even in the presence of alkaline urine as the patient in our case was on acetazolamide. Hence, we conclude that whenever there is such adverse reaction in the presence of phenytoin, the causal relationship can be attributed to the drug. Further detailed studies are warranted to know the exact pathophysiology behind this finding.

#### Conflict of Interest

None declared.

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