



Reemergence of Neurological Deficit with Hyponatremia—When Obvious Is Not True

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Transient worsening of residual neurological deficit or recurrence of previous neurological deficit has been observed in patients with previous stroke. Recurrent stroke or transient ischemic attack (TIA) are frequent causes with a cumulative recurrence rate around 5.4% at 1 year.¹ Other causes may include Todd's paralysis, metabolic causes like hyponatremia, hypotension or infections, and use of sedative drugs.^{2,3} Herein, we report a case of transient reemergence of old stroke deficit with review of literature.

A 42-year-old hypertensive male was admitted with complaints of altered sensorium and acute onset left-sided weakness since last evening. He had history of right middle cerebral artery (MCA) infarct 1 year back when he had left hemiparesis associated with speech abnormality and facial deviation. He was managed conservatively and had functional recovery to modified Rankin score (mRS) 1. On examination, he appeared drowsy, irritable, dehydrated and had left side limbs power of medical research council (MRC) grade 2. His vitals showed heart rate 99 per minute, blood pressure 137/87 mm Hg, respiratory rate 18 per minute, and temperature 97.1°F. He was suspected to have recurrent stroke. Diffusion-weighted magnetic resonance imaging (MRI) of brain showed no diffusion restriction and, T2 weighted and FLAIR sequences showed hyperintense area in right frontoparietal region suggestive of old infarct with gliosis along with chronic infarct in right corona radiata. Electroencephalograph showed no epileptiform discharges. Blood investigations revealed blood sugar level 106 mg/dL and hyponatremia with serum sodium 122 mEq/L. Patient was admitted to intensive care unit with a provisional diagnosis of metabolic encephalopathy with hypovolemic hyponatremia in view of signs of dehydration, low serum osmolality, and urine sodium levels. Hypertonic saline infusion (3% sodium chloride) was started to treat hyponatremia along with supportive treatment. Next day, his serum sodium level

reached 137 mEq/L and he became alert with no irritability. His left-sided limbs power improved to MRC grade 4. Later, he was shifted to ward and discharged home.

Different authors have described reemergence phenomenon as post-stroke recrudescence (PSR), recrudescence of old stroke deficits (ROSDs), or differential awakening.^{2,4,5} This phenomenon was initially described by Cucchiara as “differential awakening” when he observed that patients with cerebral ischemia or mass lesions developed neurological deficits after awakening from anesthesia, which improved and returned to normal over 10 to 30 minutes.⁴ Thal et al,⁵ investigated the pharmacological effect of fentanyl and midazolam in patients with brain tumors or carotid disease. Transient unmasking or reemergence of previous deficit was observed in 73% patients with previously resolved or persisting deficit. Later, Lazar et al,³ investigated the role of midazolam in reemergence of stroke deficit in eight patients with previous stroke. All patients demonstrated transient reemergence or worsening of previous deficit, returning back to normal after 2 hours. Among the commonly used anesthetic agents in current era, midazolam and propofol are most frequently associated with sedation-induced transient neurological deficit.⁶ Patients in propofol and midazolam group had median NIHSS (National institute of health stroke scale) change of 2 to 3 points. The majority of score change was in limb motor function. They also found that tumor type and grade also affected the sensitivity to drugs. Post sedation NIHSS change was similar between gliomas and meningiomas, with similar sensitivity to all four drugs in patients with high-grade gliomas. Role of anatomical and functional changes in synaptic connectivity and receptor density secondary to brain remodeling may be implicated. GABA_A agonists have shown to reduce brain plasticity mediated by long-term potentiation compared with anti-cholinergics.⁷

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This explains the drug specificity in causation of post-sedation neurological deficits.

Recently, various other triggers for reemergence of deficit have been identified in patients with previous stroke, which include infection, dyselectrolytemia, and hypotension.^{2,8} Exact mechanism of re-emergence phenomenon is not known, but role of neurotransmitters like GABA (BZD, propofol), altered neuronal excitability or conduction (dyselectrolytemia), or cytokine-mediated pathway (infection) have been implicated. Reemergence is more frequently associated with small vessel infarcts, diabetes, dyslipidemia, and smoking. It is predominantly seen after stroke affecting white matter, however, change in NIHSS is similar in ischemic or hemorrhagic index stroke.² Incidence of reemergence is more when MCA territory (>70%) is involved during index stroke.² The resolution of deficit usually occurs within 24 to 48 hours with correction or reversal of the trigger.

Hyponatremia is frequent in patients with ischemic stroke with incidence up to 40% and SIADH being most common cause. Risk factors for hyponatremia include poor solute intake, site of infarction (MCA territory is most common), drugs like mannitol or diuretics, secondary infections and inappropriate use of hypotonic fluids. Hyponatremia can present as stroke mimic due to symptoms like altered sensorium, seizures, focal neurological deficits, and coma. During acute change in sodium concentration aquaporin four channels fail to upregulate in astrocytes. This prevents shunting of water into astrocytes thereby increasing cellular volume and cerebral edema resulting in generalized cerebral dysfunction. But mechanism of focal neurological deficits due to hyponatremia is not well understood and is believed to be secondary to alteration in neuronal conduction and excitability. Due to underreporting of reemergence phenomenon, exact frequency of hyponatremia in PSR episodes cannot be estimated, but Topcuoglu et al² reported high frequency (18.5%) of hyponatremia in these episodes.

Reemergence phenomenon can be seen in emergency setting, postoperative period, or after sedation for brain imaging. It should be promptly distinguished from mimics like acute stroke, TIA, or Todd's paralysis as it may have management-related implications. Therapy like intravenous thrombolysis (IVT) has associated risks and repeated imaging increases radiation exposure, length of stay, and cost. Although IVT should not be withheld in eligible patients

suspected to have acute stroke. Other clinical implication includes involving metabolic or infectious evaluation in suspected patients. Additionally, sedative agents should be selected based on patient factors, features of previous stroke, tumor type and grade. Neurological deficits are commonly limited to limbs motor weakness but delirium or confusion is frequent. Diagnostic criteria may include: (1) transient duration with spontaneous recovery after resolution of triggering factor, (2) MRI suggestive of old stroke with no acute ischemia, (3) no clinical or electroencephalographic evidence of seizure. Our patient developed irritability and reemergence of weakness which resolved after correction of hyponatremia. His clinical features fit the diagnostic criteria suggested by Topcuoglu et al.² To conclude, reemergence phenomenon is under-recognized due to poor knowledge or understanding. It is crucial to promptly diagnose and differentiate it from mimics to reduce error and improve outcome.

Conflict of Interest

None declared.

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