Calcineurin Inhibitor Toxicity as a Cause of Post-Operative Respiratory Arrest

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Introduction: We present a case of a child status post bone marrow transplant who had a respiratory arrest in the post-operative period related to tacrolimus toxicity.

Case Report: An 8 year old with a history of chronic pain and severe sickle cell anemia, status post bone marrow transplant, was scheduled to undergo a laparoscopic splenectomy.

Anesthesia was induced with midazolam, remifentanil, propofol, and pancuronium and maintained with isoflurane in 50% air/oxygen. Morphine and fentanyl were titrated and a ketamine infusion at 5mg/hr was continued from the patient’s chronic pain regimen. At the end of the case the patient was extubated uneventfully and taken to the PACU for recovery. Approximately one hour later the patient returned to his hospital room and continued on his pre-operative pain regime of a ketamine infusion, methadone, and dilaudid PCA. Nine hours after his discharge from the PACU the patient complained of loss of vision and then went apneic. He was unresponsive to physical stimulation and two doses of naloxone were ineffective in restoring spontaneous ventilation. He was emergently intubated and taken to the CT scanner. His CT scan revealed multifocal bilateral parietal and temporal lobe infarcts. Subsequent MRI showed diffuse cortical white matter involvement consistent with cyclosporine toxicity versus multifocal infarct. The patient was then transported to the pediatric intensive care unit for further management.

He was unresponsive to painful stimuli and was unable to move his bilateral upper or lower extremities. In the PICU, he began to have intractable seizures and was placed on a high-dose midazolam infusion to control his seizures. Dopamine was used to increase cerebral perfusion since his initial CT scan was consistent with multiple embolic strokes and he was taken off his tacrolimus because the MRI was suggestive of calcineurin inhibitor toxicity. Over the next three days, his seizures abated and he slowly regained neurologic function. A repeat MRI showed significant improvement in the multifocal cortical lesions with a normal MRV and mild irregularities in the middle cerebral arteries on MRA. He was then diagnosed with a posterior reversible encephalopathy related to calcineurin inhibitor toxicity.

Discussion: This is the first case report of calcineurin inhibitor toxicity as a cause of post-anesthetic respiratory arrest. Most cases of posterior reversible encephalopathy syndrome (PRES) resolve with cessation of calcineurin inhibitors and normalization of blood pressure. In our case, the patient markedly improved within 3 days of stopping the tacrolimus. Calcineurin inhibitor-induced neurotoxicity is a very rare side effect of post-transplant therapy but should be considered early as cessation of these drugs may completely reverse neurologic deficits.

References: