Status Epilepticus Due to Hyperfusion Injury Post Cardiac Surgery

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Status epilepticus is a neurologic emergency that mandates urgent administration of appropriate anti-epileptic drugs (AED) and sedatives to prevent underlying brain injury. Although seizures often respond to initial, small doses of traditional sedatives, often large doses are required to achieve seizure arrest, and in rare instances, general anaesthesia is required, together with intubation and transfer to an intensive care setting[1]. In addition to prompt medical management, the treating physician should initiate a search for the cause of seizure activity, and the differential diagnosis here can be broad (Table 1). If intubation and paralysis is required, regular and, ideally continuous electroencephalogram (EEG) monitoring should be used to guide the rational use of anaesthesia and AEDs and will also allow a gradual weaning off medication.

Here we present a case of status epilepticus post cardiac surgery for repair of aortic dissection. This case is notable because of the young age of the patient and a previous medical history devoid of neurologic dysfunction. The cause of her intractable seizures was believed to be intraoperative cerebral hyperperfusion injury, representing an unrecognized neurologic sequela for this type of operation. We then review hyperperfusion injury in the context of vascular surgery as well as its associated neurologic complications, and recommend steps that could be taken to avoid such injury.

Table 1: Differential diagnosis for status epilepticus

Trauma
Cerebrovascular event (ischemic or hemorrhagic)
Medication related (overdose, withdrawal)
Anoxic brain injury
Metabolic derangement (electrolyte disturbance, hypoglycemia)
Drug (alcohol, illicit)
Subtherapeutic levels of anti-epileptic medications
Structural cause (tumour, vascular malformation)
Infection (meningitis)

Case Report

A 29-year-old female university student presented with an asymptomatic type A ascending aortic dissection, detected on screening cardiac MRI. She had a known history of Turner's Syndrome, as well as an aortic coarctation, repaired at age 4 and a more recent repair, at the age of 17, of a hypoplastic transverse aortic arch. Her past medical history otherwise was positive for hypertension, for which she was on atenolol, and depression, for which she was on no medication. She was taking an oral contraceptive. On the morning following admission, she underwent cardiac surgery to fix her ascending dissecting aortic aneurysm. The surgery was done under cardio-pulmonary bypass conditions, with cerebral perfusion during aortic repair, accomplished in an antegrade fashion through the right subclavian and innominate artery, with the use of a Dacron graft. Blood pressure was monitored using bilateral radial arterial lines, and the patient was hemodynamically stable throughout the case. The right femoral vein was cannulated and a large venous cannula was introduced into the right atrium. The patient was cooled to 18 degrees Celsius before sternotomy. The minimum esophageal temperature reached was 14 degrees Celsius. Sternotomy was done and the aorta was dissected. Hypothermic circulatory arrest was started and the proximal innominate artery was clamped and antegrade cerebral perfusion was initiated. The total time of circulatory arrest with cerebral perfusion was 76 minutes and cerebral perfusion was maintained at 16 degrees at a rate of 1 litre/minute. The aneurysm in the ascending aorta and proximal arch was then excised and a Dacron graft was anastomosed to the distal aortic arch. The repaired arch was deaired and clamped and the innominate artery clamp removed. Cardiopulmonary bypass was restarted and rewarming commenced. After rewarming to 36.5 degrees celcius cardiopulmonary bypass was weaned. At the end of the case, the patient was transferred to the cardiac intensive care unit (ICU) sedated under propofol as per our institution's protocol post-cardiac surgery.

On attempted weaning off propofol at four hours post-op, the patient had a witnessed generalized seizure episode. Propofol

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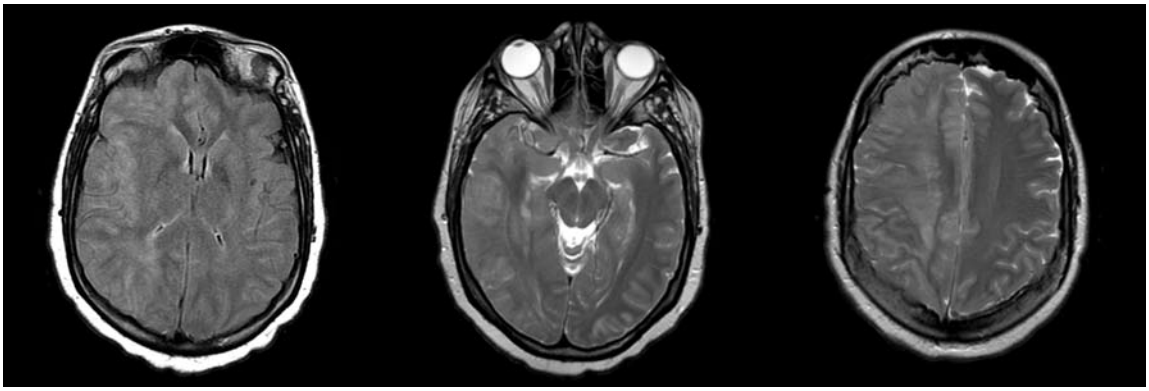

Figure 1: *Axial FLAIR MRI and Axial T2 weighted MRI on post-operative Day 2.*

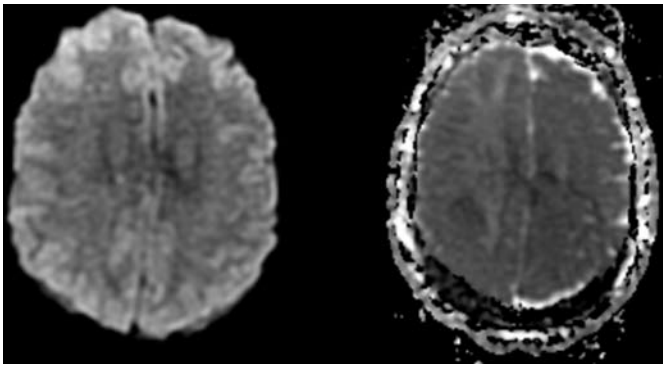

Figure 2: *DWI and ADC map on post-op Day 2 showing no evidence of infarction or ischemia.*

was restarted and another wean was attempted overnight, resulting in another generalized seizure. Plain head CT revealed no abnormalities. The patient was loaded with dilantin and prescribed sedation as needed for further seizure. Generalized seizures continued and became refractory to high doses of sedation, necessitating the administration of general anaesthesia with propofol. Prior to this, and in between seizure episodes, physical examination revealed reactive mid-size pupils bilaterally, present brainstem reflexes with right sided flexion to deep central pain. There was no movement detected on the left side. A brain MRI on post-op Day 2 revealed generalized right hemispheric swelling, not consistent with any particular vascular distribution (Figure 1). The diffusion weighted imaging (DWI) sequence, and the Acquired diffusion co-efficient (ADC) map, showed no evidence of infarction or ischemic lesions to account for the patients clinical condition (Figure 2), and the imaging was most consistent with vasogenic edema involving both cortical and subcortical white matter. An electroencephalogram on post-op Day 3 showed subclinical seizure activity, even while under high-dose propofol, and subsequent EEG's demonstrated diffuse epileptiform discharges, with a predominance in the right hemisphere. Given hemodynamic concerns with propofol, the patient was switched to thiopental after even higher doses of propofol finally managed to convert the patient to a burst suppressed EEG pattern. The patient was started on valproic acid as well, and daily EEG demonstrated continued burst suppression. A repeat MRI on post-op Day 7 demonstrated no improvement in right hemispheric swelling. On post-op Day 9 the patient was weaned off thiopental given concerns regarding its long half-life, and she was started on intravenous midazolam. Continued daily EEG began to show an emergence from burst-

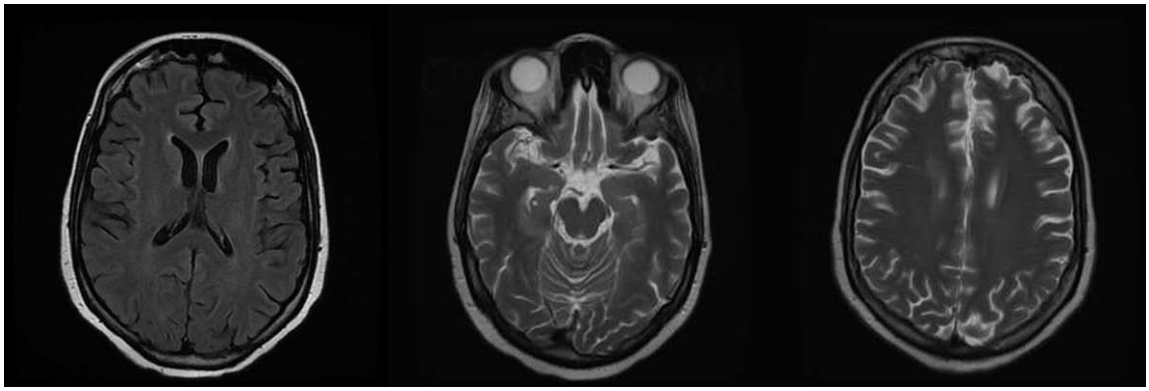

Figure 3: *Axial FLAIR MRI and Axial T2 weighted MRI at four months post-op (i.e. most recent neurology follow-up). Note complete resolution of T2 hyperintensity and FLAIR signal in right hemisphere compared to the images on post-op Day 2.*

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Table 2: Imaging findings of hyperperfusion syndrome, acute ischemia and status epilepticus

	Hyperperfusion	Acute Ischemia	Status Epilepticus
CT	Typically normal	May be normal; or with clot visible in MCA, and /or subtle features of ischemia such as cortical hypodensity, insular swelling, loss of grey-white interface	Typically normal
CTA	Typically normal	May be normal; or filling defect in major vessels (e.g. MCA)	Typically normal
MRI T2	Hyperintense	Hyperintense	Variable hyperintensity, with atrophy of involved region(s) with time
DWI	Hypo- to iso-intense	Hyperintense region in area of infarction	Hyperintense
ADC	Normal to slightly increased	Hypointense region in area of infarction that corresponds to bright region on DWI	Early decrease, then late increase

CT: computed tomography, CTA: computed tomography angiogram, MRI T2: T2 weighted magnetic resonance imaging. DWI: diffusion weighted imaging, ADC: Acquired diffusion co-efficient, MCA: middle cerebral artery.

suppression with no seizure activity. On post-op Day 19 both the thiopental and midazolam had been weaned, culminating on post-op Day 24 with evidence of intact brain stem function, representing the first sign of emergence from her medication-induced coma. An MRI done at the point revealed significantly decreased edema in the right hemisphere. Gradually the patient recovered neurologic function, and was extubated and transferred out of the cardiac intensive care unit. On the ward, she regained her strength, suffering only mild weakness from a chronic ICU myopathy affecting her proximal musculature and neck muscles. On discharge from hospital, the patient was fully ambulatory, fluently conversant, eating independently, and seizure-free. She was discharged on a single AED, with plans to have it discontinued, if she remained seizure-free at the first neurology follow-up. When seen by neurology at four months post-op, the patient remained seizure-free, with no abnormalities detected on ambulatory EEG, and a complete resolution of the right hemispheric swelling on MRI (Figure 3).

Discussion

Cerebral hyperperfusion is a recognized but rare complication of cardiovascular surgery. Although most commonly associated with carotid endarterectomy for carotid stenosis[2,3], some case reports do exist that describe it in the context of arterial bypass[4] and valve replacement surgery[5]. We have reported, what we believe is the first case of hyperperfusion injury occurring post aortic aneurysm/dissection repair, and resulting in a prolonged, severe, and ultimately reversible, neurologic deficit.

The mechanism of cerebral hyperperfusion syndrome is believed to be impaired autoregulation following a period of hypotension. Vasodilated vessels are exposed to relatively large perfusion pressures, leading to endothelial injury, vasogenic edema, localized inflammation, and neuronal dysfunction[6]. The clinical picture is broad, ranging from relatively mild self-limiting symptoms, such as headache, hypertension and focal neurological deficits, to life-threatening conditions such as intracerebral or subarachnoid hemorrhage[7].

Hyperperfusion has been variably defined in the literature, with some authors suggesting a cerebral blood flow rate that is greater than 100% of the baseline flow rate[3]. Other authors suggest it is a cerebral flow rate that is "a major increase…well above the metabolic demands of brain tissue"[8]. Although rates of occurrence vary in the literature, some estimate that as many as 14% of carotid endarterecomy cases are complicated by this hemodynamic phenomenon, although only a very small minority, typically 0.5-3%, become symptomatic[3,9]. Rates of hyperperfusion during and after cardiac surgery, especially following cardio-pulmonary bypass procedures, are unknown.

Most neurologic complications following cardiac surgery are typically ischemic, involving cardio-embolic events occurring usually intra-operatively and detected in the post-operative period. As many of these events are clinically silent, exact prevalence figures are difficult to calculate. One recent study, however, in 34 patients who underwent cardiac surgery for bypass and valve replacement, found evidence of new infarction on diffusion weighted MRI in 40% of patients who received aortic valve repair[10]. Seizures, both focal and generalized, and focal motor deficits, are all recognized features of the cerebral hyperperfusion syndrome, however they typically don't occur until 24 hours after the procedure[11]. In one case report, a man undergoing aortic root replacement and closure of a patent foramen ovale suffered a post-operative unilateral flaccid hemiplegia and anosagnosia, both of which resolved spontaneously on the third post-operative day[5]. Magnetic resonance imaging revealed diffuse right hemispheric T2 hyperintensity involving cortical and subcortical white matter. As with our case, DWI was negative, and T2 signal did not conform to any specific vascular territory.

In our case we were able to exclude the possibility that the MRI illustrated ischemia in the absence of infarction, as even in such cases DWI would have demonstrated some early restriction, and would certainly be abnormal, in the context of such extensive T2 changes as those seen on the second post-operative day. The imaging findings of ischemia and hyperperfusion, as well as those of status epilepticus, can sometimes be similar, however, particularly in early stages, and we summarize their respective findings in Table 2. The clinical context, follow-up imaging and clinical examination typically help to distinguish between the diagnoses.

As mentioned, status epilepticus itself can result in changes detectable on MRI, including the development of T2 hyperintensity, as well as changes in diffusion restriction[12-14]. Although the differential diagnosis of T2 hyperintensity in our patient's clinical context includes refractory status, the absence of significant DWI and related ADC findings argue against status as the main cause of the imaging findings. Additional MRI findings, typical of status, such as ipsilateral thalamic abnormalities, gyral and leptomeningeal enhancement, as well as atrophy of affected regions on follow-up imaging, were also

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absent in our patient[15-17]. Furthermore, status epilepticus is a symptom, not a diagnosis, and although the cause and effect relationship of clinical picture and imaging can be ambiguous, it must be remembered, that status is most frequently a consequence of an exacerbating, underlying pathological condition, which in our patient, was likely excessive cerebral hyperperfusion in dysregulated cortex.

Reversible encephalopathy is very well known in neurological practice, most commonly in the form of PRES, or posterior reversible encephalopathy syndrome. Seen as a complication of some pregnancies, as well as in association with certain chemotherapy agents, it has previously been referred to as hypertensive encephalopathy[18]. There is usually a predilection for the vasogenic edema to develop in the bilateral occipital lobes[18]. As a similar pathophysiology underlies PRES and cerebral hyperperfusion, it may well be that our patient experienced a variant of PRES following her surgery. It remains unclear why the edema in our patient was limited only to the right hemisphere, and why it spared the posterior fossa, but interestingly, this was also the case for the patient with transient unilateral hemiplegia described above. One possible explanation is related to the operative procedure itself, whereby cerebral perfusion was maintained via a cannula inserted into the right innominate artery, and common carotid, while the left common carotid was clamped to facilitate work on the aorta. Excessive and prolonged right sided perfusion, in the context of an occluded left common carotid, could theoretically expose the right brain to excessive perfusion. Furthermore, an incomplete circle of Willis is present in up to 20% of healthy individuals[19], and our patient's MRA demonstrated a fetal type left posterior communicating artery with hypoplastic anterior communicating and left posterior cerebral arteries. It could be that this variant somehow predisposed our patient to hyperperfusion injury by over-perfusing the right side of her brain relative to the left hemisphere. One possible means of avoiding this type of injury in future patients is obtaining circle of Willis imaging as part of the pre-operative work-up prior to any procedure in which cerebral perfusion will be manipulated, such as circulatory-arrest surgery. This case also illustrates the importance of regular, and continuous if necessary, EEG monitoring in ICU patients experiencing ongoing seizure activity that is difficult to control. Daily EEG's in our patient allowed us to rationalize her AED regime and gradually wean her off high dose anaesthesia and barbiturate-induced coma.

Status epilepticus as a result of diffuse hemispheric hyperperfusion post-cardiac surgery has not been reported. Judicious use of clinical tools, medications, and neuroimaging allowed us to guide this patient to a full and successful recovery. Pre-operative cerebrovascular imaging prior to surgery that may compromise cerebral perfusion may aid in preventing this type of injury in future patients.

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