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Case report

Amiodarone induced movement disorder after cardiac arrest – A case report

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Abstract

We describe a case of new onset movement disorder in a patient with ventricular tachycardia storm supported with peripheral VA ECMO. The differential diagnosis of abnormal movements in a post cardiac arrest patient requiring temporary mechanical circulatory support for cardiogenic shock is explored.

Keywords: Ventricular tachycardia, Cardiac transplant, ECMO, Cardiomyopathy, Seizures, Amiodarone

Introduction

The patient was a 52-year-old male with NYHA IV non-ischemic cardiomyopathy undergoing outpatient workup for heart transplantation. He presented for a scheduled right heart catheterization (RHC) with reports of worsening dyspnea on exertion, fatigue and lower extremity edema. Labs revealed acute kidney injury and hyperbilirubinemia (Table 1). The RHC revealed elevated biventricular filling pressures and low cardiac output consistent with Society for Cardiovascular Angiography & Interventions C cardiogenic shock including pulmonary capillary wedge pressure of 17 mmHg, Fick cardiac output 2.7 L/min, Fick cardiac index 1.3 L/min/m2 and Pulmonary artery oxygen saturation 49%. The patient was transferred to the cardiac intensive care unit and treated with inotropic support and diuresis with normalization of cardiac index and filling pressures and improvement in renal function.

Methods/ethical statement

The authors obtained written informed consent from the patient who was able to sign for himself as per our local institutional protocol. All data was de-identified and reviewed in a secure manner.

Clinical record

Upon awakening the following morning, he developed pulseless ventricular tachycardia (VT). His CRT-D (cardiac resynchronization therapy) began anti-tachycardia pacing (ATP) which accelerated the rhythm into ventricular fibrillation (VF), requiring brief CPR with successful internal defibrillation and ROSC. The patient immediately awakened and followed commands with no focal deficits noted on examination. No post-anoxic myoclonus was identified. The patient had incessant non-sustained VT which was poorly tolerated hemodynamically and was loaded with infusions of amiodarone and lidocaine per standard dosing. Given continued electrical instability and cardiogenic shock, he was taken to the operating room and successfully cannulated for peripheral veno-arterial extracorporeal membrane oxygenation (VA ECMO). Induction was performed with high dose fentanyl and low dose etomidate.

On post-arrest day zero he was transferred to the cardiothoracic intensive care unit and listed status 1A for cardiac transplantation. The CRT-D tachytherapies were turned off. Despite mechanical circulatory support, he continued to have VT with low pulsatility requiring additional boluses of amiodarone and multiple electrical cardioversions which terminated the dysrhythmias. Later that day, nursing staff witnessed movements at rest described as head turn-

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https://doi.org/10.1016/j.resplu.2022.100272
Received 20 May 2022; Received in revised form 21 June 2022; Accepted 23 June 2022
Available online xxxx

Table 1 – Admission laboratory data.

Laboratory test	Patient result	Reference range
Creatinine	2.8 mg/dL	0.5–1.4 mg/dL
Serum bicarbonate	25 mMol/L	21–31 mMol/L
Lactate	3.2 mMol/L	0.5–1.6 mMol/L
Sodium	132 mMol/L	136–146 mMol/L
Potassium	3.7 mMol/L	3.5–5.0 mMol/L
Total bilirubin	3.6 mg/dL	0.3–1.5 mg/dL
AST	64 IU/L	17–63 IU/L
ALT	60 IU/L	15–41 IU/L

ALT: alanine aminotransferase; AST: aspartate aminotransferase.

ing, stiffening and shaking of extremities – worse on the right side compared to the left. During these episodes the patient was awake, oriented to self and intermittently following commands.

Past medical history

His past medical history included non-ischemic cardiomyopathy with ejection fraction 20–25%, non-obstructive coronary artery disease, VT on mexiletine and implanted CRT-D seven months prior to admission. He continued to have VT treated with ATP and was started on amiodarone 400 mg daily four months prior to admission. His outpatient heart failure regimen also included aspirin 81 mg daily, bumetanide 2 mg twice daily, melatonin 10 mg at night, metolazone 2.5 mg daily, metoprolol succinate 12.5 mg daily, mexiletine 150 mg twice daily, potassium chloride 20 mEq daily and sacubitril-valsartan 24–26 mg half tab twice daily. The patient had no prior history of seizure or non-epileptic spells.

Diagnostic testing:

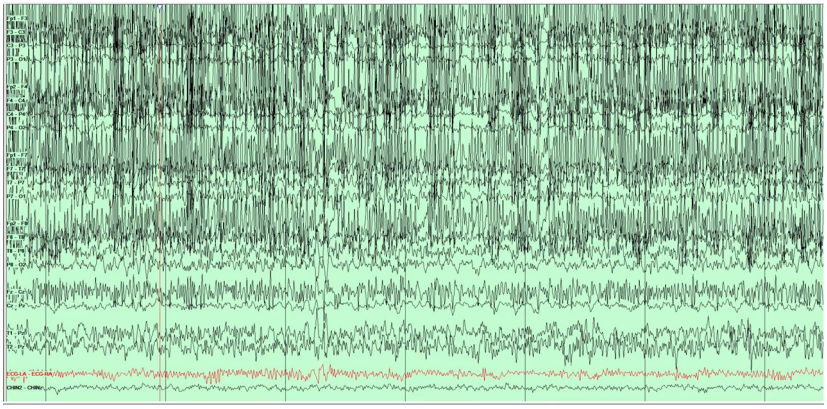
The critical care medicine team engaged neurology for evaluation. The patient had a continuous electroencephalogram (cEEG) monitoring placed to evaluate for seizure which showed a continuous, variable and reactive background without cortical cortical discharges or electrographic seizure (Fig. 1). He then underwent short interval computed tomography (CT) scans of the brain to evaluate for intracranial pathology (Fig. 2) which were negative. Magnetic resonance imaging (MRI) could not be obtained given ECMO support. Relevant laboratory tests were not suggestive of a metabolic etiology (Table 2). The movement episodes persisted throughout the following day. Levetiracetam was administered without change in the patient's movements or cEEG pattern. The patient was then intubated and initiated on propofol infusion for potential seizure control due to concern that myogenic artifact may be obscuring underlying epileptiform discharges (Supplemental video 1). Lidocaine was held due to concern for neurotoxicity. The patient's heart transplantation listing was changed to status 7 due to concern for new onset seizure, other debilitating post-anoxic injury or movement disorder.

On post-arrest day two, our local post cardiac arrest service and psychiatry teams were engaged as episodes persisted to consider a broader differential: post-anoxic movement disorders and non-epileptic spells. The differential diagnosis included ischemic stroke, intracranial hemorrhage, status epilepticus, post-anoxic myoclonus, Lance Adams Syndrome, non-epileptic spells and adverse drug reactions including serotonin syndrome or other medication toxicity.

Physical examination

With sedation held the patient had eyes open spontaneously, tracked the examiner and nodded appropriately to questions. He had cogwheel rigidity of upper extremities and at rest, a pill rolling tremor of his right hand greater than left that improved with movement to follow commands. There was no inducible clonus. His strength was symmetrical without apparent sensory deficits. Ataxia and bradykinesia could not fully be assessed due to femoral cannulation. The patient was endotracheally intubated with bilateral breath sounds on minimal ventilator settings. His heart rhythm was paced at 75 beats per minute on amiodarone infusion at 0.5 mg/min. His extrem-

video 1.



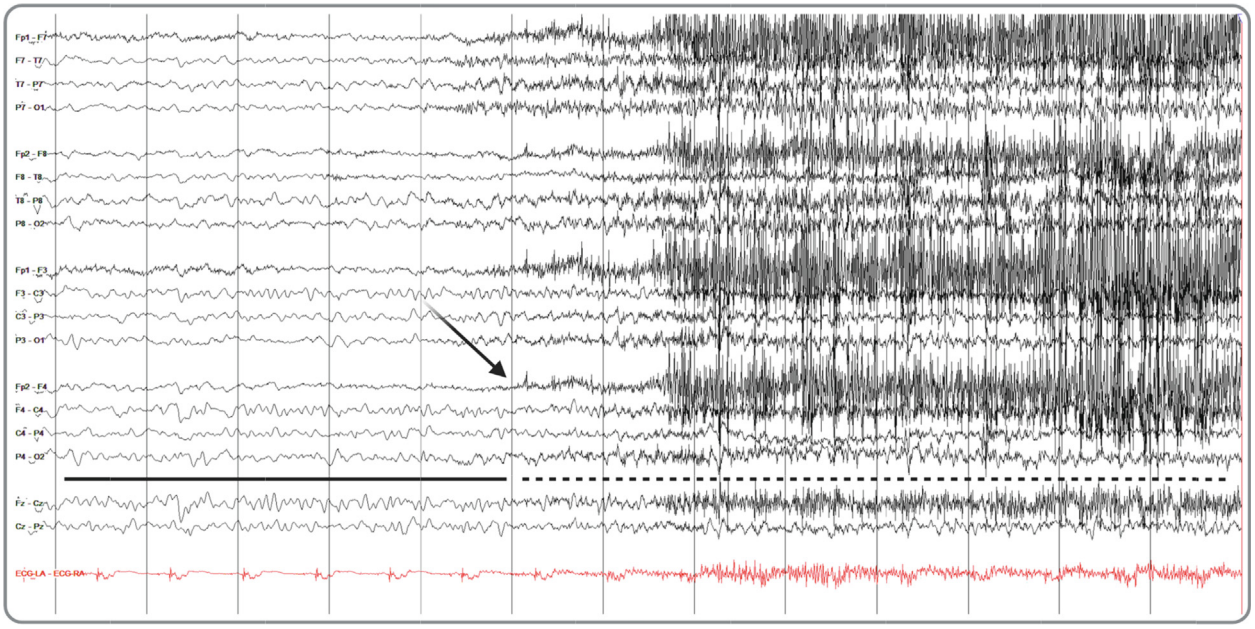


Fig. 1 – Initial electroencephalography, Background is continuous, variable and reactive (solid bar) with onset of tremor (arrow) and myogenic artifact (dotted bar).

ities were warm and well-perfused on VA ECMO with an epinephrine infusion at 0.02 mcg/kg/min.

Management

The patient received a total of 1100 mg of IV amiodarone during the preceding 12 hours to the abnormal movements. After multidisciplinary discussion between the cardiothoracic surgery and critical care teams, amiodarone was discontinued. Both propofol and levetiracetam were stopped and he was started on scheduled clonazepam to ablate movement disorder.

Discussion

We had a high suspicion that the patient's movements were amiodarone-induced Parkinsonism after obtaining a negative workup, detailed history and neurological exam positive for cogwheel rigidity and pill rolling. The Naranjo probability scale score for amiodarone in this patient was 6 (probable).[1] Gait ataxia and upper extremity intention tremor associated with amiodarone use were common in the 1980s when daily doses were frequently much higher compared to contemporary practice. Symptoms often improved or resolved with dose reduction or discontinuation of medication.[2,3] More recent studies report a much lower incidence, with approximately 3% of patients on amiodarone as outpatients experiencing neurological symptoms including tremors, ataxia, cognitive impairment, and peripheral neuropathy.[3] The pathophysiology of amiodarone neurological toxicity is unknown. Hyperthyroidism induced by amiodarone may cause such symptoms, but thyroid levels checked later in the patient's hospitalization were within normal limits.

Other diagnoses were considered and excluded in the context of the patient's critical illness and mechanical circulatory support. Ischemic or hemorrhagic stroke as well as seizures are known complications of VA ECMO.[4] We were unable to obtain a brain MRI due to ECMO and later due to retained epicardial pacer wires but short interval CTs were negative. There have been cases that demonstrate the relatively rapid improvement of symptoms with discontinuing amiodarone despite its long half-life.[5,6] Partial status epilepticus may cause abnormal movements and intact mental status; however no clear seizures were captured in this case and the remainder of recordings were without any epileptiform or inter-ictal abnormalities. Patients may develop myoclonus or Lance Adams syndrome following cardiac arrest. Such patients are initially comatose and have distinct EEG findings not observed in our case.[7] In patients with potential Lance Adams syndrome, awakening is typically delayed on the course of days to week after return of spontaneous circulation (ROSC). Neither the patient nor family endorsed a history of non-epileptic spells. Other toxicities were considered, specifically serotonin syndrome given a cardiac induction dose of fentanyl was used to facilitate intubation prior to cannulation, but the patient had no clonus making serotonin syndrome less likely. No fever was noted but this can be masked by extracorporeal support.

Follow-up

The following day, the abnormal movements rapidly improved with discontinuing amiodarone and starting clonazepam. The patient was extubated and re-listed for orthotopic heart transplantation. On further questioning, he told us he noted a mild intention tremor after starting amiodarone as an outpatient. Holding home mexiletine and loading of IV amiodarone may have unmasked and worsened symptoms. The patient underwent successful heart transplant on post-

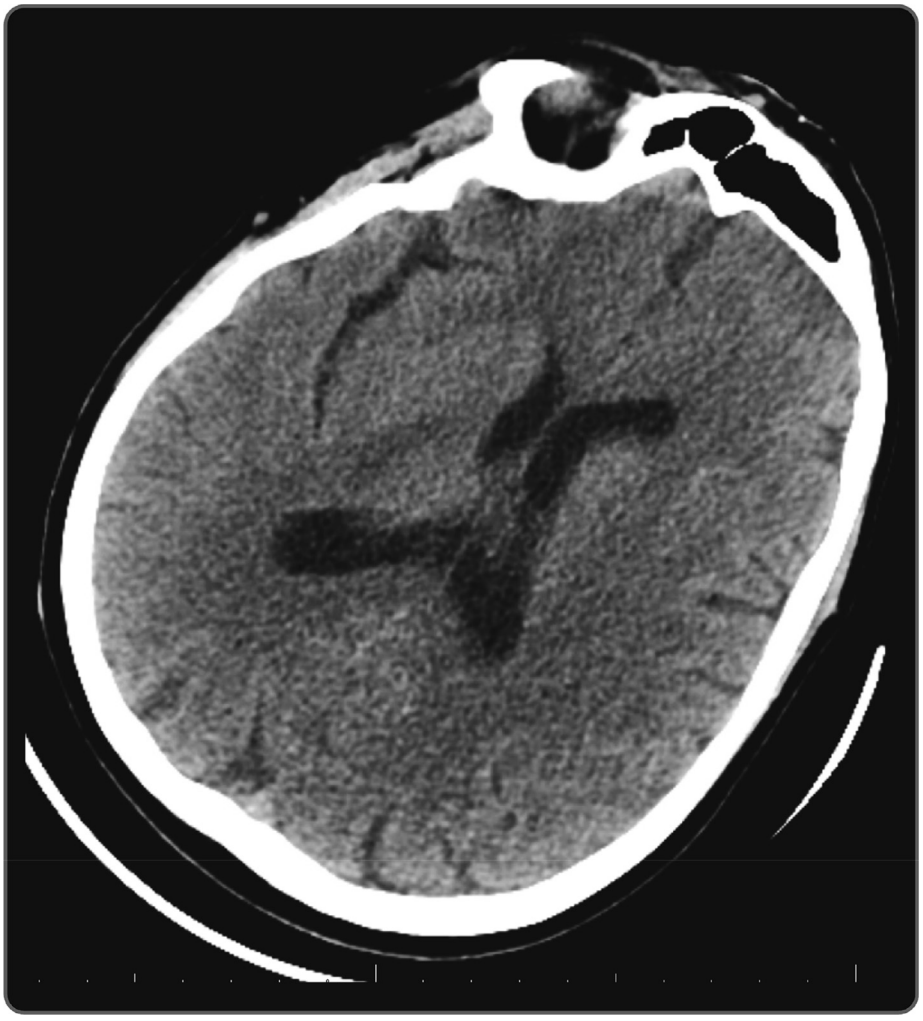


Fig. 2 – Initial brain CT. Grey to white differentiation was maintained and no findings suggestive of anoxic brain injury were noted. A short interval CT was obtained without evidence of evolving infarction or hemorrhage.

Table 2 – Laboratory data obtained following onset of abnormal movements.

Laboratory test	Patient result	Reference range
Arterial pH	7.40	7.35–7.45
Arterial PaCO2	52 mmHg	35–45 mmHg
Serum bicarbonate	30 mMol/L	21–31 mMol/L
Blood Urea Nitrogen	41 mg/dL	8–26 mg/dL
Blood glucose	152 mg/dL	70–99 mg/dL
Sodium	141 mMol/L	136–146 mMol/L
Total bilirubin	2.8 mg/dL	0.3–1.5 mg/dL
ALT	43 IU/L	17–63 IU/L
AST	70 IU/L	15–41 IU/L
Lactate	2.1 mMol/L	0.5–1.6 mMol/L
Ammonia	43 uMol/L	9–33 μMol/L
Lidocaine	1.9 ug/mL	1.5–5.0 μg/mL

PaCO2: partial pressure of carbon dioxide.

arrest day six and was decannulated from ECMO perioperatively. At about two months post-transplant the patient was still having a mild tremor with writing and was discharged home following inpatient rehabilitation having been weaned off clonazepam without return of prior movement disorder.

Conclusions

Neurological complications in patients requiring mechanical circulatory support are common and potential etiologies are broad. The prognosis of these complications varies widely and may affect eligibility for transplantation listing and durable left ventricular assist devices. Although neurological symptoms related to amiodarone use may be rare in outpatients, patients with refractory electrical instability who have escalating doses of amiodarone may be at particular risk for amiodarone-induced parkinsonism. In our case the movements were rapidly reversible with discontinuation of amiodarone and addition of clonazepam, thus the care team proceeded with heart transplantation.

CRediT authorship contribution statement

Cecelia R. Ratay: Conceptualization, Data curation, Writing – original draft, Visualization. **Ankur A. Doshi:** Supervision, Writing – review & editing. **Alexis Steinberg:** Supervision, Writing – review & editing. **David Kaczorowski:** Supervision, Writing – review & edit-

ing. **Dennis P. Phillips:** Supervision, Writing – review & editing. **Zachary J. Rhinehart:** Supervision, Writing – review & editing. **Jessica Fozard:** Writing – review & editing. **Ryan M. Rivosecchi:** Writing – review & editing. **Kimberly W. Schatz:** Writing – review & editing. **Katherine D. Bahl:** Writing – review & editing. **Paul Schwarm:** Writing – review & editing. **Patrick J. Coppler:** Writing – review & editing, Visualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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