

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
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1. REPORT DATE (DD-MM-YYYY) 22/02/2018		2. REPORT TYPE poster		3. DATES COVERED (From - To) 02/22/2018-02/23/2018	
4. TITLE AND SUBTITLE An Elusive Diagnosis Following Cardiac Arrest				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Fullam, Capt Timothy R.				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) 59th Clinical Research Division 1100 Willford Hall Loop, Bldg 4430 JB SA-Lackland, TX 78236-9908 210-292-7141				8. PERFORMING ORGANIZATION REPORT NUMBER 17573	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) 59th Clinical Research Division 1100 Willford Hall Loop, Bldg 4430 JB SA-Lackland, TX 78236-9908 210-292-7141				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release. Distribution is unlimited.					
13. SUPPLEMENTARY NOTES 40th Annual Carrell-Krusen Neuromuscular Symposium, Dallas TX, 22-23 February 2018					
14. ABSTRACT					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Clarice Longoria
			19b. TELEPHONE NUMBER (Include area code) 210-292-7141		



An Elusive Diagnosis Following Cardiac Arrest

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Case Presentation

49-year-old female was admitted after found unresponsive in bed. Cardiopulmonary resuscitation (CPR) was initiated by the husband followed by emergency medical services (EMS) who diagnosed ventricular fibrillation. She was intubated and advanced cardiac life support administered with return of spontaneous circulation (ROSC) in the emergency department. Amiodarone was loaded and maintenance initiated. Workup for etiology of her ventricular fibrillation, including computed tomography (CT) of the head and CT angiogram of the pulmonary arteries, was negative. Left heart catheterization and ventriculography demonstrated no evidence for coronary artery disease, a reduced ejection fraction (EF) with global hypokinesia and dilated left ventricle. Episodes of ventricular tachycardia continued causing recurrent arrests with concomitant worsening metabolic acidosis and cardiac function. She was transitioned to venous-arterial extracorporeal membrane oxygenation (VA ECMO) with improved arrhythmias and metabolic acidosis but continued cardiogenic shock and increasing vasopressor requirements. Given concern for potential myocarditis and need for a left ventricular assist device (LVAD) or cardiac transplant, she was transferred to an outside hospital for further care.

Myocardial biopsy was negative for inflammatory changes consistent with myocarditis. Her hemodynamic stability and cardiac function improved from a nadir EF of 10-15% to 40-50% after 8 days of ECMO. While at the facility, she was treated with intermittent cisatracurium (Nimbex[®]), dexmedetomidine (Precedex[®]), and fentanyl. ECMO was discontinued and she was transferred back to our hospital given no further need for LVAD or transplant. Cisatracurium was discontinued prior to transfer and dexmedetomidine and fentanyl were discontinued on arrival. Due to persistent flaccid paralysis and inability to follow commands, Neurology was consulted.

Neurology Consultation/Exam

Additional History Obtained: Bilateral cataract removal over the past year reported by husband, mother of 3 healthy adolescent children with no history of miscarriage

MS: Would attend to examiners when her name was spoken. Would not follow any simple commands to stick out tongue or close eyes and inconsistently appears to track to command

CN: Bilateral ptosis of eyelids with inability to fully close eyes; bilateral temporal wasting noted. Otherwise grossly intact.

Motor/Sensation: Flaccid bilateral upper and lower extremities. 0/5 strength with volitional movement but with deep nailbed pressure patient able to withdraw both lower extremities against gravity

Reflexes: bi BR pat Achilles plantar
R 2- 2- 2- 0 0 equivocal
L 2- 2- 2- 0 0 down

- Trace/Possible Percussion myotonia of L thenar eminence

Gait: Unable to obtain.

Inpatient Evaluations/Studies

Serum Studies: Na 150 (down-trending from high of 158), NH3, TSH, CK, Lactate, VBG WNL

CSF Studies: Unremarkable

EEG: Abnormal EEG (Awake, Drowsy, ATE): Slowing, continuous, generalized, theta-delta

MRI Brain w/w/o contrast: No acute intracranial abnormality

Train of Four: No evidence for persistent neuromuscular blockade

NCS/EMG:

NCS, including repetitive stimulation, unremarkable

Muscle	Ins	Spontaneous Activity	Voluntary Act	Comments
	Activit y	Fibs Fasc Other Recruitment	Dur Amp Poly	
Tibialis anterior.L	Incr	- - -	Shor Low t++ ++	25%
Vastus lateralis.L	NML	- - -	-	No activation
Abductor pollicis brevis.L	Incr	2+	-	No activation
1st dorsal interosseous.L	Incr	2+	-	No activation
Biceps brachii.L	NML	- - -	-	No activation

DMPK Gene Analysis: 12 CTG Repeats on both alleles (No evidence of a repeat expansion identified)

CNBP Gene Analysis: No evidence of repeat expansion in the CNBP gene detected

4 Month Follow-Up

Repeat examination (notable findings):

- Bilateral ptosis with no fatigability, bilateral weakness of orbicularis oculi as well as cheek puff/lip pursing, Neck Flexion/Extension 4/5.

- Significant atrophy of bilateral temporalis muscles

- Diffusely decreased bulk with strength as follows:

Upper:	Del	Tri	Bi	WE	WF	FE	FF	HI
Right	5/5	5/5	5/5	5/5	5/5	5/5	5/5	4/5
Left	5/5	5/5	5/5	5/5	5/5	5/5	5/5	4/5
Lower:	HF	KE	KF	ADF	APF	EHL		
Right	4+/5	5/5	5/5	4+/5	4+/5	4+/5		
Left	4+/5	5/5	5/5	4+/5	4+/5	4+/5		

- Reflexes 1/4 in bilateral upper extremities; absent at the patella and Achilles'

bilaterally, trace percussion myotonia of thenar eminence on left but absent at extensor compartment of forearm and tongue

- Gait with exaggerated lordosis and 'waddling' type pattern

Final Workup/Diagnosis

Repeat EMG:	Ins Act	Spontaneous Activity	Voluntary Motor Unit Potentials
Muscle	Fibs Fasc Other Recruitment	Dur Amp	
Deltoid.R	NML	- - -	NML NML
Triceps brachii (Lateral head).R	Inc	1+ - Myot	Long + High + 25%
Flexor digitorum profundus, dig 4 & 5.R	Inc	1+ - Myot	Rapid + Short + Low + 75%
Sternocleidomastoid.R	Inc	- - Myot	Short + Low + 25%
Tibialis anterior.R	Inc	- - NML	Short + Low + 15%
Gastrocnemius (Medial head).R	Inc	- - Myot	Short + Low + None
Quadriceps.R	Inc	1+ - Myot	NML NML
T10 paraspinal.R	NML	- - NML	NML NML
T10 paraspinal.R	NML	- - NML	NML NML

DMPK Gene Analysis: 790 and 12 repeats (Pathogenic)

Amended initial report: PCR Analysis with 12 CTG Repeats and Inconclusive allele 2 Southern blot (initial sample): 800-1300 CTG repeats on allele 2

Discussion

-Myotonic Dystrophy Type 1 is the most common muscular dystrophy of adulthood which affects between 1 per 8000-9000 individuals worldwide

-Neuromuscular manifestations of myotonia and skeletal muscle disease may be subtle or overlooked by patients making exact onset of the disease difficult to ascertain and raises the possibility that a non-neurologist physician may be the first to evaluate these patients^{1,2}

-EM is the result of decreased expression of muscle-specific chloride channel type 1 (ClC-1) due to abnormal RNA processing from toxic gain of function of the transcribed DMPK repeat protein^{3,4}

-Membrane hyper-excitability can be curtailed by altering sodium channel opening frequency or duration which is the basis for mexilitine therapy for myotonia⁵. Our patient's lack of EM initially may be explained by the acute effects of amiodarone (shown to have Class IB antiarrhythmic properties acutely) versus her critical illness⁶

-Genetic testing has a low false negative rate, however, 3-5% of the DM1 population can have interrupting CCG, CTC, and CCG repeats within the CTC repeat which can cause false negative studies⁷

-A potential confounder is dilution of the sample sent for testing. Average ECMO patients require 2 to 3 packed red blood cells and up to 14 plasma units and cryoprecipitate daily which, in our patient, obscured her initial serum genetic testing⁸

-DM1 patients have a hypersensitivity to anesthetic agents with prolonged recovery from sedation and propensity for potential prolonged mechanical ventilation, which likely contributed to our patient's initial presentation and prolonged hospital course⁹

-This case re-affirms the importance of recognition of the stigmata of DM1, especially in care settings where the diagnosis may be missed. Typically, genetic testing and EMG/NCS can confirm the diagnosis; however, providers should be aware of potential false negatives to avoid abandoning the correct diagnosis in the face of initial negative results.

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A 49-year-old female was admitted following ventricular fibrillation associated cardiac arrest with return of spontaneous circulation (ROSC) with advanced cardiac life support. Past medical and surgical history was notable for bilateral cataract removals over the preceding year. Family history was non-contributory. Workup for the arrest was unremarkable including computed tomography (CT) of the pulmonary arteries, left heart catheterization, and ventriculography. Her initial course was complicated by newly diagnosed dilated cardiomyopathy with reduced ejection fraction, ventricular tachycardia, and cardiogenic shock requiring venous-arterial extracorporeal membrane oxygenation (ECMO). Given concern for myocarditis, a myocardial biopsy was performed and negative for inflammatory changes. After discontinuation of ECMO, neurology was consulted due to failure to wean from the ventilator. Initial exam was significant for bilateral temporal wasting and ptosis with subtle percussion myotonia of the left thenar eminence. She had no volitional movement of her extremities and reflexes were hypoactive.

Electroencephalogram and magnetic resonance imaging of the brain were unremarkable for seizure activity or evidence of anoxic injury, respectively. Given the findings of bilateral ptosis, possible percussion myotonia, temporal wasting, recent cardiac arrest, and early cataracts, a workup for myotonic dystrophy type I was pursued. Nerve conduction study and electromyography (NCS/EMG) did not demonstrate myotonic discharges and was only remarkable for reduced amplitudes of the left median and ulnar motor studies. DMPK gene analysis was negative, with only 12 CTG repeats. Follow up CNBP gene analysis for myotonic dystrophy type 2 (DM2) was also negative. The patient's mental status and clinical state improved and she was discharged to a rehabilitation facility after placement of an implantable cardioverter defibrillator 2 weeks after initial consultation. The patient returned for further evaluation after recovery from her acute illness and repeat clinical exam, EMG/NCS, and ultimately genetic testing confirmed the underlying diagnosis.