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Neurocritical Care Special Issue

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Vickie and Jack Farber Institute for Neuroscience at Jefferson

Dear Colleague,

There's a tremendous synergy surging through the departments of neurosurgery, neurology, psychiatry and neuroscience at Jefferson. We've brought our research scientists and physicians specializing in each of these disciplines together, under the auspices of the Vickie and Jack Farber Institute for Neuroscience.

These distinguished scientists and clinicians have achieved groundbreaking results that have earned Jefferson and the Vickie and Jack Farber Institute for Neuroscience worldwide recognition and respect among their peers. Now, more than ever, we are confident that these synergies will accelerate our translation of research into new treatments and minimally invasive neurosurgical procedures for neurodegenerative and other devastating disorders.

An exciting outcome of our expansion of the Vickie and Jack Farber Institute for Neuroscience is the establishment of the Jefferson Weinberg ALS Center. It is a truly comprehensive center, with clinicians and scientists working together to provide hope to patients with ALS. Our seamless integration of clinical care with basic, translational and clinical research to develop new, leading-edge therapies will exemplify the purpose of the Farber Institute at Jefferson.

Further enriching Jefferson's research and services in the neurosciences is the new partnership between Abington Health and Jefferson. Jefferson Hospital for Neuroscience is the area's only dedicated hospital for neuroscience; it offers advanced treatments for stroke, concussion, aneurysm, spine problems, multiple sclerosis and more. Abington – Jefferson Health is also one of the Philadelphia area's leaders in treating neurological conditions, and we're honored to be collaborating with its excellent staff.

Above all, we are deeply grateful to Vickie and Jack Farber and the Farber Family Foundation. Vickie and Jack Farber have been more than generous: they have been steadfast partners, wise counselors, engaged leaders and visionary investors who put the power of scientific discovery behind a commitment to find effective treatments, preventative therapies—maybe even a cure—for life-robbing brain diseases.

Finally, we thank you for your interest in our work through readership of this publication. Going forward, we hope, more than ever, that our work stimulates and inspires our fellow researchers and clinicians.

Sincerely,

Robert H. Rosenwasser, MD, FACS, FAHA
Jewell L. Osterholm, MD, Professor and Chair of the Department of Neurological Surgery
President, Vickie and Jack Farber Institute for Neuroscience
Thomas Jefferson University and Jefferson Health

NEUROCRITICAL CARE AT JEFFERSON

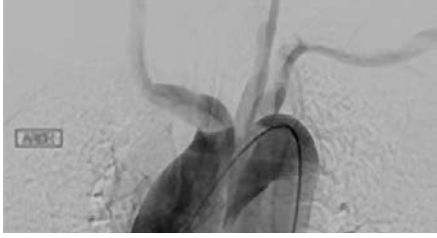
This special edition of the *JHN Journa*l highlights neurocritical care at Jefferson, which is one of the largest neurocritical care programs in the country and a major referral center for stroke and critically ill neurology and neurosurgery patients in the tri-state area. The authors report on novel aspects of diseases most commonly encountered in the neurologic ICU – ischemic stroke and intracerebral hemorrhage – as well as some unusual conditions, such as uncommon inflammatory encephalitis. Two authors discuss important aspects of seizures and status epilepticus, common in brain injured patients. Overall, this edition of the *Journal* offers a glimpse of the complexities and challenges encountered by practitioners in this exciting and rapidly evolving critical care specialty.

The expertise of these authors comes from a strong practice at Jefferson Hospital for Neuroscience, the only dedicated hospital for neuroscience in the Philadelphia region. These neurosurgeons treat the highest volume of patients with aneurysms, brain AVMs, angioplasty and stenting occlusive carotids in the region. Our neurocritical units are staffed by specialists who have been highly trained to meet the specific, often dire needs of critically ill neurological patients. Our highly specialized neurointensivists provide a multidisciplinary team approach to patient care on units that are equipped with advanced neuromonitoring tools and new technologies such as:

- **Advanced Intracranial Monitoring (Brain Tissue Oxygenation)**
- **Intracranial Pressure Monitoring**
- **Arterial Pressure Monitoring**
- **Central Venous Pressure Monitoring**
- **Noninvasive Cardiac Output Monitoring - pulse contour analysis and transpulmonary thermodilution**
- **Hypothermia devices - Intravascular catheters and body surface cooling**
- **Transcranial Doppler Ultrasound**
- **Continuous and Quantitative Video EEG**
- **Direct and Video Laryngoscopy and Adjunctive Airway Management Tools**
- **Bronchoscopy**
- **Comprehensive Ultrasonography for Volume Status and Cardiopulmonary Assessment, and Vascular Access**
- **EMG**
- **Evoked Potential Assessment**
- **Telemedicine**

As part of our commitment to education, Jefferson offers neurocritical care fellowship training, accredited by the United Council for Neurologic Subspecialties (UCNS), which provides core clinical training in the Neuro-ICU and general critical care in the SICU, MICU, CCU and CTICU. Fellows engage in formal one-on-one procedural training as well as clinical research that often yields national presentations. Our nationally renowned faculty members have played a role in developing guidelines for management of status epilepticus, space occupying cerebral swelling, diagnosis of death by neurologic criteria and targeted temperature management.

We enjoyed preparing this journal and hope that the knowledge we share will be of use to readers who seek further understanding about the important field of neurocritical care.



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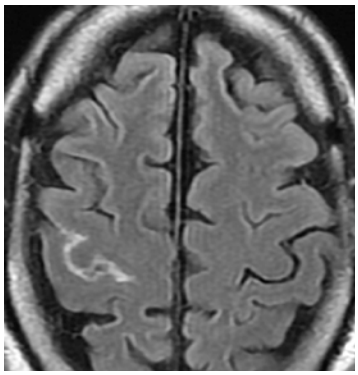

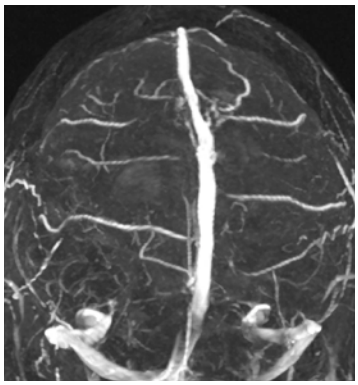

Acute Ischemic Stroke and Thrombolysis in the Setting of Aortic Dissection: Case Report and Literature Review

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Key Words

cerebral infarction, aortic dissection, thrombolysis, outcomes, type a dissection

ABSTRACT

Objective

Aortic dissections (AD) can present with neurologic deficits concerning for stroke, rather than with chest or back pain, a symptom usually seen in acute AD. As a result, these patients may be treated with thrombolytics for their stroke symptoms. The use of thrombolytics in a patient with AD can complicate their surgical management. Rapid identification requires education in this rare subpopulation of patients with aortic dissection and ischemic stroke.

Data Sources

Systematic literature search in databases (MEDLINE, EMBASE, Cochrane CENTRAL, CINAHL; 1984–2014), reference lists, personal files, and hand search. Search terms included: *aortic dissection, thrombolysis, cerebral ischemia, and stroke.*

Study Selection

Any study involving the administration of intravenous thrombolytics to acute stroke patients with aortic dissections was included.

Data Extraction

Two reviewers extracted data and assessed risk of bias independently. 24 studies were reviewed, 10 case reports were included.

Data Synthesis

We present two cases from our institution where ischemic stroke patients received recombinant tissue plasminogen activator (rt-PA), intravenous (IV) and intra-arterial, and survived. Ten prior case reports of thrombolytic administration to acute ischemic stroke patients in the setting of a concurrent aortic dissection were reviewed. 75 % (3/4) of the patients who received the full dose IV thrombolytic did not survive. The patients that received partial dose IV rt-PA survived in 83.4 % (5/6) of cases. The range of neurologic outcomes in the latter group varied from asymptomatic to a modified Rankin score (MRS) of 4.

Conclusion

Identifying stroke patients with AD can be very difficult early in the presentation when treatment decisions must be made quickly. Despite the unfavorable outcomes in the few prior case reports of cerebral ischemia patients receiving thrombolytics, there may be a subpopulation that can survive the use of thrombolytics in AD with intensive monitoring. Our cases demonstrate the feasibility of successfully performing thrombolysis in the setting of an aortic dissection.

INTRODUCTION

Aortic dissection (AD) is a tear in the media layer of the aorta with bleeding within the aortic wall. Stanford type A aortic dissections, which involve the ascending aorta and arch, usually prompt cerebral manifestations. AD can produce a wide range of symptoms by obstructing arterial outflow. This can manifest as neurologic symptoms if the carotid, vertebral, spinal arteries or vaso-vasorum supplying peripheral nerves are affected. The incidence of aortic dissection is between 5 and 40 cases per million people per year and type A dissections account for more than fifty percent of this number.[1,2] Neurologic deficit was reported in the reviews of Gaul et al. and Grupper et al. to occur in 17-40% of patients with 5-10% of this accounting for cerebral ischemia.[3,4] Grupper et al. also estimated 10-50% of patients will not experience any pain associated with the aortic dissection.[3] These patients can present as acute stroke patients eligible for intravenous recombinant tissue plasminogen activator (rt-PA). We present the case of a patient who received both intravenous and intra-arterial rt-PA, and was subsequently found to have a Stanford type A aortic dissection, which was repaired within twenty-four hours.

CASE ONE

A 78-year-old man was brought in by EMS with left-sided weakness, after falling in the bathroom. On arrival to the emergency department (ED) his NIHSS score was 16 (Table 1). He had transient hypotension with a blood pressure of 86/41, which improved to 102/64. His cardiac exam was normal. His pulses were equal in all extremities; rest of his physical exam was unremarkable. A non-contrast head CT showed no intracranial hemorrhage. He was given weight based dosing intravenous (IV) rt-PA, 0.9mg/kg, at 120 minutes after symptom onset per protocol.

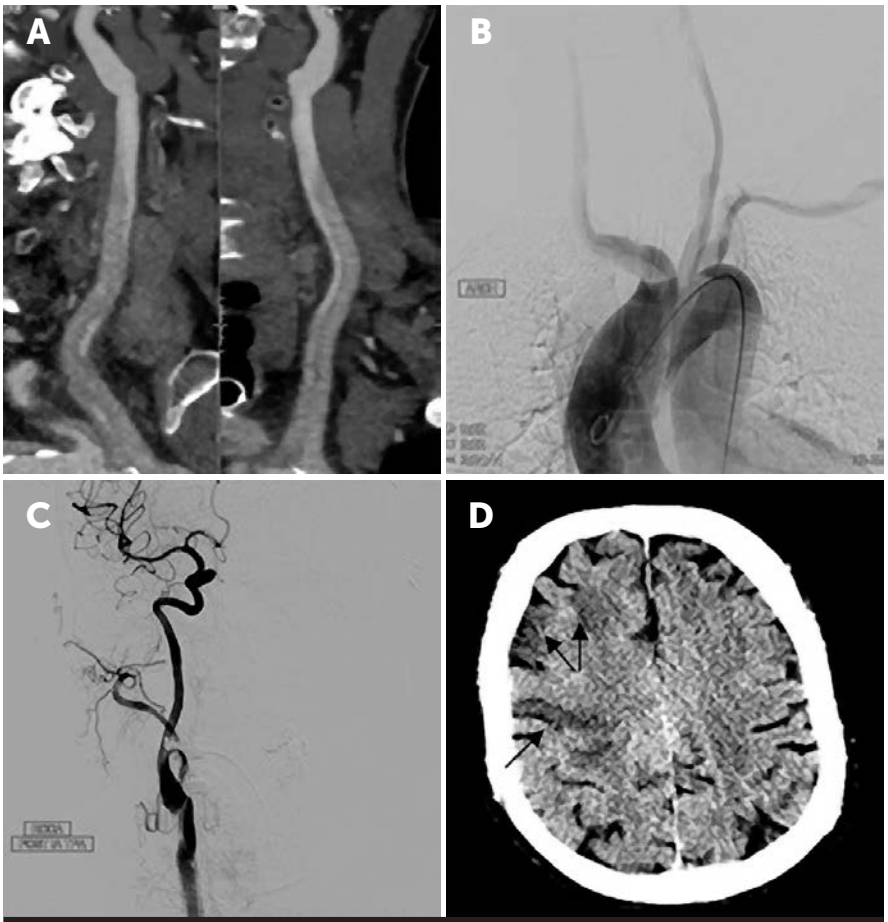

Figure 1

A. CT angiogram showing hypodensity creating a false lumen in bilateral common carotids. **B.** Cerebral angiogram: Hypodense dissection flaps in all three vessels coming off aortic arch. **C.** Cerebral angiogram showing reconstitution of carotid and patent MCA/ACA on the right after mechanical thrombectomy and IA rt-PA. **D.** CT head showing three intermediate areas of infarction (black arrows).

The ED then initiated transfer to a comprehensive stroke center for evaluation for possible intra-arterial intervention.

En route, the patient was intubated for a decreased level of responsiveness. On arrival to the stroke center his repeat NIHSS was 12 (Table 1). CT-angiography head and neck as well as CT brain perfusion studies were completed.

CT angiography revealed a Stanford Type A aortic dissection with extension to all three neck vessels, right brachiocephalic trunk, left common carotid and left subclavian arteries. His right internal carotid had a non-occlusive dissection and distally there were non-occlusive thrombi in the first middle cerebral artery branch (M1) and the first anterior cerebral artery branch (A1) (Figure 1). After discussion with the family, the endovascular neurosurgeon performed intra-arterial intervention. The right internal carotid was selectively catheterized via a femoral approach and 10mg intra-arterial (IA) rt-PA was administered. A repeat injection demonstrated resolution of the M1 and improvement in the A1 thrombi. The patient had improvement in his left-sided strength to a motor score of 2/5 after anesthesia wore off.

He was transferred to the intensive care unit and placed on intravenous beta-blocker infusion. Since he had received systemic rt-PA, the decision was made to monitor him for twenty four hours and trend fibrinogen levels. A non-contrast head CT the next morning showed no intracranial hemorrhage; however, three intermediate-sized areas of cerebral infarct were seen. Because of the rt-PA, he was not taken immediately to surgery but was treated conservatively for 24 hours. He underwent a hemiarch replacement with a 28 mm Dacron graft on the following morning. The aortic valve was intact, and was re-suspended with three 4-0 pledgeted Prolene sutures. An intraoperative transesophageal echo after the replacement demonstrated mild aortic insufficiency and good preservation of left ventricular function.

Postoperatively, he remained in the intensive care unit for sixteen days. On hospital day nineteen, he was discharged to an acute rehabilitation facility with left hemiparesis with a motor score of 3/5, and left-sided neglect. His Modified Rankin Score on discharge was a 4; however, his language function was intact.

CASE TWO

A 49-year-old male, with a history of uncontrolled hypertension presented to an outside hospital with left-sided hemiparesis. On arrival to the emergency department (ED) his NIHSS score was 27 (Table 1). The CT scan showed loss of gray-white differentiation in the left frontal lobe, but was negative for intracranial hemorrhage. He was given weight based dosing IV rt-PA, 0.9mg/kg, at 58 minutes after symptom onset per protocol. The ED then initiated transfer to a comprehensive stroke center for evaluation for possible IA intervention.

On arrival to the stroke center his repeat NIHSS was 12 (Table 1) with improvement in his left-sided weakness. Given his improvement, it was decided he was not a candidate for IA intervention. After administration of the rt-PA, the patient began to complain of chest discomfort. An echocardiogram demonstrated a flap in the ascending aorta. CT scan showed a type A dissection from the aortic root extending to the bifurcation of the iliac arteries, with dissection of bilateral carotid arteries and cardiothoracic surgery was notified. After returning from the exam, the patient became acutely hypoxic with increased lethargy and the decision was made to intubate. The initial plan was to

delay the operation for 24 hours due to the rt-PA and the concern for a high risk of bleeding complications with early operation. However, the patient's neurologic status deteriorated with development of worsening left hemiplegia approximately ten hours after rt-PA administration. A repeat CT scan was negative for hemorrhage and there was concern that the hemiplegia may be due to malperfusion.

Approximately 12 hours post rt-PA administration, the patient underwent emergent repair of type A aortic dissection. Intraoperatively, the patient received 15 units of Platelets, Profilnine (Grifols Biologicals Inc, Los Angeles, CA, USA), Amicar, and three liters of crystalloids. Intraoperative transesophageal echocardiogram demonstrated significant aortic insufficiency. The aorta was opened, and a large transverse intimal tear at the level of the sinotubular junction over the noncoronary cusp was found. The annulus appeared to be moderately dilated. Due to recent administration of rt-PA , it was felt that replacement of the ascending aorta was a better option to minimize the chance of severe hemorrhage, rather than a root and/or hemiarch replacement. The ascending aorta was replaced with a 36 mm Dacron graft. There was significant bleeding from the anastomosis, but no surgical bleeding was present. The bleeding appeared to subside enough to tolerate closure, and the patient was transferred to the intensive care unit in a stable condition.

On the first post-operative day, the patient passed a spontaneous breathing trial and he was extubated. A post-extubation neurologic assessment revealed the patient continued to follow commands on the right side and was hemiplegic on the left side.

Table 1. NIHSS of patient prior to and after IV rt-PA

NIHSS	Patient 1 ED	Patient 1 After IV TPA	Patient 2 ED	Patient 2 After IV TPA
LOC	1	0	0	0
Orientation	1	1	1	2
Commands	0	1	2	1
Best Gaze	2	0	1	0
Visual Fields	0	0	2	1
Facial Symmetry	1	0	2	1
Motor	–	–	–	–
Left Upper Extremity	3	4	4	1
Right Upper Extremity	2	0	3	0
Left Lower Extremity	3	4	4	1
Right Lower Extremity	2	0	3	0
Ataxia	0	0	0	2
Sensation	0	0	1	0
Language	1	2	1	2
Dysarthia	0	0	1	1
Extinction	0	0	2	1
TOTAL	**16**	**12**	**27**	**13**

GENERAL SURGICAL APPROACH FOR BOTH PATIENTS

In both cases, surgery was performed under general anesthesia, through a standard median sternotomy. Cardiopulmonary bypass was initiated through femoral arterial and cavoatrial cannulation. Activated clotting time was maintained over 450 seconds with systemic heparin. A vent was inserted through the right superior pulmonary vein to the left ventricle. Cardioplegia was administered through a retrograde coronary sinus catheter that was placed through the right atrium, and blood cardioplegia was given every 20 minutes. Both patients were cooled to 18° C for circulatory arrest. Retrograde cerebral perfusion was administered through a catheter placed in the superior vena cava. The layers of the dissection in the aorta were reapproximated using Teflon-felt and BioGlue (Cryolife, Inc., Kennesaw, GA, USA). The anastomosis was constructed with a running 4-0 Prolene suture with felt buttresses. After the anastomoses, the patient was rewarmed and weaned from cardiopulmonary bypass. Heparin was fully reversed with protamine and blood products were given as necessary, chest tubes were placed and the chest was closed with wires in a standard fashion.

MATERIALS AND METHODS

Systematic literature search in databases (MEDLINE, EMBASE, Cochrane CENTRAL, CINAHL; 1984–2014), reference lists, personal files, and hand search were performed. Search terms included: aortic dissection, thrombolysis, cerebral ischemia, and stroke. Any study involving the administration of IV thrombolytics to acute stroke patients with aortic dissection was included. Two reviewers extracted data and assessed risk of bias independently. 24 studies were reviewed, 10 case reports were included.

RESULTS

To date, the case reports of patients with aortic dissections who received thrombolytics have had mixed outcomes. In a

review of the prior ten cases reported, four patients received full dose rt-PA (Table 2). 75% (3/4) of the patients who received the full dose IV thrombolytic did not survive. The patients that received partial dose IV rt-PA survived in 83.4% (5/6) of cases. The range of neurologic outcomes in the latter group varied from asymptomatic to a modified Rankin score (MRS) of 4. Perhaps the dismal outcomes of these patients who receive thrombolytic therapy for cerebral ischemic syndromes have been over-estimated. There still are not many cases reported to analyze this effect.

DISCUSSION

Need for Rapid Identification

Patients experiencing aortic dissections may present with a neurologic deficit with or without accompanying chest pain. This can mask the underlying cause which is a tear in the wall of the aorta that needs to be addressed. These patients will present with neurologic symptoms concerning for ischemic stroke and may be in the appropriate 3-4.5 hour time window for IV rt-PA. It is imperative to evaluate the patient for appropriateness of intravenous thrombolytics and administer them as soon as possible. However, an aortic dissection causing cerebral ischemia is a contraindication for such therapy. A painless aortic dissection presenting only with neurologic deficits will more often have left hemiparesis or hemiplegia, hypotension, and bradycardia.[5] This symptom complex is referable to the right carotid artery and possible involvement of the carotid sinus.[6] All patients being considered for thrombolytics should undergo a thorough cardiac physical examination. An analysis of the International Registry of Acute Aortic Dissection (IRAD) database showed AD patients with stroke presented more often with syncope, pulse deficit, hypotension or shock; and less often with chest pain.[7] The 2010 Guidelines for the Diagnosis of Patients with Thoracic Aortic Disease make a level C recommendation that all patients presenting with a neurologic deficit be questioned about chest, back, or abdominal pain and examined for peripheral pulse deficits.[8] A plain CXR can be helpful to demonstrate a wide mediastinum or abnormal aortic contour, but may be negative in 20% of patients.[2, 7, 9] Iguchi et al. suggested use of carotid ultrasonography prior to the administration of rt-PA.[10] This may not be feasible in institutions without twenty-four hour access to this imaging modality and proper interpretation.

Debate among Cardiothoracic Surgeons to Operate on AD Patients with Cerebral Malperfusion

The cardiothoracic literature debates whether to take patients with a significant neurologic deficit to surgery or not. The diagnosis of untreated Stanford Type A

Table 2. Prior cases reported of AD patients who received IV rt-PA and their outcomes if reported. *=not available.

Author	Year	Patient	NIHSS	Therapy	Disposition
Mendes et al.[17]	2012	70 YO M	NIHSS 9	IV rt-PA (full dose)	Alive, 12 Month NIHSS 2
Rodriguez-Luna[18]	2011	80 YO F	*	IV rt-PA (partial dose)	Expired
Noel[19]	2010	81 YO F	NIHSS 22	IV rt-PA (partial dose)	Alive, MRS 3
Ramalingam[20]	2010	55 YO F	NIHSS 6	IV rt-PA (partial dose)	Alive, 18 Month NIHSS 0
Hong[21]	2009	69 YO F	NIHSS 6	IV rt-PA (partial dose)	Alive, 3 Month NIHSS 0
Takeuchi[22]	2009	72 YO F	NIHSS 16	IV rt-PA (full dose)	Expired
Gaul[23]	2007	76 YO F	*	IV rt-PA (full dose)	Expired
Uchino[24]	2005	56 YO F	NIHSS 16	IV rt-PA (loading dose only)	Alive, 3 Month MRS 4
Chua[25]	2005	44 YO M	NIHSS 18	IV rt-PA (loading dose only)	Alive
Fessler[26]	2000	54 YO M	*	IV rt-PA (full dose)	Expired

dissections carries a mortality rate of 1-3% per hour, and 25% during first twenty-four hours.[1, 11] In-hospital mortality data from IRAD shows an over-all mortality of 42% (stroke) versus 24% (non-stroke), medically treated patient mortality 77% (stroke) versus 54% (non-stroke), and in the surgically treated group 31% (stroke) versus 19% (non-stroke).[7, 12] Some surgeons consider intervention in patients with coma at presentation or severe neurologic deficits futile.[1, 13] Studies do show that conscious patients with a neurologic deficit have a similar operative mortality as those without and over half of these patients will improve neurologically after surgery.[12, 14-16] Early reperfusion may lead to better outcomes in this patient subpopulation. One study demonstrated complete symptom recovery in 14%, improvement in 43%, no neurologic change in 43%, and none of the patients worsened when operated on within nine hours of symptom onset.[16]

Possible Better Outcomes if Intra-arterial Intervention?

The neurologic deficit may be caused by a temporary occlusion of the arterial true lumen by pressure of a false lumen created by extension of the dissection to the cerebral arteries. Another mechanism may be embolism of clot from the false lumen through an exit tear. If one were able to identify these patients, a neurosurgical endovascular procedure could be considered.

Endovascular treatments such as carotid stenting or intra-arterial thrombolytics in place of IV thrombolytics would address the mechanisms of cerebral ischemia in these patients without exposing them to systemic anticoagulation. This would allow the neurologic intervention and prevent the delay for the cardiovascular repair.

Timing of Surgical Intervention after Tissue Plasminogen Activator administration

Each hour that passes until surgical intervention of an AD, increases mortality. Thus patient care is directed toward optimizing the patient for earliest possible surgical intervention. This becomes muddled in patients who receive rt-PA and when is it safe for these patients to undergo repair. There are a few case reports published on patients who have successfully been repaired after receiving rt-PA for their stroke symptoms.[21,27-29] Although Alteplase has been shown to be rapidly cleared from the plasma with an initial half-life of less than 5 minutes[31], the effects can remain up to 24 hours and thus post IV rt-PA protocols require that surgeries be performed only if they are life-saving. Surgical interventions too early can cause intraoperative complications such as prolonged hemostasis. Hong et al reported a case in which they went for emergent aortic surgical repair within 2 hours of rt-PA administration, but note that the surgery took more than ten hours secondary to prolonged hemostasis.[21] Following administration of 100 mg Activase, there is a decrease (16%–36%) in circulating fibrinogen.[30,31] In a controlled trial, 8 of 73 patients (11%) receiving Activase (1.25 mg/kg body weight over 3 hours) experienced a decrease in fibrinogen to below 100 mg/dL.[31] With coagulopathies such as these, the risks of early versus late surgical intervention must be weighed. For our patients, one was stable enough to wait 24 hours for surgical repair, while the other patient had worsening of his neurological symptoms and required urgent repair within 12 hours of TPA administration. Further research is warranted to determine the optimum timing of surgical intervention post IV rt-PA.

CONCLUSION

Acute AD is a life-threatening disease process which may be complicated by cerebral malperfusion syndromes. The patients may present with focal neurologic deficits and qualify for IV rt-PA. A thorough history and physical exam, including palpating peripheral pulses, may be the only clues to the coexistent AD in stroke patients. Future consideration may be given to whether emergent neurosurgical endovascular therapies should be offered in lieu of systemic thrombolytics when a stroke patient with and AD is identified. Finally, the timing in which safe surgical intervention can be performed after administration of IV rt-PA remains to be determined.

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Continuous EEG Monitoring in Critical Care

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INTRODUCTION

Continuous video-EEG monitoring (cEEG) has increasingly been used in the critical care population in large part due to the recognition that a wide variety of conditions are associated with the risk of developing seizures. As most seizures in this population are nonconvulsive, EEG provides the only reliable means to detect them and monitor response to their treatment. Below are common questions on the role of continuous EEG in the critical care patient followed by a brief overview.

ARE SEIZURES COMMON IN CRITICAL CARE PATIENTS ?

Seizures have been detected in 8-34% of critical care patients.[1,2] The etiologies associated with a high risk of seizures include subarachnoid hemorrhage, intracerebral hemorrhage, traumatic brain injury, acute ischemic stroke, encephalitis, cardiac arrest (hypoxic-ischemic encephalopathy), sepsis, and pre-existing epilepsy. In a study of 570 patients with a variety of predominantly neurological etiologies undergoing cEEG for the detection of nonconvulsive seizures or unexplained impairment of consciousness, seizures were detected in 19%, of which 92% were exclusively nonconvulsive.[2] A more recent study of 625 adult inpatients undergoing cEEG (for > 18h) found an overall seizure frequency of 27%.[1] The frequency of nonconvulsive seizures is especially high after the control of convulsive status epilepticus. A prospective study of 164 patients with convulsive status epilepticus undergoing cEEG for a minimum of 24 hours found persistence of non-convulsive electrographic seizures after the control of convulsive status epilepticus in 48% of patients.[3]

While most studies have concentrated on critically ill neurological patients, cEEG often detects seizures in patients hospitalized in medical (MICU) and surgical (SICU) intensive care units. Oddo et.al. found a 10% rate of electrographic seizures among 201 MICU patients without known acute neurological injury undergoing cEEG (with purely electrographic seizures on 67% of cases); sepsis was a significant predictor of electrographic seizures and seizures were associated with poor outcome in this study.[4] In another study of 105 patients without acute brain injury undergoing cEEG in the MICU and SICU, electrographic seizures were found in 11% of patients and they too were associated with worse functional outcome.[5] Recently, Kurtz et.al. reported a 16% rate of nonconvulsive seizures among 154 SICU patients undergoing cEEG for altered mental status; nonconvulsive seizures were again associated with poor outcome.[6]

DO SEIZURES HAVE AN IMPACT IN CRITICAL CARE PATIENTS ?

Seizures induce physiological changes and have been associated with secondary brain injury. Vespa et.al. found an electrographic seizure rate of 6% in 46 patients with ischemic stroke and 28% in 63 patients with intraparenchymal hemorrhage (ICH) undergoing cEEG (76% had only electrographic seizures). In the ICH patients, seizures were associated with greater neurological deterioration and increase in midline shift on CT scans during the initial 72 hours after symptom onset.[7] More recently, a study of 48 comatose subarachnoid hemorrhage patients undergoing multimodality monitoring including intracranial EEG recordings, showed a seizure rate of 38% for intracranial and 8% for surface seizures; intracranial seizures were associated with increases in heart rate, mean arterial pressure and respiratory rate reflecting a sympathetic response and with trends for increased intracranial and cerebral perfusion pressure.[8] Seizures, and more specifically seizure burden, has recently been shown to independently contribute to neurological decline in a large prospective study in a pediatric critical care population.[9] These associations suggest the potential impact of seizures in worsening the already fragile clinical state of the critical care patient.

WHAT ARE SOME COMMON USES OF CEEG MONITORING IN CRITICAL CARE PATIENTS ?

The most common indication for peforming cEEG in critical care patients is when there is a suspicion for seizures. As described above, there are many potential neurological and non-neurological etiologies that have a risk for seizures. Seizures might have a wide range of presentations. Critical care patients frequently have changes in the level of consciousness and/or altered mental status and the clinical exam alone is usually a poor marker for seizure detection in this setting, thus requiring cEEG for reliable diagnosis. When nonconvulsive seizures have clinical manifestations, they are typically subtle (e.g. non-overt rhythmic or repetitive movements, clonic, myoclonic, or tonic movements, gaze deviation, eyelid fluttering, etc) in contrast with the more overt rhythmic movements of the extremities seen in convulsive seizures. Critical care patients also frequently have paroxysmal events (e.g. motor or autonomic repetitive episodes) where an epileptic etiology is suspected and continuous EEG is a useful tool in establishing their potential epileptic origin. Given the subtle seizure semiology and the frequent occurrence of artifacts in the critical care setting, the video component of the EEG recording is of great importance.

In patients with status epilepticus, cEEG is key to assess the effectiveness of therapy. Its use in this setting is recommended by the recent neurocritical care guidelines for the treatment of status epilepticus.[10] There are other indications for cEEG beyond seizure detection and seizure treatment monitoring including neurologic prognostication after cardiac arrest (as part of a multimodal approach);[11,12] there are also studies describing cEEG (quantitative EEG) use for ischemia detection in poor-grade subarachnoid hemorrhage patients,[13,14] and cEEG use for burst suppression monitoring to determine therapeutic endpoints during barbiturate coma.[15]

The 2012 Neurocritical Care Society guidelines are a valuable source for detailed recommendations on the indications for EEG monitoring in the critical care setting. These suggest strategies for evaluation and management of status epilepticus. In addition, the 2013 consensus statement on the use of EEG monitoring in critically ill patients from the Neurointensive Care Section of the European Society of Intensive Care Medicine is helpful.[10,16]

WHAT IS THE TYPICAL DURATION OF CEEG MONITORING AND WHICH EEG FINDINGS ARE ASSOCIATED WITH HIGH RISK OF SEIZURES ?

There is no standard duration of cEEG monitoring. Factors such as the clinical state of the patient (e.g. comatose vs non-comatose), EEG findings (e.g. presence or absence of epileptiform abnormalities, periodic or rhythmic patterns), and underlying etiology may play a role in defining the individual duration of monitoring. Close communication between the intensivist and the neurophysiology teams can help in assessing monitoring duration for each patient. However, the literature contains data suggesting how EEG monitoring might be used.

In the retrospective study of 570 critical care patients undergoing cEEG, most seizures were detected within 24 hours of recording in non-comatose patients but longer monitoring periods were needed in comatose patients. Only 80% of the comatose patients had their first seizure within 24 hours of recording, with 13% of the comatose patients needing > 48 hours of recording to capture their first seizure.

The authors suggest that this data doesn't provide a guide for how long to monitor a patient but rather helps in the decision for cEEG discontinuation.[2] In a recent study analyzing cEEG data from 625 inpatients monitored for varied, primarily neurological etiologies, the 72 hour risk of seizure could be determined based on the presence of epileptiform discharges. The 72 hour risk of seizure decreases to < 5% in patients with no epileptiform activity over the first 2 hours of the recording and for patients with epileptiform activity but no seizures over the first 16 hours of the recording.

Only 4% of patients without epileptiform abnormalities had seizures, and 58% of patients who had seizures had their first seizure early in the recording (<30min of monitoring).[1,17]

The association of specific EEG patterns such as periodic or lateralized rhythmic patterns with seizures has been described in the literature. In a study of 67 comatose neuro-ICU patients undergoing prolonged cEEG monitoring (ten or more days), the presence of prolonged (≥ 5 days), intermittent (1-5 days), or no recording of periodic epileptiform discharges (PED) was seen in 37%, 31%, and 31% of patients, respectively. Prolonged PEDs were associated with the presence of electrographic seizures.[18] Foreman et.al. reported data on 200 patients with generalized periodic discharges (GPDs) matched with 200 controls. Overall, 46% of patients with GPDs had a seizure (clinical or electrographic) during the hospital stay compared with 34% in controls. Nonconvulsive seizures and nonconvulsive status epilepticus were seen in 27% and 22% respectively in GPD patients compared with 8% and 7% in controls.[19] In a study by Gaspard et.al. of 558 patients undergoing urgent EEG or cEEG, lateralized rhythmic delta activity (LRDA) was found in 27 subjects (5%); lateralized periodic discharges (LPD) in 49 (9%); focal nonrhythmic slowing in 136 (24%); and no focal, periodic, or rhythmic patterns (labeled as controls) in 241 (43%). Almost all subjects with LRDA, LPD or focal nonrhythmic slowing had an acute or remote cerebral injury. Almost two-thirds of patients with LRDA were stuporous or comatose.

A 63% rate of seizures during the acute illness (almost all electrographic) was seen for patients with LRDA, similar to the rate seen for subjects with LPDs (57%), and higher than in nonrhythmic slowing and controls (20% and 16% respectively).[20]

The presence of patterns that have an association with electrographic seizures in a given recording may warrant a longer recording than in ones where they are absent.

IS THERE PRACTICE VARIABILITY ON THE USE OF CEEG IN CRITICAL CARE PATIENTS ?

The variability in clinical practice in the use of continuous EEG in critical care patients has been recently highlighted on a survey of neurophysiologists and neurointensivists. One-hundred thirty seven physicians from 97 institutions completed the survey (64% institutional response rate). Almost all utilize cEEG for nonconvulsive seizure detection in patients with altered mental status after clinical seizures, intracerebral hemorrhage, traumatic brain injury, and cardiac arrest, and to characterize abnormal movements suspected to be seizures. There was variability in cEEG use for altered mental status in the setting of other etiologies such as tumors, ischemic strokes, central nervous system infections and metabolic encephalopathy where > 25% do not routinely perform cEEG for these indications. The use for vasospasm detection after subarachnoid hemorrhage was low. Typical duration of monitoring was similar, with most reporting recordings lasting 24 or 48 hours (50% and 29% respectively). Almost half of respondents reported an increase in cEEG use compared to the prior year.[21]

It is important to establish institutional protocols for indications and practice of critical care video-EEG monitoring. A team approach is ideal, which includes close collaboration between intensivists and the neurophysiology team. An upcoming consensus statement on critical care EEG currently under development from the American Clinical Neurophysiology Society will provide useful guidance in this process.

CONCLUSION

In conclusion, continuous EEG plays an increasingly important role in the monitoring and treatment of critical care patients, both in the neurocritical care setting and in the general critical care population. Its role is expanding from the more typical use for seizure detection to include other uses such as prognostication of outcome and more generally for the neuromonitoring to aid management of the critically ill patient. There are still many unanswered questions and further research is needed. New insights into potential applications and overall significance in the care of the critically ill patient will be seen in years to come.

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Novel Therapies for Intracerebral Hemorrhage

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Key Words

stroke, hypertension, cerebral edema, intracranial pressure, neurological intensive care, intensive care, neurocritical care

INTRODUCTION

Intracerebral hemorrhage is by far the most destructive form of stroke[1]. Apart from the management in a specialized stroke or neurological intensive care unit (NICU), no specific therapies have been shown to consistently improve outcomes after ICH[2]. Current Guidelines endorse early aggressive optimization of physiologic derangements with ventilatory support when indicated, blood pressure control, reversal of any preexisting coagulopathy, intracranial pressure monitoring for certain cases, osmotherapy, temperature modulation, seizure prophylaxis, treatment of hyerglycemia, and nutritional support in the stroke unit or NICU. Ventriculostomy is the cornerstone of therapy for control of intracranial pressure patients with intraventricular hemorrhage.[3,4] Surgical hematoma evacuation does not improve outcome for most patients, but is a reasonable option for patients with early worsening due to mass effect due to large cerebellar or lobar hemorrhages. Promising experimental treatments involve targeting of molecular mechanisms implicated in inflammation, blood product degradation, and secondary neuronal damage.

NOVEL THERAPIES FOR ICH

Ultra-early hemostatic therapy

Hematoma volume is an important determinant of mortality after ICH and early hematoma growth which is the increase in hematoma size within 6 hrs of onset, is consistently associated with poor clinical outcomes and an increased mortality.[5-8] Recombinant factor VII (rFVIIa, Novoseven®, Novo Nordisk), a powerful initiator of hemostasis, was studied in a randomized, double blind, placebo-controlled study, in which 399 patients with spontaneous ICH received treatment with rFVIIa at doses of 40, 80, or 160 µg/kg within four hours after ICH onset. Use of rFVII was associated with a 38% reduction in mortality and significantly improved functional outcomes at 90 days despite a five percent increase in the frequency of arterial thromboembolic adverse events.[9] The phase III FAST study compared doses of 80 and 20 µg/kg of rFVIIa with placebo in an overall trial population of 841 patients. No significant difference was found in the main outcome measure, which was the proportion of patients with death or severe disability according to the modified Rankin scale at 90 days (score of 5 or 6 but the hemostatic effect and side effect profiles were confirmed.[10] On the basis of these results, routine use of rFVIIa as a hemostatic therapy for all patients with ICH within a four-hour time window cannot be recommended. The lack of effect of rfVII in ICH, despite its ability to halt hematoma expansion, suggests that additional or targeted therapy to sub-groups of patients may alter the outcome after ICH. In a FAST trial sub-group analysis, a potential effect of rFVII was seen in patients <70 years, baseline hematoma volumes of <60ml, baseline IVH <5ml and time from onset <2.5hrs[11]. Future research is needed to address to potential effects of rFVII in this sub-groups and if the use of CT technology can improve the identification of candidates for rFVII.[12]

Argatroban

A potent inhibitor of fibrin-bound and free thrombin has been used successfully as an alternative for anticoagulation in patients with heparin-induced thrombocytopenia, acute ischemic stroke, and vascular occlusive disease. Animal models have shown that this agent reduces brain edema within six hours of administration and therefore, may be an effective therapy for hematoma-induced edema.

Minocycline

A type of tetracycline has been associated with neuroprotective properties related to MMP inhibition, antioxidant and anti-inflammatory activity. The effects of this agent have demonstrated in experimental models of ICH.[13-15]

Deferoxamine

A potent iron-chelating compound promotes excretion of iron when administered orally or intravenously. Based on the toxicity of iron and oxidative stress related to hematoma, deferoxamine was shown to reduce ICH mediated peri-lesional brain injury in rats[16] and piglets[17] injected with autologous blood into the basal ganglia.

Statins

Rosuvastatin, a potent statin used for reduction of cardiovascular risk was used in a small study of ICH patients providing modest benefits.[18]

Free radical scavenger (NXY-59)

In a recent clinical trial, the effects of NXY-59, a free radical scavenger, were investigated in 607 patients with ICH. NXY-59 was associated with slightly less hematoma growth than placebo at 72 hrs after treatment but without effect on mortality or functional outcomes at 3 months.[19]

Pioglitazone

A thiazolidinedione is currently approved for the management of type II diabetes mellitus and found to modulate peroxisome proliferator-activated receptor gamma agonists in microglia and macrophages, has demonstrated the ability to increase hematoma reabsorption and neuronal protection in animal models.[20] A phase II clinical trial is currently underway to test the hypothesis that pioglitazone is safe and tolerable after ICH.[21] Additional human trials with deferoxamine,[22] statins[23] are currently underway.

Temperature modulation (TTM)

Temperature control could potentially offer benefits related to metabolic control, ICP control, and inhibition of the inflammatory cascade, which is associated with apoptosis and neuronal death[24,25]. Hyperthermia is considered to have detrimental effects to the injured brain and may well be an initial response to the initial ictus [26] Several studies have shown the direct association between hyperthermia and poor outcomes after all types of brain injury.[26-28] Szczudlik et al[29] showed that ICH patients with onset of hyperthermia on the first day of hospitalization have greater mortality and worse functional status 30-days after the ictus. Sustained fever has been shown to be independently associated with poor outcome after ICH.[29] A large body of experimental evidence indicates that even small degrees of hyperthermia can worsen ischemic brain injury by exacerbating excitotoxic neurotransmitter release, proteolysis, free radical and cytokine production, blood-brain barrier compromise, and apoptosis[30], [31]. Brain temperature elevations have also been associated with hyperemia, exacerbation of cerebral edema, and elevated intracranial pressure.[32,33] Recent experimental data from animal models of ICH that used bacterial collagenase infusions, suggested that temperature modulation improved recovery and lessened neuronal injury when hypothermia was initiated after 12-hours of onset[34] but this effect was not seen in a different animal model of "whole blood" infusion.[35] A recent study of ICH patients suggested that mild induced hypothermia was associated with less cerebral edema without change in hematoma growth or functional outcome when hypothermia was started after 6-hours of onset.[36] The American Heart Association (AHA) has recommended normothermia in the setting of acute ICH.[37] No method to accomplish this has been evaluated in a prospective fashion. Although acetaminophen and cooling blankets are generally used, efficacy in the intensive care setting has been questioned.[38]

Craniotomy and clot evacuation

Craniotomy has been the most studied intervention for the surgical management of ICH. Two earlier smaller trials showed that for patients presenting with moderate alterations in the state of consciousness, surgery reduced the risk of death without improving the functional outcome[39] and that ultra-early evacuation of hematoma improved the 3-month NIHSS[40] without an effect in mortality but a meta-analysis of all prior trials of surgical intervention for supratentorial ICH showed no significant benefit from this intervention.[41] The STICH study, a landmark trial of over 1000 ICH patients, showed that emergent surgical hematoma evacuation by craniotomy within 72 hours of onset fails to improve outcome compared to a policy of initial medical management.[42] In a post-hoc analysis of STICH, the sub-group of patients with superficial hematomas and no IVH had better outcomes in the surgical arm.[43] This observation provided support for the STICH-II trial, which is currently enrolling patients. In contrast to supratentorial ICH, there is much better evidence that cerebellar hemorrhages exceeding 3 cm in diameter benefit from emergent surgical evacuation as abrupt and dramatic deterioration to coma can occur within the first 24 hours of onset in these patients.[44] For this reason, it is generally unwise to defer surgery in these patients until further clinical deterioration occurs.

Emergency hemicraniectomy

Hemicraniectomy with duraplasty has been proposed as a life-saving intervention for several neurological catastrophes such as malignant MCA infarction and poor grade SAH. No randomized controlled trial has been conducted in patients with ICH. In a recent report of 12 consecutive patients with hypertensive ICH and treated with hemicraniectomy, 92% survived at discharge and 55% had a good functional outcome at discharge.[45] This preliminary data supports the need for better-controlled studies addressing the role of this surgical technique in ICH patients.

Minimally invasive surgery (MIS)

The advantages of MIS over conventional craniotomy include reduced operative time, the possibility of performance under local anesthesia, and reduced surgical trauma. Endoscopic aspiration of supratentorial ICH was studied in a small single-center randomized controlled trial.[46] The study showed that this technique provided a reduction of mortality at 6 months in the surgical group but surgery was more effective in superficial hematomas and in younger patients (<60 years).[46] Similarly, a recent report from China evaluated the effects of minimally invasive craniopuncture versus medical therapy in a cohort of 465 patients with basal ganglia ICH. Improvement in neurological outcome at 14 days and 3-months was better in the treatment group, though no differences were seen in long-term mortality.[47]

Thrombolysis and clot evacuation

Thrombolytic therapy and surgical removal of hematomas is another technique that has been studied in a single center randomized clinical trial.[40] Patients in the surgical group had better outcome scores than the medically treated group. Finally, a multi-center randomized control trial examined the utility of sterotactic urokinase infusion when administered within 72hrs to patients with GCS $\geq$ 5 and hematomas $\geq$10ml provided significant reduction in hematoma size and mortality rate at expense of higher rates of rebleeding but no significant differences in outcomes measures was seen.[48]

Thrombolysis after IVH

Intraventricular administration of the plasminogen activator urokinase every 12 hours may reduce hematoma size and the expected mortality rate at one month.[49] Several small studies have

reported the successful use of urokinase or tissue plasminogen activator (t-PA) for the treatment of IVH, with the goal of accelerating the clearance of IVH and improving clinical outcome.[50] A Cochrane systemic review published in 2002 summarized the experience of several case series providing evidence of safety but no definitive efficacy.[51] The ongoing Phase III Clear IVH Trial (Clot Lysis Evaluating Accelerated Resoution of Intra Ventricular Hemorrhage) is designed to investigate the optimum dose and frequency of r-tPA administered via an EVD to safely and effectively treat IVH and will soon provide some insight on this issue. When used off-label, a dose of 1 mg of rt-PA every eight hours (followed by clamping of the EVD for one hour) is reasonable until clearance of blood from the third ventricle has been achieved. Doses of 3 mg or more of t-PA for IVH thrombolysis have been associated with an unacceptably high bleeding rate.

CONCLUSION

Recent attempts to discern the pathophysiology of ICH have provided meaningful information to support plausible targets for intervention but evidence based therapies for ICH are not yet available. Treatment is primarily supportive and outcomes remain poor. Despite a long history of devastating outcomes and high mortality, there is still optimism that the management of ICH will change in the future based on new insights into the acute pathophysiology of this disease. A better understanding of the dynamic process of hematoma growth, importance of inflammation triggered by coagulation and products of blood degradation, and the deleterious effects of fever and inflammation may provide feasible targets for future interventions. Additional invasive and non-invasive treatment strategies are being tested in clinical trials and results are forthcoming.

Conflicts of Interest

Dr. Rincon reports receiving salary support from American Heart Association (12CRP12050342) and Gennentech (G-29902).

Dr. Rincon is consultant advisor for: Otsuka and Bard Medical

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A Case of Acute Disseminated Encephalomyelitis in a Middle-Aged Adult

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BACKGROUND

Acute disseminated encephalomyelitis (ADEM) is a monophasic inflammatory demyelinating disorder of the white matter that is often preceded by viral infection or recent vaccination. Encephalopathy and focal neurological deficits usually manifest one to three weeks after a prodromal illness with neurologic decline progressing rapidly over days to weeks. Approximately 25% of patients will develop multiple sclerosis (MS) within five years of initial presentation of ADEM but the majority of individuals do not progress beyond three months.[4] ADEM is most commonly seen in children and young adults, where prognosis is favorable, but very few cases have been reported of middle-aged or elderly patients. The clinical course of these patients as compared to younger patients with ADEM is unclear. Here we present a case of ADEM in a middle-aged adult that recovered well after treatment with high-dose corticosteroids.

CASE SUMMARY

A 62-year-old man with a history of hypertension initially presented with progressive development of gait dysfunction, urinary incontinence, and encephalopathy over the course of two weeks following four days of a gastrointestinal illness. Upon presentation to an outside hospital, he was non-verbal and due to his depressed mental status required intubation. He underwent an MRI of the brain on the first hospital day (HD) that revealed extensive supratentorial white matter hyperintensities extending from the periventricular region through subcortical fibers without contrast enhancement (see figure 1). Thus he was started on 250 milligrams (mg) of intravenous (IV) methylprednisolone every 6 hours for presumed ADEM. He also underwent a lumbar puncture on HD #1 prior to administration of IV steroids that revealed an opening pressure of 20, with cerebrospinal fluid (CSF) containing 0 red blood cells, 47 white blood cells of which 85% were lymphocytes, glucose of 52 and protein of 114. He was empirically treated with acyclovir and ceftriaxone for a total 5 days, which were discontinued after CSF bacterial cultures were negative. Blood cultures were also negative and a transthoracic echocardiogram was negative for evidence of vegetation to suggest endocarditis. Various viral titers including herpes simplex virus (HSV), Epstein Bar virus (EBV), varicella zoster virus (VZV), and cytomegalovirus (CMV) were negative, as were serologies for CSF Lyme and Cryptococcus neoformans. In addition, CSF oligoclonal bands and myelin basic protein were negative. Serum inflammatory markers including ANA, C reactive protein, and sedimentation rate were not elevated. EEG showed diffuse slowing suggestive of moderate diffuse cerebral dysfunction without evidence of seizures or epileptiform activity.

Despite treatment with high dose steroids for approximately 6 days at the outside hospital, his mental status did not improve and thus he was transferred to our facility to the neurological intensive care unit for further management. Upon arrival, the patient's GCS was 10T, with spontaneous eye opening, ability to localize to pain in the left upper extremity, and intact brain stem reflexes. Additionally, he displayed triple flexion in his bilateral lower extremities and decorticate posturing in his right upper extremity. A repeat lumbar puncture performed on HD #8 demonstrated a normal opening pressure, with CSF containing 0 red blood cells, 9 white blood cells of which 94% were lymphocytes, glucose of 79 and protein of 100. CSF bacterial cultures were negative, as well as no evidence of active HSV or EBV infection. CSF cytology revealed the presence of white blood cells but was negative for malignancy. RPR was also negative. Two subsequent MRIs of the brain were performed on HD #13 and HD #21 showing no significant change in the appearance of the prior white matter lesions and no new contrast enhancing lesions. In addition, an MRI of the cervical and thoracic spine with contrast performed on HD #22 did not show any prior or new enhancing white matter lesions. With continued treatment with high dose IV steroids at 250 mg of IV methylprednisolone every 6 hours for another 7 days, his mental status improved and thus he was safely extubated on HD #10 and continued on a taper of oral prednisone. He underwent a brain biopsy on HD #13 that revealed multiple small foci of macrophage accumulation and widespread white matter inflammation secondary to demyelination (figure 2). He was subsequently discharged on HD #63 to acute rehab on a prolonged oral steroid taper. His physical exam on discharge was notable for a GCS of 15, fully oriented, full strength on the left, and a residual right hemiparesis. Upon outpatient follow up four months later, he made further improvements, now ambulating without assistance, cognitively back to his baseline, and independent in his activities of daily living, with a modified Rankin score (mRS) of 0. He underwent a follow up MRI brain five months later that showed overall improvement in the diffuse white matter changes previously seen on initial presentation (see figure 1).

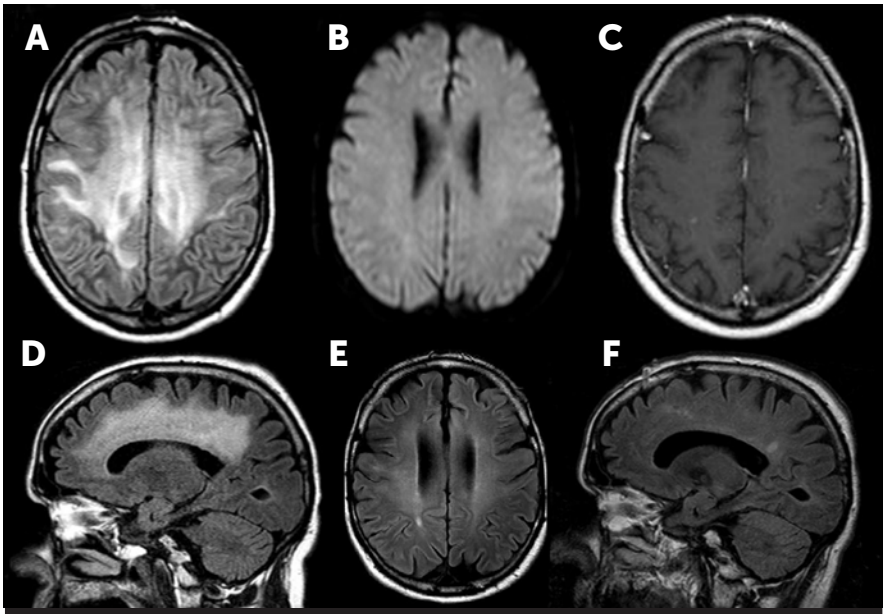

Figure 1

MRI Imaging on admission **A - D** in comparison to those obtained on 7 month follow up **E & F**. **A.** Axial t2/FLAIR showing supratentorial WM hyperintensities extending from the periventricular region through the subcortical fibers. **B.** Axial view diffusion- weighted imaging showing no restricted diffusion to suggest acute infarction. **C.** Axial T1 post-contrast image showing no contrast enhancement of the T2/FLAIR lesions. **D.** Sagittal T2/FLAIR image showing diffuse periventricular WM intensities. **E.** Axial T2/ FLAIR showing interval improvement & resolution of the periventricular WM lesions. **F.** Sagittal T2/FLAIR also demonstrating the improvement of the periventricular WM lesions.

DISCUSSION

ADEM is theorized to be an immunologically mediated demyelinating disease triggered by a febrile illness or recent vaccination, eliciting an inflammatory response affecting the central nervous system (CNS). Possible mechanisms may include either molecular mimicry or direct inflammatory damage to myelinated neurons.[2] The prevalence of ADEM is higher in children and young adults and thought to be related to the increased frequency of viral infections and vaccination in this patient population.[6] The demonstration of multifocal hyperintensities most often affecting the subcortical white matter on fluid attenuated inversion recovery (T2/FLAIR) MRI of the brain make the identification of ADEM difficult given various other inflammatory, infectious, and rheumatologic disorders that have similar clinical and radiological presentations. Given such ambiguity, the International Pediatric Multiple Sclerosis Study Group proposed a consensus definition for the pediatric population with the mandatory inclusion of encephalopathy in the criteria for diagnosis.[2] Despite this useful aid in identifying young patients, there still remains no clear diagnostic criterion for ADEM in adults, and therefore older individuals are more difficult to prognosticate given the paucity of reported cases and outcomes following standard ADEM therapies such as high dose corticosteroids, intravenous immunoglobulin (IVIG), and plasmapheresis (PLEX). Our patient presented with a suggestive clinical history of symptoms, physical exam and radiological signs, along with a CSF profile and histopathology suggestive of ADEM. Given both the therapeutic and prognostic implications of considering this a case as the first demyelinating event of MS, it important to make clear that this most likely does not represent MS given the initial subacute presentation of encephalopathy, the presence of multifocal lesions with ill-defined margins, and pathology showing widespread inflammation. In contrast, MS often presents with distinct episodes of focal neurological deficits with concordant confluent demyelinating lesions of varying ages appearing ovoid in shape, often affecting the white matter more than gray matter, the latter of which is seen more commonly in ADEM[4]. CSF studies reveal the persistent presence of oligoclonal bands more frequently in MS in comparison to ADEM[5]. Furthermore in this patient, subsequent MRIs confirmed no evidence of new contrast enhancing lesions, with follow up MRI five months later showing resolution of a monophasic demyelinating event with concomitant clinical resolution of neurological deficits. Additionally, due to the negative aforementioned serologies and inflammatory markers, as well as the lack of systemic symptoms, this case likely does not represent a manifestation of an underlying infectious, neoplastic, or rheumatologic condition that may mimic a demyelinating CNS insult.

A small case series of middle-aged adults presenting with ADEM has been described by Wang et al[1], in which all three patients had a single episode of focal neurological deficits and encephalopathy with typical MRI findings, and clinically improved with steroid treatment. Although typically reserved for more fulminant forms of ADEM, there have also been individual reports of the concomitant use of steroids along with IVIG and PLEX in the treatment of ADEM in older patients with favorable outcomes, suggesting that this presentation in older adults may in fact be of the similar pathophysiology that is well-described in children and young adults.[3,7]

ADEM rarely presents in the middle-aged to elderly adult and due to the paucity of cases reported in the literature, the prognosis in this age group is unknown. We present a case of ADEM in a middle-aged adult in which the patient had an excellent response to treatment with high dose steroids, resulting in a remarkable neurological recovery. Thus it behooves us to treat suspected cases of ADEM in an adult patient aggressively, as outcome may be favorable.

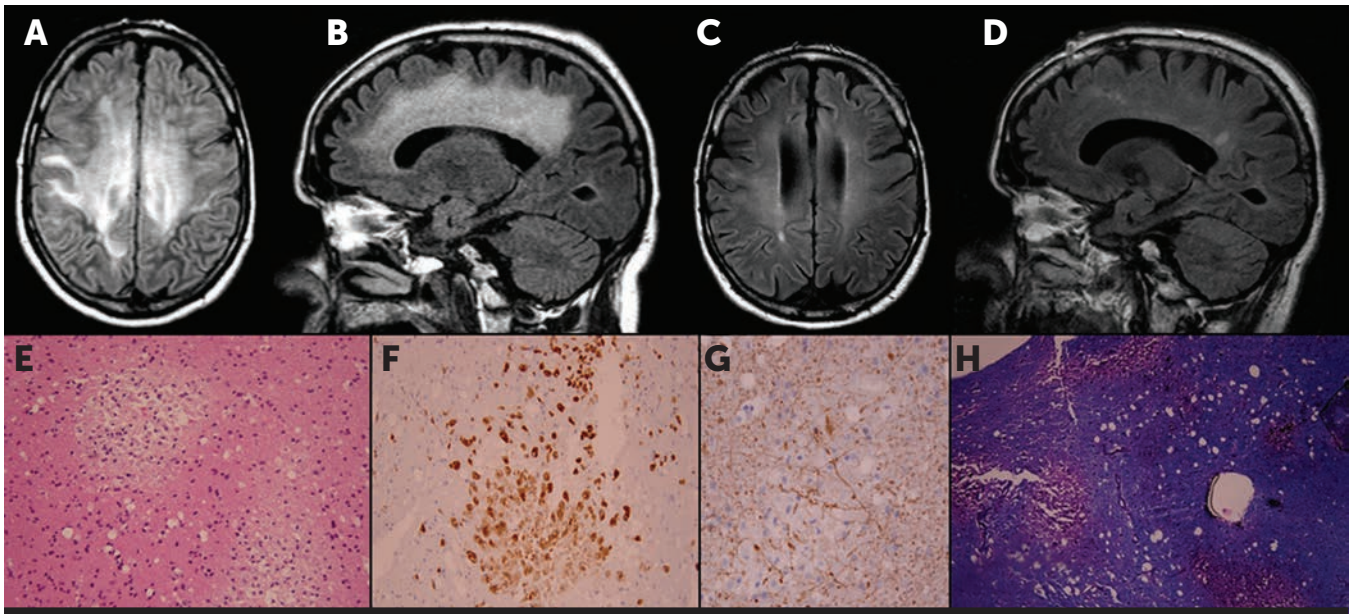

Figure 2

A. Axial T2/FLAIR showing supratentorial WM hyperintensities extdending from the periventricular region through the subcortical fibers. **B.** Sagittal T2/FLAIR MRI showing diffuse periventricular WM intensities. **C.** Axial T2/ FLAIR MRI showing interval improvement & resolution of the periventicular WM lesions. **D.** Sagittal T2/FLAIR also demonstrating the improvment of the periventricular WM lesions. **E.** H&E Stain (200x) showing areas devoid of pink-stained myelin consistent with demyelinating plaques. **F.** Immunohistochemistry stain for CD68 (200x) which is a marker for macrophages. This image shows the detection of dark pigment structures that represent macrophages infiltrating the areas of demyelination. **G.** Stain of neurofilaments (brown strands, 400x) confirming the relative conservation of axons even within the areas of demyelination. **H.** Luxol Bluestain (100x) showing staining of lipophilic myelinated axons (blue) with patchy areas of demyelination (purple) with dark structures representing infiltrating macrophages.

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Strategies for Optimizing Acute Ischemic Stroke by Reducing Door-to-Needle Time in a Major Academic Center

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INTRODUCTION

Acute ischemic stroke affects nearly 795,000 people per year in the United States.[1] In fact, 1.9 million neurons are lost for every minute that the brain is deprived of oxygen.[2] For patients who present to an emergency department within 4.5 hours, they may be eligible for treatment with intravenous thrombolytic therapy (tPA). Currently, IV tPA is the only treatment with level 1A evidence for acute ischemic stroke[3]. Multiple studies have confirmed that there is a direct correlation between a faster Door-to-Needle (DTN) time and better patient outcomes.[4-5] The current Target: Stroke Quality Improvement Initiative sets a Door to Needle time goal of less than 60 minutes. Prior to 2014, our institution's time median DTN time was 83 minutes.

OBJECTIVE AND METHODS

The purpose of this study was to evaluate the stroke alert pathway for delays and identify improvements and resolutions to mitigate out-of-window tPA delivery. A retrospective analysis was conducted by identifying data from both the Emergency Department and Neurology initial encounter documentation which identified specific time metrics deemed critical to tPA administration to the neurologist's ability to administer tPA. These metrics were identified based off of existing information, along with interviews of the Neurology residents and attendings. Our areas of study included Symptom Onset, Time of Presentation to ED, Stroke Alert Received, Neurology at Bedside, Time of tPA Decision, Time tPA Ordered, Time of tPA at Bedside, and Time of tPA Administration.

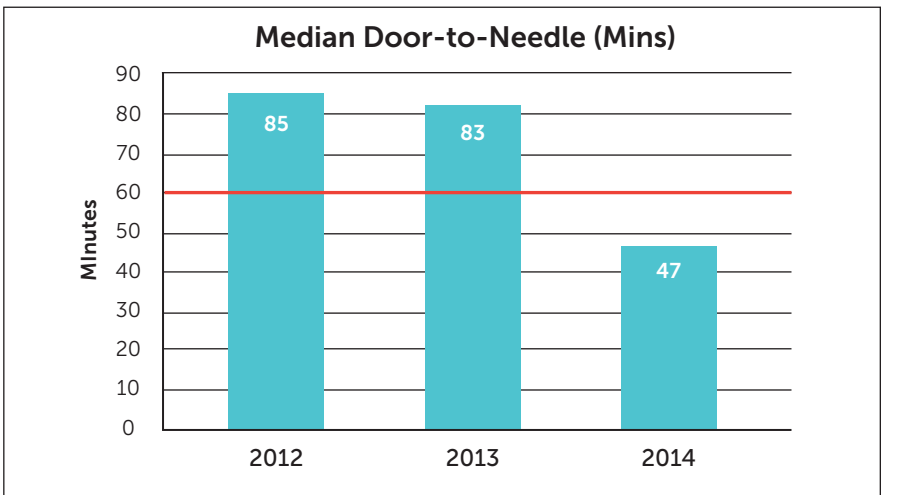

Figure 1
Median DTN time

Other patient data that we identified included the National Institute of Health Stroke Scale (NIHSS) on presentation, disposition, symptomatic intracranial hemorrhage and past medical history, including hypertension, coronary artery disease, hyperlipidemia, atrial fibrillation, and demographic factors, including gender, age, and smoking history.

The study was approved by our Institutional Review Board. The inclusion criteria for patients in our study were all patients who were eligible to receive tPA between January 1, 2014 and September 31, 2014. 31 eligible patients were identified. The DTN times of tPA administration for these eligible patients that presented to the emergency department were compared to all patients who received tPA in 2013.

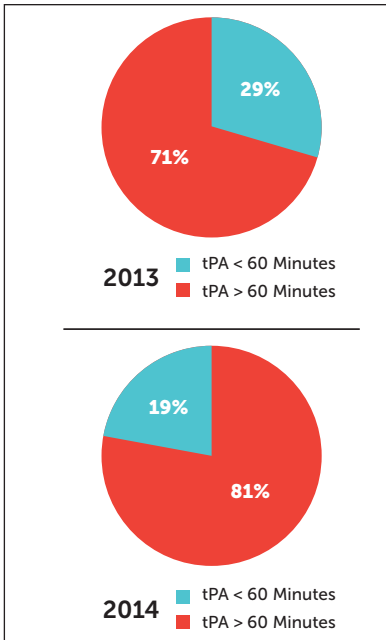

Figure 2
Proportion of patients receiving tPA within 60 minutes

RESULTS

We evaluated 30 patients who met our inclusion criteria. By evaluating our current time measurements, we were able to determine which areas needed to be improved. Using the time metrics we described above, we were able to decrease the median DTN time from 83 minutes in 2013 to 47 minutes (see below) up to September 31st, 2014 (see Figure 1). The proportion of patients receiving tPA in under 60 minutes increased from 29% to 81% (see Figure 2). Our rate of symptomatic intracranial hemorrhage dropped from 14% to 3% (see Figure 3). The proportion of patients who were discharged home increased from 43% to 71% (see Figure 4).

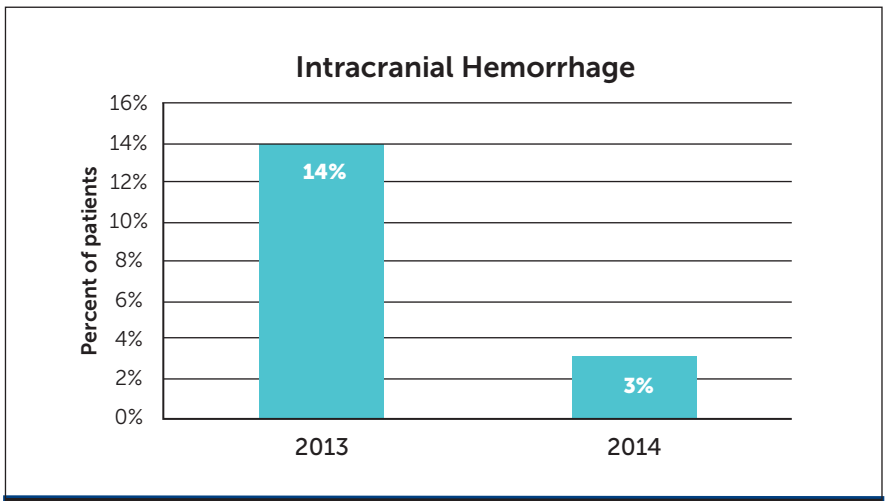

Figure 3
Proportion of Symptomatic Intracranial Hemorrhage post IV tPA

CONCLUSION

Through the identification and analysis of key metrics in the acute stroke pathway by the neurology team, we were able to implement new strategies, including pre-mixing, and aggressive blood pressure management, while providing immediate feedback to the neurologists involved in each case about areas in which improvements could be made. As such, DTN times and the proportion improved within a brief period of time. As the benefits of IV tPA are time dependent, it is critical that hospitals work to optimize acute stroke protocols. By implementing the innovative changes of the neurology house staff, institutions nationwide can achieve similar rapid gains in DTN times and provide effective treatment to a greater percentage of patients with acute ischemic stroke.

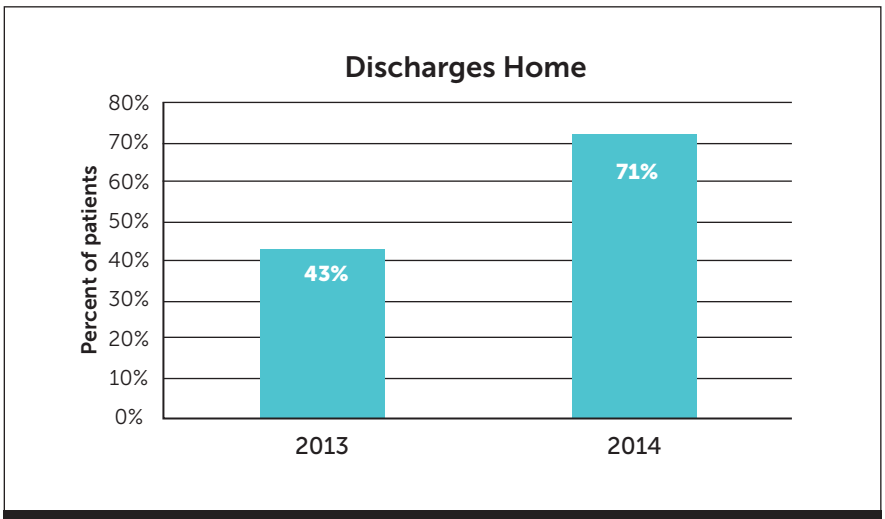

Figure 4
Proportion of Patients Discharged Home

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Managing Hyperglycemia in Critically Ill Patients: Where Are We Now?

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Hyperglycemia is common in critically ill patients and is associated with increased morbidity, mortality, rate of infections and length of hospital stay. For decades, hyperglycemia in critically ill population was considered an adaptive response and interventions were only considered if diabetic ketoacidosis (DKA) or severe hyperosmolar states developed. Furnary et al published studies showing lower sternal wound infection rates in cardiac surgical patients with control of glucose (180-220 mg/dl). This led to the dissemination of the "Portland Protocol," but it was not widely accepted.[1, 2]

Management of hyperglycemia changed with the publication of Van Den Berghe study.[3] This was a prospective, randomized, controlled study involving adults admitted to a surgical intensive care unit (ICU) who were receiving mechanical ventilation (MV). A total of 1548 patients were enrolled with patients randomly assigned to two groups. One group received intensive insulin therapy (IIT) with goal blood glucose of 80-110 mg/dl. The second group received conventional treatment whereby insulin was given only if the blood glucose level exceeded 215 mg/dl with goal glucose level of 180-200 mg/dl.

The primary outcome measure was death from any cause during intensive care. The main secondary outcome measures were in-hospital death; the number of days in the intensive care unit and the need for prolonged intensive care (more than 14 days) or readmission; the need for ventilatory support, renal replacement therapy, or inotropic or vasopressor support. At 12 months, IIT reduced mortality during intensive care from 8.0% with conventional treatment to 4.6% (P<0.04) in intensive treatment group. The benefit of intensive insulin therapy was attributable to its effect on mortality among patients who remained in the intensive care unit for more than five days (20.2% with conventional treatment, as compared with 10.6% with IIT; P=0.005). The greatest reduction in mortality involved deaths due to multiple-organ failure with a proven septic focus. IIT also reduced overall in-hospital mortality by 34%.

Subsequently, in another single center study,[4] Van Den Berghe randomly assigned 1200 patients in medical ICU to strict normalization of blood glucose levels (80-110 mg/dl) with the use of insulin infusion or to conventional therapy. The study showed no significant difference in hospital mortality (40.0% in the conventional-treatment group vs. 37.3% in the intensive-treatment group, p=0.33). However, IIT reduced morbidity and mortality in patients that stayed in ICU for three or more days. The reasons for reduced morbidity in patients who received IIT were the prevention of acquired kidney injury, earlier weaning from MV, and earlier discharge from the medical ICU and hospital.

A number of multicenter studies were performed following the initial Van Den Berghe trial in an attempt to replicate the earlier results. VISEP (Volume Substitution and Insulin Therapy in Severe Sepsis) study[5] and Glucocontrol study[6] were prospective, multicenter randomized control trials whereas Wiener study[7] was a meta-analysis of 29 randomized controlled trials having a total of 8432 patients. The results of these studies showed no significant difference in mortality in the conventional and tight control groups but increased episodes of severe hypoglycemia.

Given the conflicting data regarding tight glycemic control, the NICE-SUGAR study [8] was undertaken. This was a multicenter randomized control trial which enrolled 6104 patients. Study compared intensive target glucose of 80 to 108 mg/dl to the conventional target of 180 mg/dl or less.

Primary outcome was death from any cause within 90 days after randomization. Secondary outcomes were survival in first 90 days, cause-specific death, duration of MV, length of stay in the ICU, and total length of stay in the hospital. The intervention was discontinued when patients were discharged from ICU or eating and were resumed if the patient was readmitted within 90 days. Blood glucose <40 mg/dl was considered a serious adverse event. One-third of the patients were surgical patients and two-thirds were medical patients. Mortality in intensive target group was 27.5% compared to 24.9% in conventional group (p=0.02). The incidence of severe hypoglycemia (<40 mg/dl) was 6.8% in intensive group compared with 0.5% in conventional group (p<0.001).

There were a number of differences between Van Den Berghe trial and NICE-SUGAR trial, which may help explain their divergent results. Van Den Berghe study was performed at a single center and considered reduction of glucose level only if it was markedly elevated (>215 mg/dl). In contrast, NICE-SUGAR study was multinational and the glucose level in conventional group was targeted at only a mildly elevated range of 144 to 180 mg/dl. Most patients in Van Den Berghe trial received parenteral nutrition whereas enteral nutrition was the rule in NICE-SUGAR study.

The strengths of NICE trial include its large, multicenter patient population, vigorous statistical analysis and broad representative spectrum of critically ill patients. However, some of the downfalls were open-label study design and premature discontinuation of treatment in 10% of the patients. Increased risk of death from IIT in NICE-SUGAR study can be attributed to multiple factors including direct harmful effects of insulin and neuroglycopenia that warrants further studies.[9]

An summary, IIT seems to save lives in the initial Van Der Berghe trial but its results are yet to be replicated, particularly in any multicenter trial. Critical care and endocrinologic societies have backed away from recommending intensive insulin therapy. ADA/AACE Inpatient Task Force recommends that insulin infusion should be used to control hyperglycemia with the starting threshold of 180 mg/dl. Once IV insulin is started, the target glucose is between 140 and 180 mg/dl. Lower glucose targets (110-140 mg/dl) may be appropriate in selected patients. Targets <110 mg/dl are not recommended.[10]

HYPERGLYCEMIA IN BRAIN INJURED PATIENTS

Hyperglycemia is a common secondary insult in traumatic brain injury (TBI), subarachnoid hemorrhage (SAH), and acute ischemic stroke and has been consistently associated with poor neurological outcome.[11]

ISCHEMIC STROKE

Several studies have evaluated the effect of IIT in acute ischemic stroke patients with hyperglycemia.[12,13] UK Glucose Insulin in Stroke Trial was the largest randomized clinical trial, which enrolled 933 patients and showed no clinical benefit of IIT.[14]

INSULINFARCT trial randomized 180 patients with acute stroke to receive IIT or subcutaneous insulin treatment during the first 24 h.[15] It demonstrated that IIT in the first 24 h was associated with larger infarct growth and was not recommended.

Mortality

Study	IIT (%)	Conventional (%)	p value
Van Den Berghe (2001)	4.6	8	<0.04
Van Den Berghe (2006)	37.3	40	0.33
VISEP (2008) (At 28 days)	24.7	26	0.74
Glucocontrol (2009) (At 28 days)	18.7	15.3	0.14
NICE-SUGAR (2009)	27.5	24.9	0.02

Hypoglycemia

Study	IIT (%)	Conventional (%)	p value
VISEP (2008)	17	4.1	<0.001
NICE-SUGAR (2009)	6.8	0.5	<0.001
Glucocontrol (2009)	8.7	2.7	<0.0001

Sample Size

Study	n (Total)	n (Conventional)	n (IIT)
Van Den Berghe (2001)	1548	783	765
Van Den Berghe (2006)	1200	605	595
VISEP (2008)	537	290	247
Glucocontrol (2009)	1101	551	550
NICE-SUGAR	6104	3050	3054

AHA/ASA recommends that it is reasonable to treat hyperglycemia to achieve blood glucose levels in a range of 140 to 180 mg/dl and to closely monitor to prevent hypoglycemia in patients with acute ischemic stroke[16] (Class II a; Level of Evidence C).

SUBARACHNOID HEMORRHAGE

Hyperglycemia may have detrimental effects in patients with subarachnoid hemorrahge by increasing chances of infection, cerebral ischemia and by facilitating the progression from ischemia to irreversible infarction.

The majority of the studies using IIT reported episodes of hypoglycemia. Insulin therapy inducing episodes of low glucose was associated with cerebral infarction, vasospasm, and worse functional outcome 3 months following SAH.[17] There is only one randomized trial where 40 patients receive IIT. This study showed no significant improvement in clinical outcome or the incidence of vasospasm.[18]

Currently there is no evidence that hyperglycemia in SAH patients should be treated with IIT. This treatment is accompanied by an increase in hypoglycemic episodes.

AHA/ASA recommends that glucose management with strict avoidance of hypoglycemia may be considered as part of the general critical care management of patients with Aneurysmal SAH[19] (Class IIb; Level of Evidence B).

TRAUMATIC BRAIN INJURY

Hyperglycemia contributes to poor outcome in TBI patients. Hyperglycemia has been shown to worsen ischemic brain injury in experimental studies with animals. One study analyzing cortical contusion injury in rats found that hyperglycemia worsens the injury with superimposed ischemia.[20] In two class III human studies, hyperglycemia has been associated with worsened outcome.[21,22] A randomized controlled trial of 97 patients with severe TBI compared a regimen of IIT versus conventional management. No significant differences were observed in mortality and poor functional outcome at 6 months. Meanwhile, the incidence of hypoglycemic events was markedly increased among patients treated with IIT.[23] This was confirmed in an additional randomized trial with total of 523 patients including 94 TBI patients. IIT was not associated with improved survival and was associated with increased occurrence of hypoglycemia.[24]

Current clinical trials do not show any benefit of tight glucose control with IIT in TBI patients with increased episodes of hypoglycemia.[25]

CONCLUSION

In summary, significant body of literature has shown that hyperglycemia is common in patients with TBI, SAH, and ischemic stroke and that it is related to poor outcome. However, no concrete evidence exists that tight glycemic control improves outcome in these patients. It might on the contrary lead to hypoglycemic episode with deleterious effects on the injured brain due to secondary neuronal injury.

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Brain Abscess Presenting as Non-Traumatic Convexal Subarachnoid Hemorrhage

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ABSTRACT

We report a case of isolated brain abscess presenting as non-traumatic convexal subarachnoid hemorrhage (cSAH) 6 days before radiologic signs could be seen. A literature review provides only one other case with similar presentation.

INTRODUCTION

Non traumatic non aneurysmal convexal subarachnoid hemorrhage (SAH) is a poorly defined and rare clinical entity that comprises less than 7% of all subarachnoid hemorrhages.[1] Convexal SAH (cSAH) is characterized by blood collections in 1 or several adjacent sulci in the absence of blood at the base of the brain or elsewhere.[2] Various causes of cSAH have been described in literature ranging from Cerebral Amylod angiopathy (CAA), Reversible cerebral vasoconstriction syndrome RCVS), Corcitcal vein thrombosis (CVT), lupus vasculitis, moya-moya disease and septic emboli.[3,4,5,6,7,8] But, careful review of literature revealed only one other case of brain abscess causing cSAH.[9] Here we present another case of brain abscess heralded by cSAH.

CASE PRESENTATION

A 42-year-old man with no significant past medical history and no history of trauma presented with acute onset of transient left hemi-anesthesia lasting ten minutes. He first noticed the numbness during the day, without any preceding trauma. It started in his left arm and migrated to his hand and left flank within a few minutes. He was transferred to our facilities for a stroke workup. He denied any loss of consciousness, confusion, visual changes, and word finding difficulties, slurred speech, fever, nausea, vomiting, or headache. Past social history revealed that he is an elementary school teacher with no recent travels within the past year or exposures to toxins. He denied any use of tobacco, alcohol, or illicit drugs and currently takes no medications. His physical exam revealed extensive left arm numbness to light touch, temperature and pinprick and his strength was 4/5 throughout all muscle groups in his left arm, sparing the hand where it was 5/5 as per MRC scale. His CT scan revealed a subarachnoid hemorrhage as shown in figure 1 through 3.

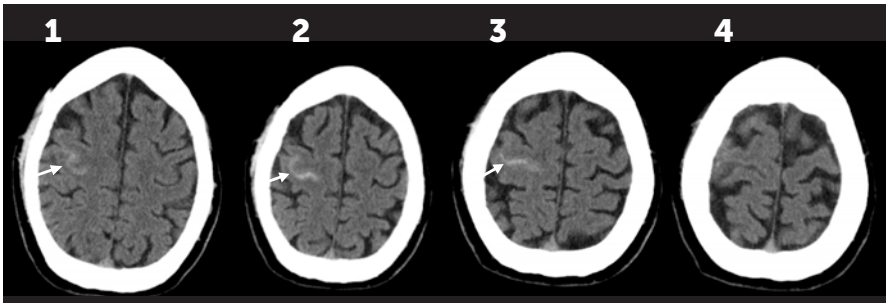

Figure 1 - 4

An MRI, MRA of the head and neck confirmed the finding of a subarachnoid hemorrhage within the right central sulcus in the right frontoparietal region. There was no evidence of infarction, and an MRV was normal.

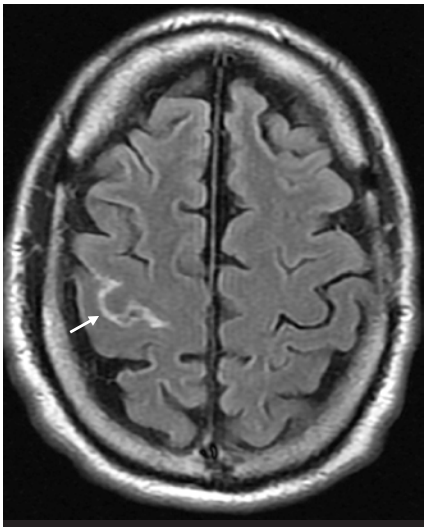

Figure 5 - Flair 1

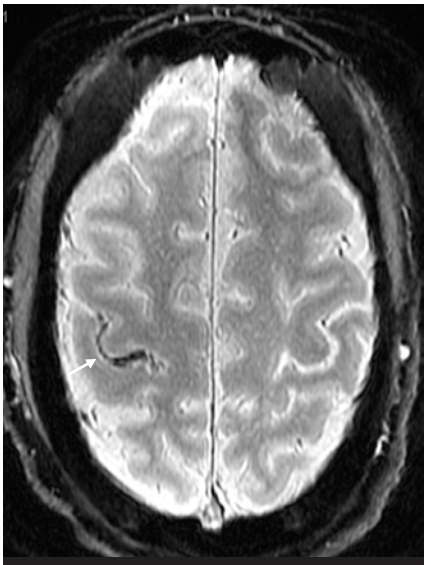

Figure 6 - GRE 1

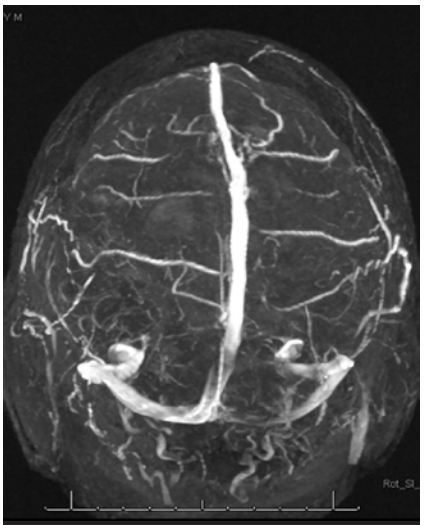

Figure 7 - MRV 1

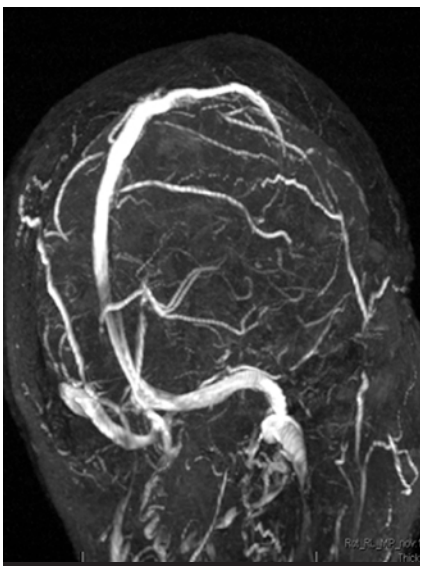

Figure 8 - MRV 2

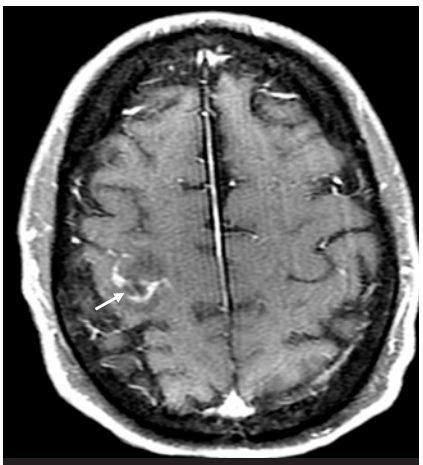

Figure 9 - Ax T1C1

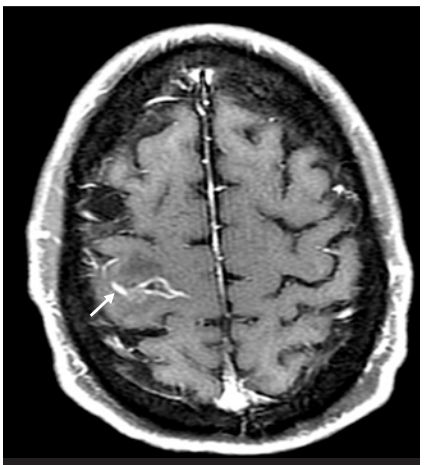

Figure 10 - Ax T1C2

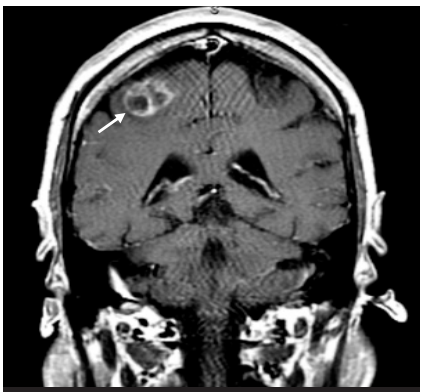

Figure 11 - Cor T1C1

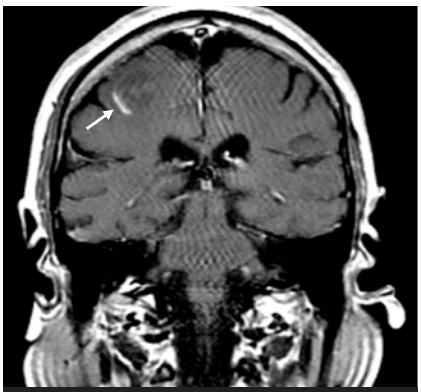

Figure 12 - Cor T1C2

He then received MRI of the brain, MRA of the head and MRV. The MRI of the brain confirmed the finding of a subarachnoid hemorrhage within the right central sulcus in the right frontoparietal region. There was no evidence of infarction. MRA of the head and MRV were unremarkable. After a stable exam for 48 hours from time of onset, he was discharged home on prophylactic levetiracetam. Five days later, his symptoms returned, this time involving loss of fine motor skills in his left hand. A conventional angiogram did not find any aneurysms, arteriovenous malformations (AVMs), or evidence of vasculitis. A transthoracic echocardiogram did not reveal any evidence of thrombi, patent foramen ovale, or shunt. CT of the chest, abdomen, and pelvis did not reveal any evidence of malignancy. His maxillofacial CT did now show any oral/maxillary abscess. His subsequent MRI showed an area of hypointensity with ring enhancement suggestive of brain abscess (Figures 9, 10, 11, 12).

He was subsequently taken to the operating room (OR) for a washout procedure. His OR cultures grew Streptococcus viridians, streptococcus anginosus and presumptive fastidious gram negative rods.

DISCUSSION

SAH has classically being described as traumatic vs non traumatic. A ruptured aneurysm is the most common cause of non traumatic SAH; accounting for approximately 85% of the cases (10). Of the rest, about two thirds are idiopathic perimesencephalic in origin and the rest are from multiple causes (11). Since non enhanced CT is the first diagnostic modality in patients presenting with suspected SAH, location of the bleed could be an important clue as to the etiology of the bleed.

SAH can be classified into three distinct patterns by location on the initial unenhanced CT. In the first pattern, SAH is centered in the suprasellar or central basal cisterns and extends peripherally in a diffuse manner. This pattern is characteristic of saccular aneurysm rupture. In the second pattern, SAH is centered in the perimesencephalic or

low basal cisterns and does not extend peripherally. This pattern is characteristic of idiopathic perimesencephalic hemorrhage. In the third pattern, SAH is localized to the cerebral convexities alone. This pattern is infrequent, and the differential diagnosis encompasses a heterogeneous group of diseases, including reversible cerebral vasoconstriction syndrome, cerebral amyloid angiopathy (CAA), posterior reversible encephalopathy syndrome (PRES), cerebral venous thrombosis (CVT), and other less common causes.[11] In our patient, the bleed was only confined to a few cuts in the right central sulcus.

SAH typically presents with sudden and severe headache (usually described as "the worst headache ever") accompanied by nausea, vomiting, photophobia, neck pain, and loss of consciousness.[12]The clinical presentation of cSAH might be different from the classic thunderclap headache reported in aneurysmal SAH; cSAH presents with focal deficits, especially in older patients (>60), which might suggest a TIA, migraine with aura, or epileptic seizures.[5] Our patient did not have headache or seizures on presentation. His initial imaging including non-contrast CT head and MRI with contrast failed to to raise suspicion for any disease process in the location of the hemorrhage. When he did come back in 6 days, the area around the hemorrhage showed hypodensity on the unenhanced CT head which on subsequent MRI with contrast showed ring enhancing lesion. We suggest in cases of cSAH where imaging techniques present no abnormalities, follow-up imaging within seven days should be considered.

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Neurogenic Stunned Myocardium in Status Epilepticus – A Report of Two Cases and Cohort Analysis

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BACKGROUND

Status epilepticus is a condition in which the patient suffers five minutes or more of either continuous clinical or electrographic seizure or recurrent seizure activity without return to baseline between seizures.[1] This a problem commonly encountered in the neurologic ICU. Among brain injured patients, the incidence of convulsive status epilepticus is about 27%[2] but incidence of non-convulsive status epilepticus can range from 20% to as high as 50%-55%.[3,4,5] Status epilepticus is a dangerous disease with a reported in hospital mortality rates ranging from 9-61%.[6,7,8,9] Ongoing, uncontrolled seizure causes a direct neuronal injury that contributes to this high risk of mortality. Patients with status epilepticus, however, also suffer a number of systemic complications, thought to be related to excitotoxicity, [10] mitochondrial failure[11,12] and systemic inflammatory response driven by uncontrolled seizure.[13,14,15,16] Notably, patients with status epilepticus frequently suffer a transient reduction in cardiac systolic function.[17,18] In some cases, decreased systolic function may be part of a syndrome of decreased cardiac function, echocardiographic abnormalities, troponin elevation, and non-specific EKG changes that has a number of names in the literature, including tako-tsubo syndrome, stress cardiomyopathy, and neurogenic stunned myocardium. Neurogenic stunned myocardium is known to be common in many classes of acute neurologic injury and has been described in subarachnoid hemorrhage, traumatic brain injury, cerebral infarction, and intracranial hemorrhage.[19,20,21] In the setting of status epilepticus, case reports of neurogenic stunned myocardium date from at least the early 1990s.[23,26] While the exact mechanism by which seizure causes myocardial dysfunction is unclear, it is thought likely to be mediated by excitotoxicty associated with release of endogenous catecholamines during prolonged seizure.[20,22,24,25] The prevalence and clinical impact of neurogenic stunned myocardium in the setting of status epilepticus is not fully described to date in the literature.

METHOD

We conducted a retrospective cohort study of 100 consecutive patients diagnosed with generalized status epilepticus. Patients were identified from administrative data including ICD 9 codes associated with the admission. Patients with a concurrent diagnosis of anoxic brain injury or cardiac arrest were excluded. Forty-two patients in this sample underwent echocardiography. We analyzed demographic characteristics, co-morbidities, echocardiographic findings, and treatment patterns in these patients. We sought to describe the prevalence of echocardiographic findings suggestive of neurogenic stunned myocardium in this cohort. Further, we abstracted two recent cases for a more detailed presentation and discussion.

CASE ONE

A 32-year-old woman without prior medical history was admitted to the neurologic ICU with convulsive status epilepticus. She was treated with benzodiazepine agents and fosphenytoin and clinical seizure activity abated. Continuous EEG was placed and showed diffuse slowing with alternating theta frequency discharges and rhythmic delta frequency discharges. During ICU day 1, the patient developed tachycardia with sustained heart rates of 160-170 beats per minute coupled with hypotension with a blood pressure nadir or 60/40 mmHG. The patient remained hypotensive after bolus administration of crystalloid fluids. The patient was placed on norepinephrine. Transthoracic echocardiography demonstrated an ejection fraction of 15% and severe global hypokinesis with sparing of the basal segments (figure 1). A pulmonary artery catheter was inserted and a cardiac index of 2.1 L/kg/min was measured. The patient was started on a dobutamine infusion to maintain a target cardiac index of 2.4L/kg/min or greater. The patient was weaned from the dobutamine four days later with normalization of her cardiac index.

CASE TWO

A 64-year-old woman with no known neurologic or cardiac disease history was found unresponsive. Continuous EEG demonstrated non-convulsive status epilepticus. The patient was admitted to the neurologic ICU and treated with benzodiazepines and levetiracetam. On ICU day 2, the patient developed hypoxia and tachycardia. CT angiography of the chest revealed bilateral sub-segmental pulmonary emboli and bilateral infiltrates as well as new pulmonary edema. Transthoracic echocardiography demonstrated a mild decreased ejection fraction (40%) together with significant wall motion abnormalities described as

basal to mid-septal akinesis and global hypokinesis with sparing of anterolateral, inferolateral, and periapical contraction (figure 2). The patient developed hypotension and was supported with norepinephrine. A repeat echocardiogram was obtained nine days later and demonstrated resolution of the wall motion abnormalities.

COHORT ANALYSIS

A cohort of 100 consecutive patients with status epilepticus not related to anoxic brain injury or cardiac arrest were identified from administrative data. The mean age of this cohort was 56 years. Forty patients were female and 56 were Caucasian. Of the 100 patients, 43 underwent transthoracic echocardiography. Echocardiography was divided into four categories: normal (30/43), apical hypokinesis typical of neurogenic stunned myocardium (1/43), other segmental wall motion abnormalities (6/43), and hyperdynamic left ventricular function (6/43). No correlation was found between the presence of the abnormal echo patterns and pressor use, ICU length of stay, hospital length of stay, or in hospital mortality.

DISCUSSION

In this analysis, echocardiographic patterns most typical of neurogenic stunned myocardium occurred infrequently. Abnormal contractility was found in 7% of the total cohort and in 16% of patients who underwent echocardiography. These data permit only limited conclusions. No data were captured regarding the treatments rendered to these patients; many of the treatments commonly used in the setting of status epilepticus, including barbiturate, propofol, and phenytoin infusions may have influenced cardiac function. In addition, factors that may have informed the clinical decision to obtain echocardiography were not captured in this analysis. Therefore, it is difficult to draw conclusions regarding the true prevalence of neurogenic stunned myocardium in status epilepticus. It is clear, however, that an important subpopulation of patients with status epilepticus have abnormal cardiac contractility. Routine assessment of cardiac function in this patient population is warranted. Future analysis will focus on gathering more robust epidemiologic data regarding the prevalence of neurogenic stunned myocardium and will explore the relationship between abnormal cardiac function and seizure localization, semiology, treatment practices, and clinical outcomes.

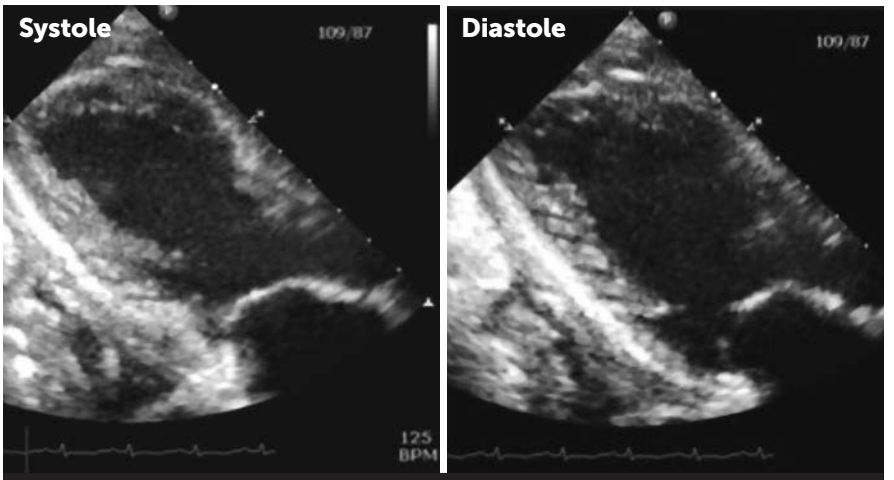

Figure 1 - Case One

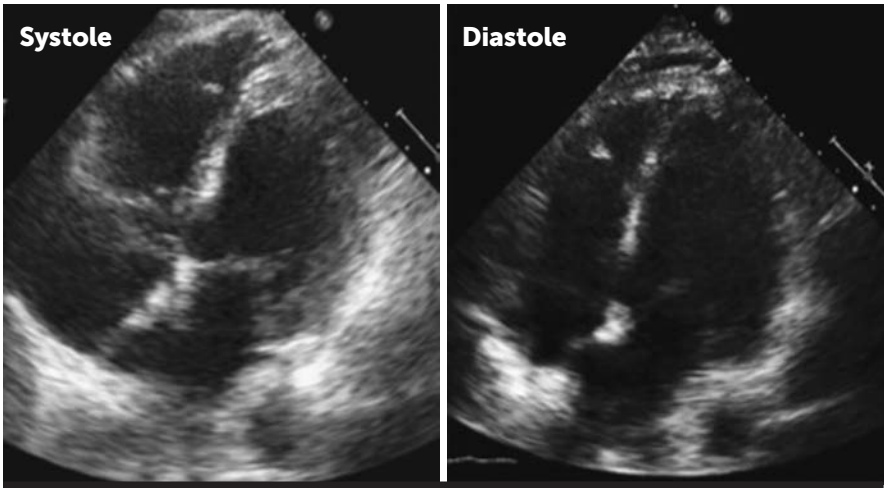

Figure 2 - Case Two

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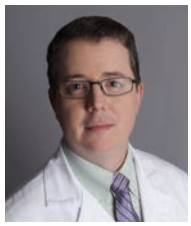

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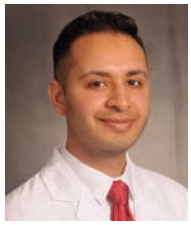

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Recent Publications

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Time 6:30-8:30 p.m.

Place 900 Walnut Street, 3rd Floor, Conference Room
Philadelphia, PA 19107

Moderator/ Secretary Jill Galvao

Parking Complimentary parking is provided in the parking garage located in the JHN Building (Jefferson Hospital for Neuroscience) on 9th Street (between Locust & Walnut)

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The Delaware Valley Brain Tumor Support Group at Jefferson provides an opportunity for patients and their families to gain support in obtaining their optimum level of well-being while coping with, and adjusting to the diagnosis of brain tumor. Members are encouraged to share their support strategies so members can confront the challenges that this disease process has imposed on their lives. The strength gained from group can be a source of comfort and hope for whatever lies ahead.

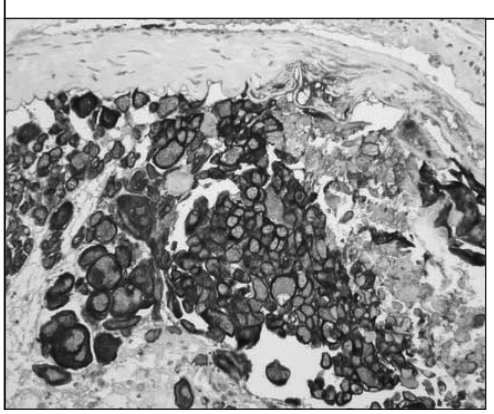
When Second Thursday of every month

Time 7-8:30 p.m.

Place Jefferson Hospital for Neuroscience,
3rd Floor conference room
900 Walnut Street Philadelphia, PA 19107

Facilitator Joseph McBride, BSN, RN and Katelyn Salvatore, BSN, RN.
215-955-4429 or katlyn.salvatore@jefferson.edu

Light refreshments and snacks will be served. Free parking is available at the Jefferson Hospital for Neuroscience parking lot.



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  January 29-30, 2016
  The College of Physicians of Philadelphia
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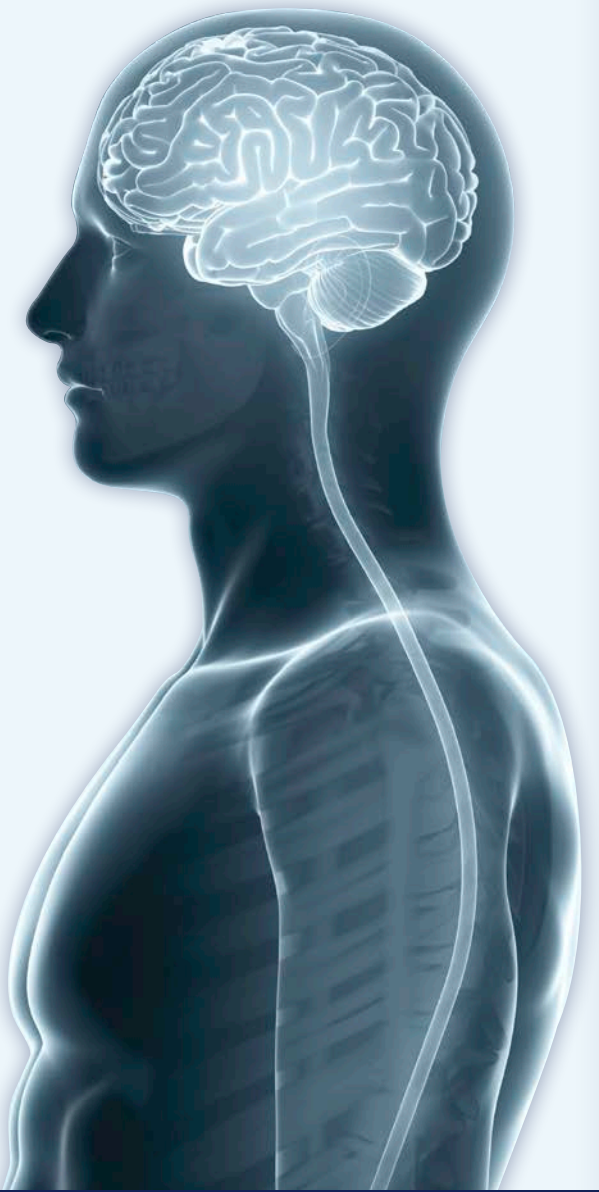

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Sidney Kimmel Medical College at Thomas Jefferson University designates this live activity for a maximum of ***11.75 AMA PRA Category 1 Credits™***. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

To obtain the maximum 11.75 credit hours, you must complete the pre-test, attend the live conference, and complete two post-conference tasks: take the post test and view the web-based discussion of the post test responses providing the rationale for each correct response. In addition, you will need to attend the Saturday simulation workshops.

Thomas Jefferson University Hospital is an approved provider of Continuing Nursing Education (CNE) by the PA State Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation. A maximum of 11.75 nursing contact hours will be awarded for this program. The participant must complete the pre and post tests, attend the entire program, and attend the Saturday simulation workshops to be eligible for full contact hour credit.

All faculty at continuing educating activities for nurses, physicians and allied health professionals are required to disclose to the audience (1) any significant financial relationships with the manufacturer(s) of any commercial products, goods or services and (2) any unlabeled/unapproved uses of drugs or devices discussed in their presentations. Such disclosures will be made in writing in the course presentation materials.

Sidney Kimmel Medical College™ at Thomas Jefferson University

ENDORSED BY Neurocritical Care Society

Friday, January 29, 2016
The College of Physicians of Philadelphia, 19 South 22nd Street, Philadelphia, PA 19103
Saturday, January 30, 2016
Case-Based Practical Workshop at Thomas Jefferson University, 1001 Locust Street, Philadelphia, PA 19107