LEE HEALTH NEUROVASCULAR NEWS LETTER

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LETTER FROM THE DIRECTOR

Dear All:

HCA Orange Park Medical Center is pleased to announce new initiatives for the management of acute, subacute and chronic cerebrovascular ischemia, intracranial hemorrhage, and intracranial pathology including brain tumors, vascular malformations, hydrocephalus and cranial nerve disorders. Beginning July 1, 2020, the health system will provide comprehensive care for patients with these maladies. Michael Horowitz Dr. and Youssef Al-Saghir, MD along with specialists within the departments of Neurology, Internal Medicine, Cardiology, Intensive Care, Rehabilitative Medicine, Palliative Care and Social Services will be providing 24/7/365 service to patients who require acute or non-acute care for the full spectrum of cerebrovascular and cranial disease. These conditions will include stroke, transient ischemia, aneurysms, arteriovenous malformations, cavernous malformations, arteriovenous fistulas, carotid/subclavian/ vertebral artery stenosis, epistaxis (nose bleeds), spinal vascular malformations, vascular brain and head and neck tumors, hydrocephalus, and subdural and epidural hematomas.

The newly organized effort aims to interact with the community to mutually care for at risk and acutely ill patients. Consultations and transfers can be easily arranged at any time of the day or night by dialing xxx-xxx-xxxx.

In addition to providing clinical care, our hope is to better inform the community about the various neurovascular and cranial pathologies and their management. Towards that end, OPMC will be sending a monthly newsletter that highlights a different topic each month and provides information about various providers who may be of assistance with patient care.

We at HCA OPMC look forward to working together. If you have any suggestions for how we can better serve you and the community please feel free to contact us and be assured we will take your thoughts and comments to heart.

Sincerely,

Michael Horowitz, MD
Director

PROFILE

INSERT BIO

TOPIC REVIEW: CURRENT MANAGEMENT OF ACUTE ISCHEMIC STROKE

Case Report

A 44 year old right handed woman presented to the ER with receptive aphasia and right sided upper extremity hemiparesis (1/5). Time of onset was unknown. BMI is 42. Past medical history is notable for tobacco use and hyperlipidemia. Medications include Lipitor. NIHSS is 22. CT scan (Figure 1) was normal (ASPECT Score 10). Catheter angiography revealed a left cervical ICA occlusion and a left MCA M1 large vessel occlusion (Figure 2). Revacularization of the left MCA was carried out using a Solitaire thrombectomy device (Medtronic, Minneapolis, MN). Figure 3 shows the microcatheter positioned across the MCA occlusion. Figure 5 shows the microcatheter, Solitaire device and extracted thrombus. The patient underwent an MRI 24 hours later showing a left basal ganglia infarct but no changes in the distal left MCA territories (Figure 6).

The patient was discharged home 7 days later on 81 mg ASA per day with normal speech and 4/5 left upper extremity strength. Final work up revealed a heterozygous prothrombin gene variant mutation (hypercoagulable state).

CT BRAIN IN ER

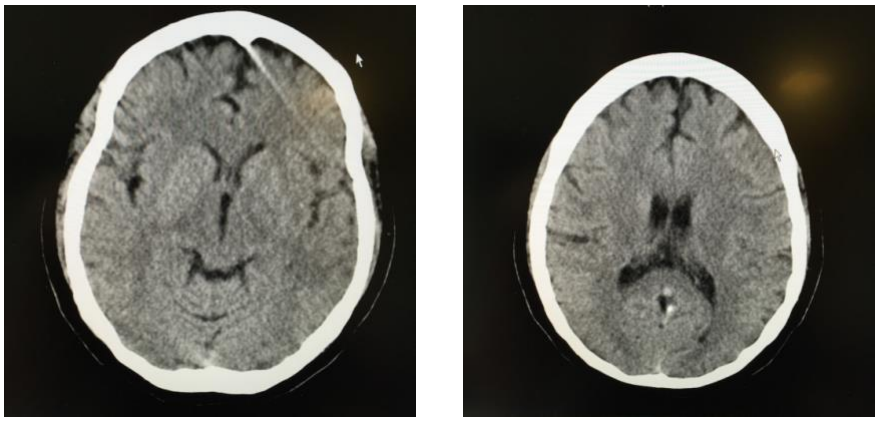

Figure 1: Normal CT upon presentation in the ER (ASPECT Score 10)

ANGIOGRAPHY PRE TREATMENT

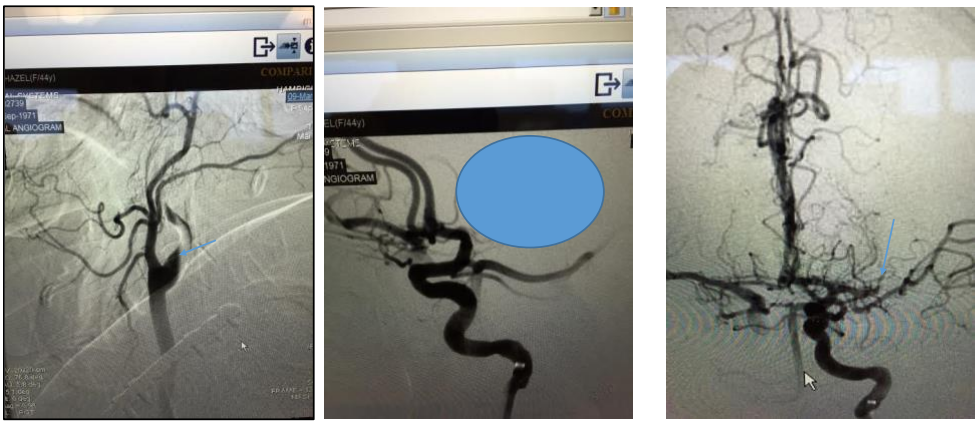

Figure 2: Angiogram showing left ICA occlusion and left MCA occlusion. The catheter has been advanced through the left ICA occlusion to better visualize the distal vaculature. The blue oval shows a region of no opacification due to the MCA occlusion

MICROCATHETER PLACED THROUGH OCCLUSION

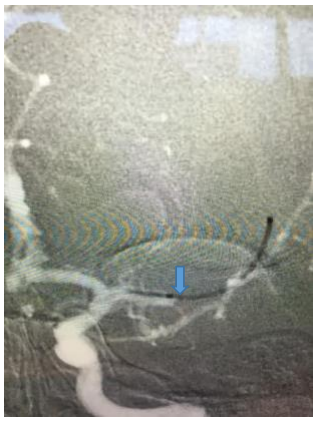

Figure 3: Angiographic image with the microcatheter positioned distal to the MCA occlusion (through the thrombus).

RETRIEVED THROMBUS

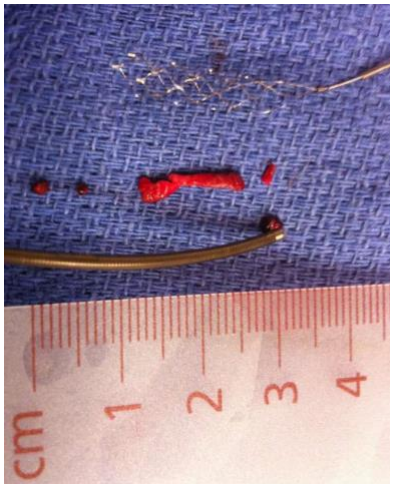

Figure 4: Microctheter, Solitaire Thrombectomy Device, and extracted MCA thrombus.

MRI BRAIN 24 HOURS POST TREATMENT

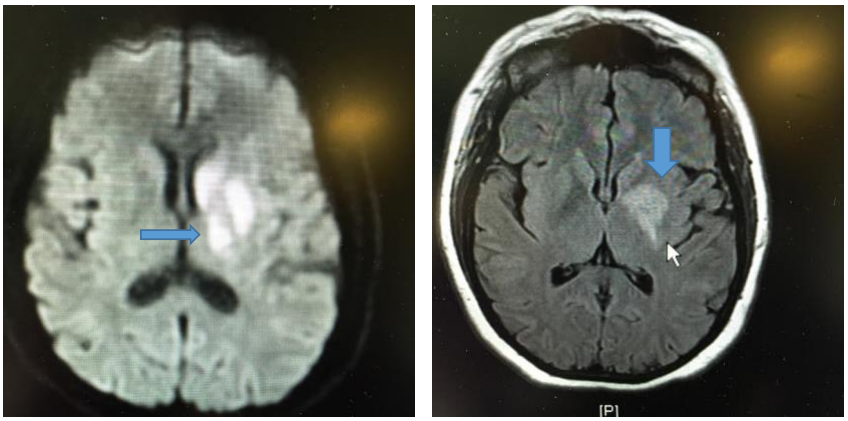

Figure 5: MRI 24 hours after the procedure showing basal ganglia stroke but no distal MCA territory ischemic changes.

Definitions

Stroke is a condition manifested by rapidly developing clinical signs of focal or global disturbance of cerebral function with symptoms lasting 24 hours or longer. This malady can include ischemic and hemorrhagic infarction, intracerebral hemorrhage and subarachnoid hemorrhage (SAH). In adults 80-85% of strokes are ischemic while in children, 55% of strokes are ischemic.

Transient ischemic attack (TIA) defines clinical signs of focal or global disturbance of cerebral function that is related to reduced blood flow to the brain that lasts less than 24 hours.

This Topic Review will focus exclusively on ischemic stroke.

Disease Impact

Stroke is the number one cause of disability among adults in the United States with 795,000 Americans affected per year (1 stroke every 40 seconds). Stroke is a major cause of death with 128,000 mortalities per year.

Basic Physiology

The brain contains 2% of the total body weight yet, as a result of its high metabolic activity, it receives 20% of the cardiac output. Normal cerebral blood flow (CBF) is 50-65 cc/100g brain/minute. Brain perfusion is not only affected by cardiac output but by intracranial pressure. As intracranial pressure rises, it becomes more difficult to perfuse the brain normally. This perfusion of the brain is measured by the cerebral perfusion pressure (CPP) which is calculated using the equation: CPP = Mean Arterial Blood Pressure – Intracranial Pressure. One can see from this equation that if mean arterial pressure drops or if intracranial pressure rises, CPP will drop. It follows, therefore that if CPP drops then CBF can drop as well. The brain tries to maintain CBF, and by dilating and constricting the arteries of the brain, the body can keep CBF constant over a range of CPP ranging between 60 and 140 mm Hg. Once CPP drops below 60 mm Hg, however, the brain can no longer maintain adequate blood flow to the brain. Once CBF drops below 20cc/100g brain/min brain dysfunction ensues. Once CBF drops below 15-18cc/100g brain/min EEG changes are seen, and once CBF drops below 8-10 cc/100g brain/minute neurons begin to die and stroke occurs.

Etiology of Acute Ischemic Strokes

For the purposes of this review on acute ischemic stroke we will focus on thromboembolic and occlusive mechanisms that can lead to reductions in CBF. These two physiologic events lead to reduction in CBF and a variety of symptoms that depend upon the affected intracranial arteries and the cerebral territories that they perfuse. The potential underlying causes for such events such as carotid stenosis, atrial fibrillation, atherosclerotic disease, metabolic disease, patent foramen ovale with paradoxical emboli, atrial myxoma, cardiac valvular disease, hypercoagulable states, inherited and acquired thrombophilia, drug use and vasculopathy will be elaborated upon in future newsletters.

Patient Evaluation

No matter what the etiology is for an acute thromboembolic or occlusive stroke, the emergent evaluation remains almost uniform. This uniformity ensures rapid triage and proper intervention when possible.

Step 1

All patients suspected of suffering a stroke should undergo an expeditious history and physical.

History should include determination of the last known time the patient was seen to be normal or at baseline. This information will define the official “time of onset”. Time of onset (TOS) will in turn help define potential future therapies. In addition to TOS, it is imperative that first responders and ER personnel note past medical history (cardiac history, stroke history), past surgical history, pregnancy status, other neurologic diseases, and current medications. It is extremely important to

determine if the patient is on any antiplatelet or anticoagulant medications as these can affect the use of certain stroke therapies.

While a detailed physical examination can be useful, this can consume precious minutes. For that reason, the physical examination, aside from vital signs, can be initially replaced by obtaining a National Institute of Health Stroke Score (NIHSS). This scoring system may seem intimidating at first, however, by using readily free downloadable applications that can be placed onto a smart device/phone such as NeuroToolkit, Stroke Scale and MDCalc, the medical provider can rapidly and consistently determine a patient's neurologic level of function. The NIHSS, like the TOS, is an important component of the initial evaluation that helps select patients for various treatment algorithms. The reliable inter-observer reliability of the NIHSS also provides the ability to follow a patient's examination over time to check for improvement or decline in neurologic function. The NIHSS point system ranges from 0–42. A score of 0 denotes a normal examination, 1-4 reflects minor symptoms, 5-15 indicates moderate symptoms, 16-20 represents moderate to severe symptoms and 21-42 marks a severe stroke.

NIHSS can help predict outcomes. Left untreated, an NIHSS >16 portends the strong possibility of death while NIHSS <6 indicates a strong possibility of a good recovery. An increase in 1 point in a patient's NIHSS decreases the likelihood of an excellent outcome by over 10%.

Step 1 can be completed in less than 5 minutes and can be obtained in the field as easily as it can in the hospital.

Step 2

All patients suspected of having any intracranial pathology should undergo immediate head CT scan to determine whether or not there has been an intracranial hemorrhage or an intracranial mass (tumor) exists. The CT scan may also demonstrate evidence for ischemic tissue. If the CT scan reveals ischemic changes then the radiologist, neurologist or neurosurgeon should determine the Alberta Stroke Program Early CT Score (ASPECT Score). This 10 point scoring system quantifies the volume of ischemic brain seen on CT scan. A score of 10 denotes no evidence on CT for ischemia (ischemia might be present, but it may be too early for the radiographic changes to be seen on CT). An ASPECT Score <7 predicts worse functional outcome at 3 months as well as the increased risk for developing delayed intracranial hemorrhage into the damaged brain tissue.

CT arteriography performed at the same time as the CT can be useful. This study rarely adds significant time to the plain CT imaging and can quickly determine if a patient harbors a large vessel occlusion (LVO) that is defined as an ICA or MCA thromboembolus. By determining the presence or lack there of of an LVO using CTA, a decision can be made as to whether or not emergent cerebral catheter arteriography and thrombectomy/thrombolysis/stenting is warranted.

While MRI, MR perfusion and CT perfusion can be helpful for evaluation of acute strokes, the time it takes to obtain and interpret such studies generally outweighs the benefits of the information these studies provide and as of this time, these modalities are not indicated or standard of care in most situations. Such imaging may be useful for patients presenting for treatment beyond the 12 hour to help guide decision making, but this is considered on a case by case basis.

Patient Treatment

Intravenous Tissue Plasminogen Activator (iv-tPA; Alteplase)

When patients present within 4.5 hours of onset of stroke symptoms (within 4.5 hours of last known normal) they are generally eligible for iv-tPA if their NIHSS exceeds 4 (0.6-0.9 mg/kg not to exceed 90 mg total dose infused over 90 minutes with 10% administered as a bolus over minute 1). This recombinant drug cleaves plasminogen into the protease plasmin that in turn degrades Fibrin. Polymerized Fibrin normally combines with platelets to form a hemostatic clot, hence degradation of Fibrin can degrade thrombus and reopen an occluded vessel. Absolute and relative contraindications to iv-tPA administration are numerous. Once again these can be retrieved on a smart device/phone using an application such as Stroke pocketcards. The use of iv-tPA was approved by the FDA in 1996 following published study results in 1995 (NEJM. 333:1581-1588, 1995). A follow-up study published in 2016 suggested that reducing the dose to 0.6 mg/kg might yield equivalent results to 0.9m/kg while reducing the risks of intracerebral hemorrhage from 2.1% to 1% (NEJM. 374:2313-2323, 2016).

The use of iv-tPA beyond the 4.5 hour window from last known normal has been investigated in the EXTEND Trial. The results of this study were reported at the International Stroke Conference in February 2019. This study used CT and MR perfusion to determine if there was a patient population that might benefit from the administration of iv-tPA in the >4.5 hour period. Results were favorable. EXTEND may ultimately lead to changes in the indications for iv-tPA administration and might increase the use of perfusion studies in certain situations.

Endovascular Therapy for LVO

Endovascular (mechanical and suction thrombectomy, superselective intra-arterial tPA infusion) treatment of acute LVO stroke is of interest because of two factors. The first is that recanalization rates for iv-tPA administered within 4.5 hours of last known normal are only 5-14% for ICA occlusions and 20-44% for MCA occlusions. The second is that the degree of recanalization is the most important determinant of the size of infarct volume (less recanalization leads to greater infarct volume and worse outcomes). As a result of these considerations, physicians have looked for ways to increase treatment efficacy.

The MR CLEAN Study (NEJM. 372:11-20, 2015) evaluated patients treated using thrombectomy and iv-tPA as opposed to iv-tPA alone. This study showed that in patients treated using combined therapy there was no difference in mortality, 71% improvement in good neurologic outcomes, and no residual occlusion in 75% of treated vessels. A subgroup analysis later showed benefit to combined therapy in patients with ASPECTS ≥5 (Lancet. 15:685. 2016). Additional studies such as SWIFT PRIME, EXTEND IA, REVASCAT, AND ESCAPE compared iv-tPA alone to iv-tPA plus thrombectomy. These investigations revealed that when combination therapy was used from 4.5 – 12 hours from last known normal time of onset, outcomes were improved over those following iv-tPA alone without any increase in morbidity or mortality.

The above studies investigated the combined use of iv-tPA and endovascular thrombectomy and demonstrated clear benefits. What about patients who are not eligible for iv-tPA? Can these individuals be helped using endovascular therapy alone? The HERMES Study addressed these questions showing benefits to thrombectomy alone, thus giving hope to another subgroup of patients (Lancet. 387 (10029):1723-1731, April 2016).

In 2017, the DAWN Study (NEJM. 378:11-21, 2018) gave hope to patients with significant deficits and small infarct volumes on CT ("Mismatch between Deficit and Infarct") presenting 6-24 hours from last known normal. In this investigation, patients with small infarct volumes (mean volume 7.6 ml; range 2-18 ml) and moderate to severe NIHSS (median 17; range 13-21) were randomly assigned to undergo either standard care for strokes that presented beyond the tPA window or thrombectomy. Ninety day functional independence was 49% in the thrombectomy group vs. 13% in the control group and mortality at 90 days was 19% in the thrombectomy group vs 18% in the control group. Symptomatic intracranial hemorrhage was less than 7% in both groups (no statistical difference). By extending the therapeutic window to 24 hours, DAWN has expanded the pool of individuals who may benefit from aggressive treatment.

Posterior Circulation Acute Strokes

There are no clear recommendations for the management of posterior circulation LVO such as those involving the basilar artery. Symptomatic occlusions are evaluated on a case-by-case basis. Revascularization attempts are indicated in most cases that do not show large areas of brainstem ischemia due to the >90% risk of symptom progression and death from such arteriopathy. All treatments are considered off label and at the discretion of the treating physician in consultation with the patient's family when possible.

Conclusion

Acute management of ischemic stroke has advanced significantly over the last decade. Study data and improvements in technology have made it now possible to intervene on patients who were previously relegated to a course of watchful waiting. Rapid referral of such patients to centers of excellence is imperative.