Stroke and Neurodegenerative Disorders

Stroke and Neurodegenerative Disorders: 2. Poststroke Medical Complications

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Objective: This self-directed learning module highlights common poststroke medical complaints encountered on an inpatient rehabilitation unit. It is part of the study guide on stroke and neurodegenerative disorders in the Self-Directed Physiatric Education Program for practitioners and trainees in physical medicine and rehabilitation. Using a case vignette format, this article specifically focuses on the differential diagnosis, evaluation and management of chest pain, mental status changes, weight loss and poor motivation in stroke patients. The goal of this article is to expand the learner’s knowledge of how to diagnose and manage common medical complications of stroke patients in rehabilitation.

2.1 Clinical Activity: A nurse requests your evaluation of a 74-year-old woman with type 2 diabetes mellitus; 10 days after a right basal ganglia hemorrhage, the woman is complaining of chest pain and shortness of breath. Discuss the differential diagnosis and assessment of chest pain and dyspnea in this patient population.

Chest pain is 1 of the more concerning complaints after a stroke, since the differential diagnosis includes several life-threatening conditions that require immediate attention. Causes of chest pain in the poststroke population include pulmonary embolism, cardiac disease, pneumonia, gastroesophageal reflux (GERD), and musculoskeletal issues.

Most stroke rehabilitation inpatients have 2 or more components of Virchow’s triad, which put them at high risk for venous thrombosis. These components include immobility and weakness resulting in venous stasis, dehydration or exacerbation of premorbid conditions that can cause a hypercoagulable state, and procedures such as angiograms that, because they penetrate the venous system, may cause endothelial injury. While deep venous thrombosis (DVT) may result in pain, low-grade fever and swelling, the most concerning complication of DVT is pulmonary embolism (PE), because persons with PE may present with sudden death in 50% of occurrences in a stroke population, according to 1 study [1].

In a study examining the National Hospital Discharge Survey [2], of 14,109,000 patients admitted to acute care hospitals with ischemic stroke, DVT occurred in 0.74%, PE in 0.51%, and the combination of both in 1.17%. The rates were higher in the 1,606,000 persons admitted with hemorrhagic stroke, with 1.37% for DVT occurrence, 0.68% for PE, and 1.93% for both [2]. Frequencies for DVT for those in rehabilitation settings screened with impedance plethysmography have been reported as higher in a study by Oczkowski et al [3] venous thromboembolism occurred in 11% in their population and 2% died of PE.

Prevention is obviously the best management for DVT and PE. In cases of ischemic stroke, chemical prophylaxis with heparinoids is commonly used, although there is some concern with causing a hemorrhagic conversion of the stroke or gastrointestinal bleeding. There is significant controversy in the literature regarding the superiority of either low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH). In two meta-analyses of the literature [4,5], LMWH was found to have greater efficacy in the prevention of DVT in patients with ischemic stroke. In the review by Andre et al [4], no evidence could be found to support the use of mechanical agents, such as sequential compression devices (SCD). In a recent multicenter, randomized, open-label trial in 1762 persons with severe ischemic stroke, enoxaparin at 40 mg given subcutaneously daily was found to be superior...
to UFH, dispensed at 5000 units subcutaneously every 12 hours, in the prevention of DVT. Both agents carried a similar rate of intracranial bleeding, but there was a slightly higher incidence in major extracranial bleeding with enoxaparin [6].

The prevention of DVT and PE in persons with hemorrhagic strokes is more complicated. The concern of initiating further intracranial bleeding with heparinoids is significant and, unfortunately, there is a dearth of literature on the safety and efficacy of chemical prophylaxis in this population. One study examined mechanical interventions of elastic stockings and SCD in 151 persons admitted to an acute hospital with intracerebral hemorrhage. SCD, used with elastic stockings reduced the risk of asymptomatic DVT by 71% in comparison with using stockings alone [7]. There was no mention of how many hours a day the SCD were applied; it is unclear how these results translate to an inpatient rehabilitation setting where patients are out of bed and thus out of the SCD for a significant number of hours daily.

In persons with ischemic strokes who have sustained a proximal DVT or PE, adjusted heparin or full-weight-based enoxaparin followed by warfarin is indicated. In the setting of hemorrhagic strokes, the risk of bleeding from anticoagulation seems to be associated with location of the original hemorrhage. A 2-fold increased risk of re-bleeding exists in lobar bleeds in comparison with deep hemispheric bleeds [8]. Unfortunately, no studies discuss the use of inferior vena cava filters as an alternative to chemical anticoagulation in this population.

Further controversy exists in the timing of mobilizing patients with DVT or PE. Many patients are kept on bedrest for some time after diagnosis to prevent embolization of an "unstable" clot. In 1 older retrospective study of rehabilitation inpatients, persons who were returned to physical therapy fewer than 48 hours after discovery of DVT were at higher risk for a PE than those kept immobilized between 48 and 72 hours [9]. In a review of a community population, bed rest had no effect on development of PE after DVT [10]; however, those who were previously immobilized before the DVT developed were excluded from this study.

For the patient in the case under discussion, if the examination shows findings consistent with a PE (tachycardia and/or oxygen desaturation) evaluation with spiral computed tomography (CT) or ventilation/perfusion scanning is indicated [11].

Because many of the risk factors for stroke (hypertension, diabetes mellitus, smoking, hypercholesterolemia, etc) are similar to those of coronary artery disease (CAD), it should come as no surprise that the potential for cardiac events is significant in this population. Any person with a history of stroke who complains of chest pain must be closely evaluated for a cardiac event, even without a specific history of CAD. Chimowitz et al [12] gave stress tests to 69 patients with different types of brain ischemia. Of the patients with large artery cerebrovascular disease, 50% had abnormal stress tests in comparison with 23% in persons with other causes of brain ischemia. They also found that 60% of the abnormal stress tests in the large artery cerebrovascular group were suggestive of severe CAD [12]. Patients with a history of CAD prior to their stroke should be closely monitored. In 1 retrospective review of stroke rehabilitation inpatients, the patients with CAD alone and CAD with congestive heart failure (CHF) had 3 times more cardiac complications than those without CAD or CHF [13]. Workup for the patient in this case should include an electrocardiogram (ECG), laboratory tests with troponin and with creatine phosphokinase (CPK) and, if indicated, brain natriuretic protein (BNP) to evaluate for CHF.

As with any other patient population, other issues (esophageal spasm; back, shoulder, rib pain; pneumonia; GERD) may present as chest pain. These possibilities can be examined after life-threatening causes of chest pain are ruled out.

### 2.2 Clinical Activity

The patient in Case 1 has been stable for the last 4 days. However, this morning she is more somnolent and difficult to arouse. Outline the possible etiology of acute mental status changes following stroke and formulate assessment and treatment strategies.

The appropriate evaluation of acute mental status changes after stroke requires a very broad list of differential diagnoses. Infection, seizures, stroke progression, hydrocephalus, and electrolyte abnormalities can commonly be seen after stroke. The stroke population is a medically complex group. The rate of medical complications seems to be associated with the severity of the stroke, with 97% of severe stroke patients having at least 1 complication during their rehabilitation stay [14]. In a study of 1029 consecutive patients admitted to a freestanding rehabilitation hospital, several factors were associated with a higher rate of complications, including severity of neurologic deficit, hypoalbuminemia, and hypertension [15]. The most common complications are reported to be depression, shoulder pain, falls, urinary tract infections (UTIs), and dehydration [15-17].

It is important to evaluate for infections. One large study found that UTIs are common after stroke and are associated with female sex, higher scores on the National Institutes of Health Stroke Scale (NIHSS) and advanced age [18]. Voiding dysfunction may include incontinence, retention frequency and urgency. Other medical comorbidities, such as DM, prostate disease and neuropathies may also contribute to the dysfunction. Urinary retention may occur immediately after stroke as a symptom of "cerebral shock," but incontinence may also appear later—not only because of the development of uninhibited bladder but also because of communication, mobility, or cognitive issues [19]. Urinary incontinence is associated with a worse medical status and a poorer outcome from stroke; in a review of 2-year poststroke outcomes, patients with urinary incontinence were more likely to have motor weakness, visual field deficits, higher fatality rates, greater disability, and higher rates of institutionalization. Urinary tract infection and pneumonia are independently associated with worse scores on the Barthel index and higher mortality rates at 3 months after stroke [18].
While rare in ischemic strokes, communicating hydrocephalus may be a complication after intracranial hemorrhage. Blood products, dead cells and other debris block uptake of cerebral spinal fluid (CSF), and cause dilatation of all portions of the ventricular system. Presentation of hydrocephalus can range from a plateau of function to a severe depression in mental status. In a study of persons with intracranial hemorrhage in an acute care setting, hydrocephalus was associated with a younger population (age 57 y vs. age 67 y), ganglionic or thalamic bleeds, and lower Glasgow Coma Scale (GCS) scores. The patients with hydrocephalus were less likely to be discharged home and had a higher mortality rate [20]. A CT scan is the most common starting point for evaluation of hydrocephalus; dilatation of the lateral ventricles and periventricular lucency (indicating transependymal CSF shifts) are commonly seen with hydrocephalus.

Patients with a generalized seizure or those in a post-ictal state may present with severe depression of consciousness. Both ischemic and hemorrhagic strokes may result in seizures, according to 1 study by Bladin et al [21]. In their examination of 1897 persons with acute strokes admitted to university hospitals, they found that seizures occurred in 10.6% of hemorrhagic patients and 8.6% of ischemic patients during the acute hospitalization. The major risk factor for hemorrhagic stroke seizures was cortical location of the bleeding. In ischemic patients, seizures were associated with cortical infarction and stroke severity. Recurrent seizures occurred in 2.5% of the total patient population. Status epilepticus may also present with acute mental status changes, and if not promptly recognized and managed, may result in further disability or death. Toxicity of antiepileptic medications, such as phenytoin and valproic acid, may present with a depressed level of consciousness and should be considered in the differential diagnosis of acute mental status changes in persons taking these medications.

Hyponatremia and poor glycemic control are both possible causes of mental status changes. Antidiuretic hormone levels have been noted to be increased in those with stroke [22]. The etiology seems to be a lack of suppression of vasopressin release to hyposmolar serum [23]. As the hyponatremia usually occurs slowly, substantial decreases in laboratory values can be seen before clinical presentation. First-line treatment of syndrome of inappropriate antidiuretic hormone (SIADH) is free water restriction. Significant increases or decreases in blood sugar can result in a change in mental status and mimic a new stroke. Fluctuation in oral intake, changes in activity patterns and other medical issues can complicate glycemic control in persons with diabetes. Close monitoring of capillary blood glucose is essential in this population. Hyperglycemia is associated with poor functional outcomes after stroke [24].

Despite advancements in the secondary prevention of stroke (see Study Guide Chapter 4), previous stroke remains a high risk factor for a recurrent stroke. Fourteen percent of persons with a new stroke will have a second stroke within a year [25]. Additionally, those with cerebral infarcts are at risk for hemorrhagic transformation. The frequency of transformation has been reported to be 8.5% of all ischemic strokes; those who are at particular risk have large infarcts, mass effect, hypodensity observed early after the stroke, exposure to antithrombotic or thrombolytic drugs, and age greater than 70 years [26].

In the evaluation of this patient, an organized approach in the workup will be essential, starting with a comprehensive history and physical examination, vital signs, capillary blood glucose and pulse oximetry; infection and dehydration may be apparent. Laboratory tests, including a complete blood count, electrolyte panel, and serum levels of any medications the patient is taking should be assessed. Urinalysis and a chest x-ray will help evaluate for infection. A CT scan of the head will help evaluate for hemorrhage, as well as development of hydrocephalus. Magnetic resonance imaging (MRI) or CT perfusion scan will help evaluate for a new infarct. If concerns for seizure exist, an electroencephalogram (EEG) should be performed.

The decision of whether to transfer a patient to an acute level of care depends on multiple factors, including the rehabilitation setting (freestanding hospital versus in an acute facility), comfort level of physician and nursing staff, availability of specialist care in rehabilitation, need for further workup or procedures, and the patient's ability to tolerate therapies. Transfer rates to acute care for persons with stroke have been reported to be 13% [17] to 19% [15]. In a study by Roth et al [15] factors associated with transfer to an acute care facility were elevated white blood cell count at admission, low admission hemoglobin levels, greater neurologic deficit, and a history of cardiac arrhythmia.

### 2.3 Clinical Activity: A 58-year-old man on your stroke rehabilitation unit has experienced significant weight loss since his hospital admission. Discuss the challenges and management of proper nutrition following stroke.

As mentioned in activity 2.2, hypoalbuminemia is associated with an increased rate of medical complications [15], suggesting that good nutrition is an important component in the recovery process after stroke. The first step is to determine whether the patient is being provided enough calories to meet his metabolic demands. Specific patient factors should be examined. For example, a patient with severe apraxia or weakness may be unable to feed himself effectively. A thorough history and review of systems should be obtained from the patient with special attention to a history of gastrointestinal disease, mood disturbance, and current nausea, last bowel movement, vertigo, heartburn, cough and depression. Gastric ulcers, GERD and constipation can all lead to reduced oral intake. Aspirin, often given to prevent stroke, may cause gastritis. Patients with cerebellar or brainstem strokes may have severe vertigo or nausea that would result in decreased oral intake; treatment of the underlying disturbance with antiemetic or scopolamine may alleviate the problem. Depression, fatigue and poor initiation can often follow stroke and result in anorexia. (See Clinical Activity 2.4.)
Considering the importance of good nutrition in stroke recovery, one might be tempted to give dietary supplements to all stroke survivors. In trial 1 of the FOOD (Feed Or Ordinary Diet) trial, the benefit of routine dietary supplementation to all persons with stroke was examined [27]. Within 7 days of a new onset stroke, over 4000 patients were enrolled from 125 acute care hospitals in 15 countries. At baseline, 8% of patients were found to be undernourished. All patients were randomized to either a standard hospital diet or a hospital diet with oral protein energy supplements until discharge. No significant benefit or harm was seen with the use of oral supplements.

Dysphagia remains the most significant dietary concern after stroke. In examinations of consecutive patients admitted to acute care hospitals with stroke, aspiration was found in 42% to 51% [28,29]. Cortical strokes may cause decreased oral-motor control and decreased pharyngeal peristalsis, while brainstem or cerebellar lesions may result in decreased swallow initiation and coordination.

Untreated, aspiration can result in pneumonia and malnutrition. Sixty-eight percent of stroke patients who were found in both clinical and videofluoroscopic evaluation to be aspirating developed lower respiratory tract infections during their acute hospital stay [28]. It is best to get at least a bedside swallow evaluation of patients soon after admission to the acute care hospital to fully evaluate for any aspiration as well as the appropriate route for feeding; however, this method lacks significant sensitivity to discover all persons who aspirate [30]. There seems to be a significant benefit from early feeding; in the FOOD trial part 2, early tube feeding in comparison with withholding tube feeding was associated with an absolute reduction in risk of death of 5.8% [31].

If a patient is diagnosed with severe dysphagia, the routes of feeding are limited primarily to nasogastric tubes (NGT) or percutaneous endoscopic gastrostomy (PEG) tubes. Often, NGT are placed in the acute care setting. Problems include irritation, dislodgement or erroneous placement, which requires x-ray verification, and sinusitis. They are not designed for long-term nutritional support. The PEG tubes do not carry many of the risks of NGT, but require an invasive procedure with sedation for placement, and may result in localized infection [32]. Patients and family members may have some reluctance to accepting a PEG tube placement; reassurance that the feeding tube will not interfere with swallowing therapies and the potential for it to be a temporary measure is often necessary. A prospective study comparing PEG tubes versus NGT in persons with stroke found higher serum albumin levels and no treatment failures after 4 weeks with PEG tube feeding; patients with NGT had reductions in serum albumin levels during the study interval and a 50% treatment failure rate [33]. The superiority of PEG tubes was not seen in an earlier Cochrane database review, however [34].

Swallowing function remains a dynamic process after acute stroke. In a study of serial clinical evaluations and video fluoroscopic examinations of stroke patients, 51% were assessed to have dysphagia on admission, and 27% persisted after the first 7 days. At 1 month, 15% were found to be aspirating, but 8 of the 12 patients identified were those who had not previously been identified as having swallowing difficulties [29]. Constant vigilance is needed to ensure swallowing safety throughout the recovery process. Those who still require tube feedings due to poor recovery of swallow at the end of their rehabilitation stay carry a higher mortality rate [35].

2.4 Clinical Activity: During team conference, the therapy staff reports that your 76-year-old stroke patient whom you are treating for a right MCA stroke is not actively participating in therapy. Describe the differential diagnosis and treatment for reduced motivation following stroke.

While depression is quite common after stroke, it is very important to consider a broad differential diagnosis to make sure other treatable etiologies of poor motivation are excluded. Any of the medical conditions discussed in Activity 2.2 (infection, additional stroke, hydrocephalus, recurrent seizure, fluctuations in blood sugar, and hyponatremia) could result in decreased participation in therapy. Further, thyroid dysfunction may also play a role; endocrine abnormalities were seen in 79% of acute stroke patients with 36% displaying thyroid dysfunction [36]. Because pain may also be contributing to poor therapy performance, a thorough interview and examination of the patient is necessary.

Fatigue is a common complaint after stroke, with reported frequencies of 30% to 68% [37] and could result in decreased therapy participation. If no specific etiology is determined, treatment is multifactorial, with attention to pacing of therapies, increasing strength and endurance, and ensuring good sleep cycle regulation. Although there is no FDA-approved medication for the treatment of fatigue for persons with stroke, several classes of medications have been suggested: stimulants (methylphenidate, pemoline, dextroamphetamine), and antidepressants [37]. To the authors’ knowledge, no trials have been published examining these medications in this population.

Apathy may present with a flattened affect, hypophonia, and shortened responses. It has been associated with hypometabolism in the frontal and anterior temporal regions in SPECT imaging, and correlated with infarcts in the posterior limb of the internal capsule [38]. Apathy can be seen independently or in conjunction with depression.

The frequency of poststroke depression has been reported in the literature as a rather large range, likely due to many different rating systems and definitions. This can be a difficult group to study, since standard tools and diagnostic lists may not be applicable to an aphasic patient. Depression seems to have several different peaks of increased frequency; in a 3-year longitudinal study, its prevalence was 25% to 30% in the first 3 months, decreased to 16% to 19% at 1 to 2 years, and then increased again to 29% at 3 years [39]. Lesion location as a predictive factor for development of stroke has been reported inconsistently in the literature; however, pre-
arious history of mood disorder is shown to be an independent predictor of poststroke depression [40]. It does seem that depression has an effect on the recovery from stroke, but the evidence of the specific influence is mixed. In a study of 117 stroke survivors, depression negatively influenced functional recovery only if it occurred after hospitalization, but not during it [41]. In another study, stroke patients who were depressed and not treated had lower mobility scores than those who were not depressed [42]. This study also highlighted the importance of treating depression; patients whose depression was treated had a similar recovery pattern to those who did not have depression. In another examination of the effect of medication treatment of depression, patients treated with selective serotonin reuptake inhibitors (SSRI) had an average improvement during rehabilitation similar to that of the non-depressed patients; however, those without depression were twice as likely to have an “excellent” recovery in ADLs and mobility [43]. Apathy is frequently associated with depression [40], and according to 1 study, may be more frequently associated with poor functional recovery than depression alone [44]. For treatment of depression, tricyclic antidepressants were the mainstay before the advent of SSRIs; both have been shown to be efficacious in the treatment of poststroke depression, with SSRIs showing fewer side effects [45].

REFERENCES