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Various neurological impairments other than traumatic brain injury (TBI) are routinely encountered in critically ill populations. While in some US centers these are managed by neurointensivists, in most cases these patients are cared for by general intensivists in consultation with a neurologist. The following chapter will describe common and important neurological conditions related to the ICU patient that the intensivist must know with familiarity.

Major Ischemic Stroke Syndromes

Ischemic stroke encompasses a wide spectrum of conditions with varying modes of presentation, clinical course, and outcome. The most serious of these involve occlusion of the principal arteries, mainly, the carotid artery, middle cerebral artery (MCA), or basilar artery. While some patients suffering these strokes will have poor functional recovery, aggressive management in selected patients may yield reasonable outcomes. Recognition of the clinical patterns of large artery occlusions is paramount as it allows for rapid stroke severity assessment and possibly helps predict neurological deterioration.

General Management of Ischemic Stroke

Stroke may present with a variety of symptoms, not all of which may be focal. When a stroke is suspected, no matter the severity or anatomical location affected, early interventions are universally recommended. The first priority will

always be to manage and stabilize the ABCs. Cardiac monitoring must be initiated while providing supplemental oxygen to maintain O₂ saturation >94% and establishing IV access (preferably 20 gauge to allow for IV contrast administration). Mechanical ventilation is sometimes necessary. In the majority of cases, laboratory tests must be obtained upon symptom recognition including serum electrolytes, renal function tests, complete blood count, markers of cardiac ischemia, coagulation labs, and an EKG to rule out cardiac ischemia [1].

In some patients it may be prudent to check a toxicology screen, alcohol level, electroencephalogram (EEG) if seizures are suspected, and lumbar puncture (if subarachnoid hemorrhage is suspected and head CT is negative for blood). It is paramount to establish the time the patient was last known to be neurologically intact or behaving normally as the knowledge of the time of symptom discovery is not sufficient. A brief but thorough neurological exam must be performed evaluating elements of the National Institutes of Health Stroke Scale (NIHSS). This standardized assessment helps facilitate communication, quantify severity of stroke, and potentially help select patients for intervention. One must remember that the NIHSS does not assess posterior circulation strokes well. A non-contrast head CT is obtained and interpreted expeditiously. If negative for intracerebral hemorrhage and no other contraindications exist (Table 6.1), alteplase is given. Alteplase must be administered within 3 h of symptom onset; however, the window is often extended to 4.5 h if no contraindications are present [1]. An important point to keep in mind is that the benefit of alteplase therapy is time dependent and treatment should be initiated as quickly as possible.

It is strongly recommended to also obtain a noninvasive intracranial vascular study during the initial evaluation of an acute stroke if either intra-arterial fibrinolysis or mechanical thrombectomy is being considered [1]. Under no circumstances, however, should obtaining vascular imaging delay administration of alteplase. Expert consultation by a neurologist should be obtained simultaneously while the initial

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Table 6.1 Contraindications for the use of alteplase in patients with stroke (United States guidelines)

Active internal bleeding
Previous intracranial hemorrhage
History of a stroke within the past 3 months
Onset of symptoms >3 h
Minor deficit or symptoms rapidly improving
Severe stroke seen on brain imaging (>1/3 cerebral hemisphere)
Heparin use within 48 h and elevated aPTT
Platelet count <100,000/mm ³
Patient receiving oral anticoagulant and INR >1.7
Seizure at onset of stroke
Severe or dangerous bleeding within prior 21 days
Suspected subarachnoid hemorrhage
Puncture of a non-compressible blood vessel within prior 7 days
Myocardial infarction in the past 3 months
Major surgery within past 14 days
Significant head trauma in past 3 months
Systolic blood pressure >185 or diastolic >110 mmHg or aggressive management necessary to reduce blood pressure to these parameters
Glucose <48.6 mg/dL
Intracranial neoplasm, arteriovenous malformation, or aneurysm

From De Keyser et al. [30]

steps of stroke management are already occurring. Before alteplase can be administered, blood pressure must be controlled to systolic levels less than 185 mmHg and diastolic levels less than 110 mmHg. Once alteplase is being administered, the blood pressure range must remain less than 180/105 mmHg to reduce to the risk of intracranial hemorrhage (ICH). Ten to 20 mg of IV labetalol may be administered for this purpose but should not be repeated more than once (two total doses) [1]. If unable to control blood pressure with labetalol, nicardipine infusion is the optimal second agent and can be titrated to maximum of 15 mg/h. Other agents may be used as necessary (hydralazine, enalaprilat, etc.) [1].

If fibrinolytic therapy is contraindicated, then permissive hypertension is recommended. In this setting, a blood pressure goal is set at 220 mmHg systolic and 120 mmHg diastolic unless there is evidence of end-organ damage. Certain conditions may coexist with an evolving stroke such as myocardial infarction, aortic dissection, heart failure, or renal failure and may be exacerbated by arterial hypertension. There is no stated blood pressure goal for these specific medical conditions. If they occur concurrently with a stroke, the blood pressure target should be based on best clinical judgment for the specific scenario. A reasonable estimate is to lower the systolic blood pressure by 15% and monitor for neurological deterioration related to pressure lowering [1].

With few exceptions, intravenous heparin utilization during an acute stroke is almost never indicated. It is, nonetheless, recommended to administer IV heparin to treat an acute stroke secondary to central venous sinus thrombosis [2]. Also, while no randomized studies exist to support its use,

IV heparin may be used in cases of extracranial carotid or vertebral artery dissection, stuttering transient ischemic attacks, or basilar artery thrombosis [13]. IV heparin may also be used to treat stump emboli from carotid occlusion (based on the TOAST subgroup analysis) [4].

Malignant Middle Cerebral Artery Stroke

An occlusion of the MCA may lead to extensive and catastrophic brain infarction. The arterial system is comprised of the M1 segment (proximal MCA), proximal to the lenticulostriate arteries, and the M2 segment. The M2 segment is further divided into the inferior and superior trunks supplying portions of the temporal lobe and frontal lobe, respectively. Further down, the M2 segment is divided into the M3 (operculum) and the M4 (cortical) branches. Occlusion of the proximal MCA (or the internal carotid artery leading to the MCA) may manifest as flaccid hemiplegia or hemiparesis of the contralateral arm and milder weakness of the contralateral leg, hemisensory loss of the contralateral arm and leg, hemianopsia, and gaze deviation or preference toward the side of the stroke. If the dominant hemisphere is involved (typically the left hemisphere), an inferior division occlusion will cause a Wernicke's aphasia. A blockage of the superior trunk will cause Broca's aphasia. If the nondominant hemisphere is involved (especially the parietal lobe), neglect will be manifested in lieu of aphasia.

If the stroke involves the lenticulostriate arteries, the basal ganglia will likely suffer infarction as well. In this setting, the greatest concern is that a proximal occlusion may

manifest as a malignant middle cerebral artery infarction (see Fig. 6.1). This may result in ischemic edema and increased intracranial pressure (ICP) resulting in brain herniation and death [5]. This devastating condition occurs in 1–10% of all supratentorial infarcts [6]. The traditional array of treatments for these strokes has been supportive care and management of increased ICP using sedation, hyperosmolar therapy, hyperventilation, barbiturates, and the strict maintenance of normothermia [15].

As of the publishing of this textbook, no medical therapy or intensive care unit strategies have proven effective in treating brain herniation from stroke syndromes and improving patient outcomes. A review of the numerous prospective studies examining fatality rates demonstrates that mortality in patients admitted with malignant MCA infarctions approaches 80% with a significant proportion of survivors being left with severe disability [5, 6]. Three large trials (DECIMAL [5], DESTINY [7, 8] and HAMLET [1, 9]) have examined alternative therapies in malignant MCA infarctions and have found that extensive decompressive hemicraniectomy (DHC) with durotomy may be an effective method of treating elevated intracranial pressure and in improving patient functional status (modified Rankin scale (mRS) [10]) at 6 and 12 months and overall survival when compared to medical therapy alone [11, 12]. Current suggested criteria to perform a DHC include age less than 60, stroke territory

involving more than half the MCA territory, or DWI infarct volume greater than 145 cm³ on MRI and ability to proceed to surgery within 48 h. In select patients with late swelling and delayed intracranial hypertension, operative timing may be further delayed. Since the publishing of these three large trials placed decompressive hemicraniectomy in the treatment armamentarium, there has been a smaller trial randomizing patients with malignant MCA strokes to undergo DHC versus medical therapy alone [6].

All similar trials found an overall mortality benefit, but some found a greater proportion of survivors with substantial disability (mRS 4 or above) where the patient was unable to walk and was dependent on others for assistance with basic bodily needs [6]. This has led to the ethical controversy of DHC as the only proven lifesaving intervention for this group of devastating strokes but resulting in poor quality of life in survivors. Thus, a discussion with the patient and/or family must be conducted when DHC is considered in these cases and decisions to perform DHC must be made on a case-by-case basis.

Basilar Strokes

Approximately 20% of ischemic strokes occur in the posterior circulation [3]. Those involving a complete occlusion of the basilar artery bear a considerable potential for a devastating outcomes. The infamous locked-in syndrome that is characterized by quadriplegia, anarthria, and preserved consciousness and perhaps preserved vertical eye movements is the result of pontine pyramidal tract ischemia from a basilar artery occlusion. If the infarct extends to include the medullary centers, respiratory drive and vasomotor control may be compromised. The majority of basilar strokes are caused by local thrombosis or artery to artery thromboembolism with other etiologies such as cardiac emboli or vertebral artery dissections also possible [3]. If left untreated, basilar artery occlusion results in fatality rates up to 90% [3]. When a basilar artery occlusion is suspected, imaging studies should include vessel imaging in the form of a MRA, CTA, or DSA.

In consultation with a stroke neurologist and interventional neuroradiologist, treatment should be administered immediately with antithrombotic and thrombolytic agents. There is considerable data supporting the use of intra-arterial thrombolysis [13]. Like other strokes, outcomes in patients suffering from a basilar artery occlusion depend on time to treatment (the earlier the better) with other factors such as presenting clinical symptoms and degree of recanalization playing an important role as well [3]. The route of administration of thrombolytics, intravenous versus intra-arterial, does not appear to have significant influence over patient outcome [3]. The chance of recanalization has been shown to be slightly higher after intra-arterial



Fig. 6.1 Non-contrast head CT of a malignant left middle cerebral artery (MCA) ischemic infarction. There is a hypodensity in a large portion of the MCA territory with loss of sulci on the left hemisphere, mass effect on the left lateral ventricle, and left to right midline shift

thrombolysis, and centers that have interventional neuro-radiology capabilities should attempt this treatment modality if possible [3]. However, delay in treatment has been clearly shown to result in patient harm and intravenous thrombolysis should be given if intra-arterial intervention is not available [1, 3].

Cerebellar Stroke

Cerebellar strokes can be deceptively perilous. A small- or moderate-sized stroke in the supratentorium is not usually life threatening, but a similar-sized stroke may be fatal in the cerebellum. The first question to be asked is if there is mass effect or not. If there is no mass effect, the stroke may be observed. If mass effect is suspected, an emergent neurosurgical consultation must be obtained. If there is obstructive hydrocephalus due to compression of the fourth ventricle or neurological deterioration due to brainstem compression, it is recommended to proceed with placement of a ventriculostomy and potentially an urgent suboccipital decompressive craniectomy with durotomy [12]. In the case of a patient without brainstem neurological deficits, hydrocephalus, or radiographic mass effect, close observation may be sufficient. It is reasonable to obtain serial CT scans to monitor for increasing edema, especially in patients with poor baseline mental status. If edema is increasing over a period of 3–5 days, one may consider prophylactic decompressive surgery. One may consider that involvement of the cerebellar vermis is particularly associated with increased risk of neurological deterioration and should lower the threshold for surgical intervention.

Cerebral Venous Thrombosis

Cerebral venous thrombosis (CVT) fortunately accounts for a small percentage of strokes, between 0.5 and 1% [2, 13]. Young women are the population most at risk. Multiple other risk factors for CVT have been identified including prior inflammatory diseases (inflammatory bowel disease), pregnancy, dehydration, infection, use of oral contraceptives or substances of abuse, recent surgery, recent trauma, or prothrombotic inherited conditions (e.g., antithrombin III, protein C, and protein S deficiency) [2, 13].

There is no uniform presentation of CVT. Clinical presenting features will vary depending on several factors including thrombosis location, presence of parenchymal involvement, and time elapsed between symptom onset and hospital admission [2, 13]. Headache is the most common symptom, present in up to 89% of patients [2]. Patients may also suffer focal neurological signs and symptoms depending on CVT location, including but not limited to motor weak-

ness, seizures, papilloedema, and sensory and visual deficits. Other factors that should lead to investigation for a CVT include a stroke without known risk factors, hemorrhagic strokes outside typical vascular distribution, unexplained intracranial hypertension, and ophthalmological symptoms in a patient with recent sinusitis [2].

Once CVT is suspected, a complete blood count, chemistry panel, prothrombin time, and activated partial thromboplastin time should be obtained. A normal D-dimer level may be helpful to identify patients with a low probability of CVT, but a normal level in the setting of a strong clinical suspicion should not preclude further investigation as up to 10% of patients with CVT have a normal D-dimer [2, 13]. In the initial evaluation of patients with possible CVT, plain CT or MRI is useful but does not rule out CVT. A venographic study, either CTV or MRV, should be obtained in conjunction with the plain films to ultimately make the diagnosis of CVT [13].

Once the diagnosis is made, anticoagulation with either IV heparin infusion or subcutaneous low-molecular-weight heparin must be initiated if there are no major contraindications; ICH secondary to CVT is not a contraindication [2, 13]. The patient will then proceed with a vitamin K antagonist for 3–12 months with a target INR of 2–3. In patients with persistent or evolving symptoms despite medical treatment or with symptoms suggestive of thrombus propagation, a follow-up CTV or MRV is recommended [13]. If repeat imaging reveals no or mild mass effect, one may consider endovascular therapy, with or without mechanical disruption. If there is severe mass effect or ICH on repeat imaging, one may consider decompressive hemicraniectomy as a life-saving procedure [13].

The routine use of prophylactic antiepileptic drugs is not recommended; however, even a single seizure with or without parenchymal involvement warrants immediate administration of antiepileptic medications [13]. In patients with evidence of increased intracranial pressure, one may consider treatment with acetazolamide. If there is any concern for visual loss, optic nerve decompression or CSF shunting may be effective and should be considered [13]. Steroid medications have not been found to be beneficial and are not recommended [13].

Primary Intracerebral Hemorrhage

Intracerebral hemorrhage (ICH) is a devastating injury most commonly related to uncontrolled hypertension. Despite aggressive medical intervention, close to one third of patients with ICH will die and only 20% will return to functional independence [14]. ICH often occurs in the deep structures of the brain with the basal ganglia (putamen) being the most affected, followed by the thalamus,

brainstem (pons), and cerebellum [14]. The second most common cause in the elderly population is cerebral amyloid angiopathy which causes cerebral bleeds that are mostly superficial and lobar [14]. Other less common but potential causes include systemic anticoagulation, hemorrhagic conversion of an ischemic stroke, vascular malformations, trauma, cerebral venous sinus thrombosis, vasculitis, and intracranial tumors [14].

Like other stroke subtypes, the presentation of ICH will depend on location. Typically there will be a sudden onset of a focal neurologic deficit, often with headache, nausea, vomiting, decreased level of consciousness, and elevated blood pressure [14]. Diagnosis of ICH is relatively straightforward with plain head CT being the preferred diagnostic method for its ease, availability, and accuracy [14]. If a secondary ICH is suspected (young age, no known hypertension or recent trauma, or prominent vascular structures), CT or MR angiography is recommended.

Initial management of ICH should focus on assessing the patient's airway and breathing. Any signs of impending respiratory failure should prompt intubation (aspiration risk, PaO₂ <60 mmHg, or pCO₂ >50 mmHg) [14]. Any evidence of elevated intracranial pressure should prompt immediate measures to control ICP. ICP management will be discussed in further detail in other sections but include elevating the head of bed to 30° or more, maintaining normocapnia to hypocapnia (pCO₂ 30–35) and in some cases hyperosmolar therapy (although this may be controversial in setting of acute hemorrhage and should be discussed with expert consultation) [14]. These measures will quickly lower ICP, albeit temporarily. Immediate neurosurgical consultation should be obtained for a definite procedure such as craniotomy, ventriculostomy, or placement of an ICP monitor [14]. Many ICH patients suffer falls prior to presentation, and their cervical spine should be carefully stabilized until any fracture or ligamentous injury is excluded [14].

The optimum blood pressure in this population is still being elucidated. Several studies have shown the safety of acutely lowering blood pressure in ICH in contrast to ischemic strokes where the blood pressure is purposefully allowed to remain elevated [14, 15]. The INTERACT II trial showed the safety of acutely lowering blood pressure to less than 140 mmHg systolic. However, the trial did not show a difference in mortality, major safety events, or hematoma expansion in patients who had aggressive blood pressure control (less than 140 mmHg vs. less than 180 mmHg) [15]. As of the publishing of this textbook, the ATACH II trial is still enrolling patients, attempting to answer the question of optimal blood pressure in the ICH population. For now, it is recommended to maintain systolic blood pressure less than 180 mmHg and, if safe and reasonable, less than 140 mmHg [14–16].

Aneurysmal Subarachnoid Hemorrhage

The most common etiology of subarachnoid hemorrhage (SAH) is traumatic injury. However, nontraumatic SAH contributes a large proportion of the mortality and morbidity from SAH [16]. Of all the nontraumatic causes of SAH, aneurysm rupture is the most common and best studied. There is considerable variation in annual incidence of aneurysmal subarachnoid hemorrhage (aSAH) between different regions of the world and even within the same country. In the United States, aSAH incidence ranges from 6 to 16 cases per 100,000 population, with approximately 30,000 episodes occurring each year [16]. The 2003 Nationwide Inpatient Sample provided an annual estimate of 14.5 patient discharges categorized as aSAH per 100,000 adults [16]. Risk factors for aSAH vary significantly depending on age, gender, and country of origin, with men and the young less likely to be affected. The reported incidence of aSAH is highest in Finland (19.7 per 100,000 person-years) and Japan (22.7 per 100,000 person-years) but lowest in South and Central America (4.2 per 100,000) [17]. Other risk factors include hypertension, history of tobacco use, alcohol abuse, use of sympathomimetic drugs (i.e., cocaine), history of previous aSAH, and family history of familial aneurysms or associated genetic syndromes. Patients suffering from an aSAH may present with diverse clinical manifestations ranging from an isolated simple headache to a comatose state. Other common presenting symptoms include nausea/vomiting, loss of consciousness, and nuchal rigidity. The patient may also demonstrate focal neurologic deficits in the setting of microemboli from the aneurysm itself or in the event of an aneurysm rupture. The initial clinical severity of the aSAH should be determined rapidly by using the Hunt and Hess or World Federation of Neurological Surgeons scales [16]. The risk of vasospasm sequela should also be determined using the Rankin or the modified Rankin scale.

Once an aSAH is suspected, a head CT must be obtained immediately. If the head CT does not demonstrate any hemorrhage, a lumbar puncture is then performed. If both are negative for hemorrhage, the evaluation is complete. If subarachnoid blood is confirmed, then vessel imaging is obtained as next step. Digital subtraction angiography with three-dimensional rotational imaging is most useful; however, a CT angiogram of the head and neck may also be utilized initially in certain cases. MRI may also be used if the head CT scan is nondiagnostic. The fluid-attenuated inversion recovery (FLAIR) sequence is the most sensitive MRI sequence for detection of SAH [17, 19].

After diagnosis of aSAH and identification of the culprit aneurysm, one must expeditiously address the high risk for aneurysmal re-rupture by securing the aneurysm as soon as possible, either via surgical clipping or endovascular coiling. Subsequent re-bleeding is associated with very poor

outcome. There are inherent delays to both surgical (operating room availability) and interventional radiological (summon the radiological team in house) securing of cerebral aneurysms, and during this time, it is essential to narrowly control the patient's blood pressure. While there is no known optimal blood pressure target, it is recommended to aim for a goal systolic pressure less than 160 mmHg although some centers advocate less than 140 mmHg [16]. A titratable continuous infusion agent (i.e., nicardipine) should be used to balance the risk of hypertension related re-bleeding and decreased cerebral perfusion pressure (from excessive blood pressure lowering). In patients with unavoidable extended delays, they may be considered for short-term (less than 72 h) therapy with tranexamic acid or aminocaproic acid to reduce the risk of early aneurysmal re-bleeding [16, 18]. The feared complications of these two therapies are thromboembolic events (i.e., acute myocardial infarction or acute pulmonary embolism). To be considered for this therapy, the patient should be deemed at significant risk of re-bleeding and must not have compelling medical contraindications [16].

Definitive management of aSAH is securing of the aneurysm with minimal delay. When the ruptured aneurysm is technically amenable to both endovascular coiling and neurosurgical clipping, endovascular coiling is preferred [16]. However, certain aneurysms possess a morphology (neck to dome ratio) and location, whereby they may be better suited for surgical clipping. Further, the choice of available treatment modality may vary between institutions as it also depends on the experience of the staff. In the ISAT [19] randomized controlled trial, both treatment methods were compared in cases suitable for either treatment modality and demonstrated that the endovascular arm fared better overall [16]. Compared to the microsurgery, the endovascular arm resulted in a decreased mortality and disability at 1 year and a lower incidence of epilepsy and cognitive decline. The risk of late re-bleeding, however, was lower in the microsurgery arm with a higher rate of complete aneurysm obliteration [16]. Typically, patients require post-procedural vascular imaging after the aneurysm has been secured by either method. If complete obliteration of the aneurysm is not seen, it is recommended to proceed with repeat coiling or microsurgical clipping [16].

In the post-procedural period, certain basic interventions should be routine in all SAH patients. These measures include maintaining strict normothermia and euolemia to help prevent delayed cerebral ischemia (DCI) [16]. Careful glucose management with strict avoidance of hypoglycemia should be maintained in all cases and nimodipine should be administered for 21 days (60 mg every 4 h). Nimodipine has been shown to consistently provide a small benefit in morbidity and mortality and is the only class 1 evidence-supported recommendation [16]. If hypotension results,

reduced nimodipine administration of 30 mg every 2 h may be considered. Nimodipine has been shown to reduce vasospasm but the exact mechanism of its effect has yet to be elucidated.

Other secondary complications may also occur after aSAH bleeds, both neurological and systemic. Delayed cerebral ischemia, acute symptomatic hydrocephalus, and cerebral vasospasm are most common. Patients should be monitored closely for DCI in an ICU setting by regular hourly neurological exams. Also, transcranial Doppler (TCD) should be performed searching for elevated velocities but more importantly, elevated Lindegaard ratios which are suggestive of vasospasm and risk of subsequent ischemia [16]. Continuous electroencephalography (EEG) should also be used to follow the alpha variability (AV) as poor AV trends may indicate relative ischemia in the affected area. The traditional "triple H" therapy of hypervolemia, hemodilution, and hypertension is no longer recommended [16]. Some evidence suggests that hypervolemia may lead to increased morbidity from fluid overload leading to recommendations of maintaining euolemia only [16]. Unless baseline hypertension, with evidence of DCI, it is recommended to induce hypertension, ideally to a blood pressure goal resulting in improvement of neurological deficits [16]. In the setting of anemia, packed red blood cell transfusion may be used for this goal though the optimal hemoglobin level has yet to be determined [16]. In patients who fail to respond to hypertensive therapy, it is reasonable to consider intra-arterial vasodilator therapy [16].

Acute hydrocephalus occurs in 15–87% of patients with aSAH, and chronic shunt-dependent hydrocephalus develops in 8.9–48% of patients [16]. Both conditions should be treated by CSF diversion, usually via an external ventricular catheter (EVD) or less commonly, via a lumbar drain. Again, neurosurgical consultation is often helpful in this setting to place and manage EVDs. Three retrospective case series have examined aneurysmal re-bleeding with EVD placement, one of which found a greater re-bleeding risk with EVD placement [16, 20, 21]. Daily EVD outputs should be measured and help determine a weaning strategy. Rapid (<24 h) weaning of the EVD does not appear to reduce the incidence of shunt-dependent hydrocephalus [16]. If the patient cannot be weaned from the EVD over 1–2 weeks, a permanent shunt, usually in the form of a ventriculoperitoneal shunt must be placed.

Seizures occurring after aSAH have been discussed at length and remain a topic of controversy. Almost one in four patients experience seizure-like episodes after aSAH but it is unclear whether these are actually epileptic in origin [16]. No randomized, controlled trials exist evaluating the existence and management of seizures associated with aSAH and as such, any potential benefit of routine anticonvulsant use in aSAH must be weighed against potential risks. One large,

single-center study found adverse reactions in 23% of patients taking anticonvulsants [16]. Another single-center retrospective study found prophylactic phenytoin to be independently associated with worsened cognitive outcome at 3 months after aSAH [16]. It is generally accepted to use prophylactic anticonvulsants in the immediate post-bleed period (typically for 7 days) [16], but the routine long-term use of anticonvulsant therapy is not recommended unless the patient is specifically at increased risk due to a history of prior seizure, an intracerebral hematoma, intractable hypertension, cerebral infarction, or middle cerebral artery aneurysm [16].

Aneurysmal SAH may also have non-neurological complications affecting multiple organ systems. Both hyponatremia and hypernatremia occur in 10–30% of the acute phase after aSAH [16]. Hyponatremia has been associated with development of both sonographic and clinical vasospasm [16], and therefore ICU providers should strive for correction of serum sodium levels in these patients employing agents such as fludrocortisone acetate and hypertonic saline [16]. All patients should have a euvolemic volume status which may be achieved with crystalloid or colloid administration. Using hypotonic fluids is not recommended, particularly in those with signs of intravascular volume contraction [16]. Several animal studies and human case series have shown an association between elevated blood glucose concentration and poor outcome after ischemic brain injury [16]. The mechanism for this effect is unclear but may be associated with promoting brain energy metabolic crisis and lactate-pyruvate ratio elevation. Anemia is common after aSAH and especially those patients at risk for vasospasm may be at risk for compromised brain oxygen delivery.

No optimal hemoglobin goal in aSAH has been established as of the publication of this textbook. While some series have shown worse outcomes with red blood cell transfusions after aSAH [16], other prospective registries and a recent prospective randomized trial have shown the safety and feasibility of maintaining a higher hemoglobin level [16]. Subarachnoid bleeding may also impart a significant risk of developing venous thrombotic events (VTE) such as deep vein thrombosis (DVT) and, also, independently is associated with a high risk (5%) of heparin-induced thrombocytopenia (HIT) [16]. The risk of developing HIT after aSAH is directly related to the number of angiographic procedures performed but not the use of heparin for DVT prophylaxis [16]. While there is no pragmatic way to prevent either DVT or HIT, it is important to have a raised index of suspicion and make a timely diagnosis when this is suspected. This will allow timely anticoagulation under the guidance of a hematologist.

After hospital discharge, aSAH patients should be referred for comprehensive psychological evaluation including cognitive, behavioral, and psychosocial assessments.

Hypoxic and Anoxic Brain Injury

Anoxic and hypoxic brain injury secondary to cardiac arrest is a devastating condition and outcomes are often poor despite aggressive care. Unlike stroke, cardiac arrest leads to a transient global loss of cerebral perfusion followed by a period of global hypoperfusion during CPR [22]. This period without return of spontaneous circulation (ROSC) causes cessation of cerebral ATP production, which leads to failure of the ATP-dependent sodium-potassium pumps on the neuronal membrane [22]. In turn, this disrupts the blood-brain barrier and leads to intracellular acidosis and neuronal edema [22]. Additionally, other mechanisms have been proposed including glutamate-mediated excitotoxicity, increased intracellular calcium, microthrombi formation in cerebral vasculature from the temporary stasis, and endothelial ischemic injury [22].

After ROSC, cerebral perfusion is restored, but cerebral autoregulation is lost. This results in regional and temporal disparities in cerebral perfusion with some cerebral territories being hypoperfused and others relatively hyperperfused [22]. Both conditions can cause distinct detriments to the patient with hypoperfusion promoting ongoing ischemic neuronal death whereas hyperperfusion causing edema and potentially progression to secondary injury [22].

Cardiac arrest and post-resuscitation care requires a multidisciplinary team. As recommended by the American Heart Association (AHA), early securing of the airway in patients with poor airway protective reflexes should be conducted, and the head of bed should be elevated by 30° to reduce the impact of cerebral edema [22]. Whether on a ventilator or receiving supplemental oxygen, the AHA further recommends titrating oxygen therapy to a goal saturation of greater than or equal to 94% while maintaining adequate ventilation to a PaCO₂ of 40–45 mm [22]. The AHA further recommends a target systolic blood pressure of greater than 90 mmHg and mean arterial pressure greater than or equal to 65 mmHg [22]. Furthermore, they recommend against overly tight glycemic control out of concerns for worsening neuronal metabolism, instead suggesting a goal level between 144 and 180 mg/dL (8–10 mmol/L) [22].

Since the early to mid-1990s, induced hypothermia (IH) has been utilized in the post-arrest setting. While important trials have suggested improvements in cognitive recovery following post-arrest IH, one recent clinical trial failed to show any benefit of hypothermia over maintenance of normothermia [22]. The principle behind hypothermia as a neuroprotective therapy after brain anoxia is to decrease cerebral metabolic rate leading to reduced ATP consumption, improve glucose metabolism, and decrease acidosis [22, 23]. Animal models have shown reduction in glutamate toxicity leading to decreased activity of downstream apoptotic pathways that contribute to neuronal injury. Other proposed effects of

hypothermia include inhibition of reactive oxygen species (ROS) production during reperfusion, associated with inhibited NF- κ B expression and reduced inflammatory cell infiltration [22].

Two clinical studies published in 2002 are of prime importance in suggesting a neuroprotective effect in hypothermia in the post-cardiac arrest setting [24, 25]. Specifically, the *Hypothermia After Cardiac Arrest* (HACA) study group randomized cardiac arrest survivors to maintenance of hypothermia (32–34° C) versus standard therapy and utilized cerebral performance categories to define favorable outcomes. Fifty-five percent of patients in the hypothermia group had a favorable outcome versus 39% in the standard treatment group. Additionally, mortality rate was 25% lower in the hypothermia group [26]. More than a decade later, after widespread adoption of hypothermia in this patient population, a multinational randomized trial tested the benefit of hypothermia by randomizing patients to hypothermia (33 °C) or euthermia (36 °C) in 36 Australian and European ICUs [25]. The mortality and incidence of poor outcomes were similar in both groups suggesting a benefit of preventing hyperthermia as being, perhaps, more important than inducing hypothermia.

Induction of hypothermia or maintenance of normothermia will require advanced neuromonitoring in the ICU and may be done using different cooling strategies. These include surface blankets and ice; administration of intravenous, intracystic, intrathoracic, or intragastric cold fluids; inhaled ventilator gases; and even venovenous bypass circulation cooling. In all cases this may lead to shivering which may increase cerebral metabolic rate and must be controlled. Several approaches may be used to control shivering including surface counterwarming, sedation (i.e., propofol), neuromuscular blockade, magnesium infusion, buspirone, and use of dexmedetomidine. While sedatives and paralytics work very effectively, they may obscure key physical signs indicative of neurological worsening or progression to brain death.

CNS Infections

Intracranial infections include a vast spectrum of conditions, each with different causative organisms producing unique clinical characteristics. They may progress rapidly and resulting in significant morbidity and mortality if appropriate interventions are not initiated promptly [27]. Patients will commonly present with altered mental status, seizures, focal weakness, or cranial nerve palsies. A head CT scan is frequently the first imaging modality obtained to assess for the presence of hydrocephalus, mass lesions, hemorrhage, or acute brain edema and is often performed prior to lumbar puncture. An MRI may logistically be more challenging to obtain in a critically ill patient but is more sensitive for

cerebral spinal fluid infection, leptomeningitis, empyema, ventriculitis, vasculitis, and infarctions [27], particularly when evaluating T1-weighted and diffusion-weighted (DWI) images. MR spectroscopy may also be useful in certain cases. Consultation with a neuroradiologist and neurosurgeon is advised when intracranial infections are suspected.

Acute Bacterial Meningitis

Meningitis, or inflammation of the meninges, is one of the most serious and morbid of all intracranial infections. One must have a high index of suspicion, perform a rapid diagnosis, and initiate treatment expeditiously to prevent severe sequelae and death. Classically, meningitis will be suspected in patient with headache, nuchal rigidity, and subsequent mental status changes. Once suspected, CSF and blood cultures should be obtained and CSF microscopy should reveal elevated white blood cells and hypoglycorrhea. Early empiric intravenous antibiotic initiation is paramount and should be effective against *S. pneumoniae*, *N. meningitidis*, and *S. aureus*.

Early complications of meningitis include hydrocephalus whereby bacterial by-products may obstruct venous sinuses leading to swelling of and hyperemia of the pia and arachnoid matter and interference with CSF drainage. Occasionally an external ventricular drain is necessary to divert CSF and prevent life-threatening herniation from hydrocephalus. Other potential complications of meningitis include brain infarction, ventriculitis, brain empyema, and venous sinus thrombosis; all conditions which may be readily diagnosed with MRI [27].

Acute Encephalitis

Encephalitis is distinguished from meningitis by the presence of abnormal brain function. Though nuchal rigidity is usually absent, patients may present with seizures or focal neurological deficits. One of the most important causative agents of encephalitis is the herpes simplex virus (HSV). As both type 1 and type 2 HSV may produce encephalitis, it is prudent to start antiviral therapy (acyclovir) as soon as viral encephalitis is suspected and to proceed with PCR or viral culture to confirm HSV infection. In these patients, CSF examination will reveal large numbers of red blood cells despite an atraumatic puncture. MRI may also classically demonstrate petechial hemorrhages with a high predilection for the temporal lobes, cingulate gyri, and inferior frontal lobes with a high signal intensity in T2 images [27].

In recent years (after 1999) the West Nile virus (WNV) has become a more common causative infection in acute encephalitis and is most often acquired from mosquitoes.

The incubation period for WNV ranges from 3 to 14 days and approximately 1 in 150 people infected with WNV will develop meningoencephalitis, with the immunocompromised, elderly, and very young at the highest risk [27]. The presenting symptoms are as for other meningitis patients (altered mental status, headache, nuchal rigidity) with the added unique feature of flaccid paralysis (from anterior horn cell disease). The MRI of WNV-infected patients is generally normal, but in some cases, an increased T2 signal has been seen in the lobar area, cerebellum, basal ganglia, and thalamus [27].

While uncommon in the United States, Lyme disease, caused by the tick-borne spirochete *Borrelia burgdorferi*, may be another causative organism in encephalitis. While the underlying pathophysiology remains poorly understood, neurological complications will occur in 10–15% of patients including cranial nerve palsies and peripheral neuropathies.

Tuberculosis (TB) remains a common and deadly worldwide infection, and central nervous system involvement is a serious manifestation of chronic infection with manifestations ranging from meningitis, intracranial tuberculoma, and spinal tuberculous arachnoiditis [27]. CSF acid fast bacillus microbiology is typically the method of choice for diagnosis, and even with effective treatment, the mortality rate for TB with CNS involvement remains high.

Brain Abscesses

Brain abscesses are focal, intracerebral infections that may occur in various anatomical locations. They begin with a localized area of cerebritis that progresses to a discrete collection of purulent fluid that eventually becomes surrounded by a well-vascularized capsule. The etiology of such infections is usually hematogenous seeding from other sources but in some cases may also occur from local spread from infected sinuses, otic or odontogenic sources [27]. Most commonly the culprit organisms are *Staphylococcus* and *Streptococcus* species. In patients with hematogenous dissemination, presenting as a brain abscess, careful evaluation must rule out endocarditis, cardiac shunts, and pulmonary vascular malformations. Cerebral imaging features of an abscess depend on the progression of the infection (pre- or post-capsule formation, etc.). Brain epidural abscesses are usually caused by a contiguous spread of infection from adjacent structures, such as mastoids or paranasal sinuses [27].

Malignant Brain Tumors

Malignant brain tumors will typically present with some type of herniation syndrome (which specific one will depend on location) or present with nonspecific signs and symptoms

of globally elevated ICP. If suspected, a head CT is the initial diagnostic test of choice. Immediate medical interventions are directed toward lowering the patient's elevated ICP and in this regard mimic the management of other conditions with elevated ICP (see prior section). Specifically for brain tumors, an immediate bolus of 10–20 mg IV dexamethasone, followed by a maintenance dose of 8–32 mg/day should be administered. Glucocorticoids reduce cerebral swelling by decreasing the permeability of the cerebral capillaries [28]. The routine use of seizure prophylaxis is not recommended [28]. A patient with concern for increased ICP and a GCS of less than 8 should be considered for an ICP monitor as in patients with any other mass lesion [29].

The next and definitive step is resection of the tumor (not every tumor will be amenable to surgical intervention). Neurosurgical consultation should be obtained expeditiously. Typically, once the patient is stabilized, an MRI with and without gadolinium enhancement is obtained for potential surgical planning. Postoperative care should be delivered in conjunction with consultation of intensive care, oncology, and neurosurgical services.

Conclusion

Many of the acute, nontraumatic neurological conditions encountered in critically ill patients ICU can be successfully managed using fundamental critical care techniques in combination with expert neurologist consultation. With an awareness of the basic nuances of specific neurological diseases, proper collaborative care can be delivered to these patients in a timely fashion.

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