Review Article

Medical Progress

Spontaneous Intracerebral Hemorrhage

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NONTRAUMATIC intracerebral hemorrhage is bleeding into the parenchyma of the brain that may extend into the ventricles and, in rare cases, the subarachnoid space. Each year, approximately 37,000 to 52,400 people in the United States have an intracerebral hemorrhage.[1,2] This rate is expected to double during the next 50 years as a result of the increasing age of the population and changes in racial demographics. Intracerebral hemorrhage accounts for 10 to 15 percent of all cases of stroke and is associated with the highest mortality rate, with only 38 percent of affected patients surviving the first year.[3] Depending on the underlying cause of bleeding, intracerebral hemorrhage is classified as either primary or secondary. Primary intracerebral hemorrhage, accounting for 78 to 88 percent of cases, originates from the spontaneous rupture of small vessels damaged by chronic hypertension or amyloid angiopathy.[4] Secondary intracerebral hemorrhage occurs in a minority of patients in association with vascular abnormalities (such as arteriovenous malformations and aneurysms), tumors, or impaired coagulation. Although hypertensive intracerebral hemorrhage remains the most common form of intracerebral hemorrhage, underlying vascular abnormalities should always be considered in appropriate circumstances because of the high risk of recurrent hemorrhage and available treatment options.[5-11] The causes of intracerebral hemorrhage are shown in Table 1. We will discuss primary, or spontaneous, intracerebral hemorrhage in this review.

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EPIDEMIOLOGIC FEATURES

Incidence

The worldwide incidence of intracerebral hemorrhage ranges from 10 to 20 cases per 100,000 population[12,13] and increases with age.[12,14] Intracerebral hemorrhage is more common in men than women, particularly those older than 55 years of age,[14,15] and in certain populations, including blacks and Japanese.[12,16] During the 20-year period covered by the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, the incidence of intracerebral hemorrhage among blacks was 50 per 100,000 — twice the incidence among whites.[17] Differences in the prevalence of hypertension and the level of educational attainment correlated with the difference in risk. The increased risk associated with lower levels of education was probably related to the lack of awareness of primary prevention and access to health care.[17] The incidence of intracerebral hemorrhage in the Japanese population (55 per 100,000) is similar to that among blacks.[16] A high prevalence of hypertension and alcohol use in the Japanese population may account for the incidence.[18] Low serum cholesterol levels observed in this population may also increase the risk of intracerebral hemorrhage.[19]

Risk Factors

Hypertension is the most important risk factor for spontaneous intracerebral hemorrhage.[20] Hypertension increases the risk of intracerebral hemorrhage, particularly in persons who are not compliant with antihypertensive medication, are 55 years of age or younger, or are smokers.[21,22] Improved control of hypertension appears to reduce the incidence of intracerebral hemorrhage.[13] In the Hypertension Detection and Follow-up Program, persons with hypertension (defined as a diastolic blood pressure of at least 95 mm Hg) who were 30 to 69 years of age and who received standardized antihypertensive therapy had a risk of stroke (including intracerebral hemorrhage) of 1.9 per 100 persons, as compared with a risk of 2.9 per 100 persons in those who received routine community care.[23] This approach was associated with an absolute reduction in risk of 46 percent in persons who were 65 years of age or older. In the Systolic Hypertension in the Elderly Program, the five-year incidence of all strokes, including intracerebral hemorrhage, in patients older than 60 years who had a systolic blood pressure of at least 160 mm Hg was 5.2 per 100 with antihypertensive treatment and 8.2 per 100 with placebo treatment.[24]

Excessive use of alcohol also increases the risk of

TABLE 1. CAUSES, MEANS OF DIAGNOSIS, AND CHARACTERISTICS OF INTRACEREBRAL HEMORRHAGES.

CAUSES	PRIMARY MEANS OF DIAGNOSIS	CHARACTERISTICS
Hypertension	Clinical history*	Rupture of small arterioles related to degenerative changes induced by uncontrolled hypertension; the annual risk of recurrent hemorrhage of 2 percent[5] can be reduced by treatment of hypertension
Amyloid angiopathy	Clinical history*	Rupture of small and medium-sized arteries, with deposition of β-amyloid protein; presents as lobar hemorrhages in persons older than 70 years of age; annual risk of recurrent hemorrhage of 10.5 percent[6]
Arteriovenous malformation	Imaging studies such as magnetic resonance imaging and conventional angiography	Rupture of abnormal small vessels connecting arteries and veins; the annual risk of recurrent hemorrhage of 18 percent[7] can be reduced by surgical excision, embolization, and radiosurgery
Intracranial aneurysm	Imaging studies such as magnetic resonance angiography and conventional angiography	Rupture of saccular dilatation from a medium-sized artery that is usually associated with subarachnoid hemorrhage; risk of recurrent hemorrhage of 50 percent within the first 6 months, which decreases to 3 percent per year[8]; surgical clipping or placement of endovascular coils can significantly reduce the risk of recurrent hemorrhage
Cavernous angioma	Imaging studies such as magnetic resonance imaging	Rupture of abnormal capillary-like vessels with intermingled connective tissue; annual risk of recurrent hemorrhage of 4.5 percent[9] can be reduced by surgical excision or radiosurgery
Venous angioma	Imaging studies such as magnetic resonance imaging and conventional angiography	Rupture of abnormal dilatation of venules; very low annual risk of recurrent hemorrhage (0.15%)[10]
Dural venous sinus thrombosis	Imaging studies such as magnetic resonance venography and conventional angiography	Result of hemorrhagic venous infarction; anticoagulation and, in rare cases, transvenous thrombolytic agents can improve outcome; risk of recurrent dural venous thrombosis of 10 percent within first 12 months and of less than 1 percent thereafter[11]
Intracranial neoplasm	Imaging studies such as magnetic resonance imaging	Results of necrosis and bleeding within hypervascular neoplasms; long-term outcome determined by the characteristics of the underlying neoplasm
Coagulopathy	Clinical history*	Most commonly associated with use of anticoagulants or thrombolytic agents; rapid correction of underlying abnormality important to avert continued bleeding
Vasculitis	Measurement of serologic and cerebrospinal fluid markers; brain biopsy	Rupture of small or medium-sized arteries with inflammation and degeneration; immunosuppressive medications may be indicated
Cocaine or alcohol use	Clinical history*	Underlying vascular abnormalities may be present
Hemorrhagic ischemic stroke	Imaging studies such as magnetic resonance imaging and conventional angiography	Hemorrhage in region of cerebral infarction as a result of ischemic damage to blood–brain barrier

*Imaging studies such as magnetic resonance imaging and conventional angiography can provide supportive evidence.

intracerebral hemorrhage by impairing coagulation and directly affecting the integrity of cerebral vessels.[25,26] Other less well established risk factors include serum cholesterol levels of less than 160 mg per deciliter (4.1 mmol per liter), particularly among patients with hypertension, and genetic factors such as mutations in genes encoding the α subunit of factor XIII (which is involved in the formation of cross-linked fibrin).[27-29] Cerebral amyloid angiopathy, which is characterized by the deposition of β-amyloid protein in the blood vessels of the cerebral cortex and leptomeninges, is another risk factor for intracerebral hemorrhage, particularly in elderly persons (Fig. 1). O'Donnell et al.[6] reported that the presence of the *ε2* and *ε4* alleles of the apolipoprotein E gene was associated with a tripling of the risk of recurrent hemorrhage among survivors of lobar intracerebral hemorrhage related to amyloid angiopathy. These alleles are associated with increased deposition of β-amyloid protein and degenerative changes (such as fibrinoid necrosis) in the vessel wall, respectively. The expression of either allele appears to increase the risk of intracerebral hemorrhage by augmenting the vasculopathic effects of amyloid deposition in cerebral vessels.

PATHOPHYSIOLOGICAL FEATURES

Pathologic Process

Intracerebral hemorrhages commonly occur in the cerebral lobes, basal ganglia, thalamus, brain stem (predominantly the pons), and cerebellum (Fig. 2).[30] Extension into the ventricles occurs in association with deep, large hematomas. Edematous parenchyma, often discolored by degradation products of hemoglobin, is visible adjacent to the clot.[31] Histologic sections are characterized by the presence of edema, neuronal damage, macrophages, and neutrophils in the region surrounding the hematoma. The hemorrhage spreads between planes of white-matter cleavage with minimal destruction, leaving nests of intact neural tissue within and surrounding the hematoma.[30,31] This pattern of spread accounts for the presence of viable and salvageable neural tissue in the immediate vicinity of the hematoma.

Origin of Hematoma

Intraparenchymal bleeding results from the rupture of the small penetrating arteries that originate from basilar arteries or the anterior, middle, or posterior

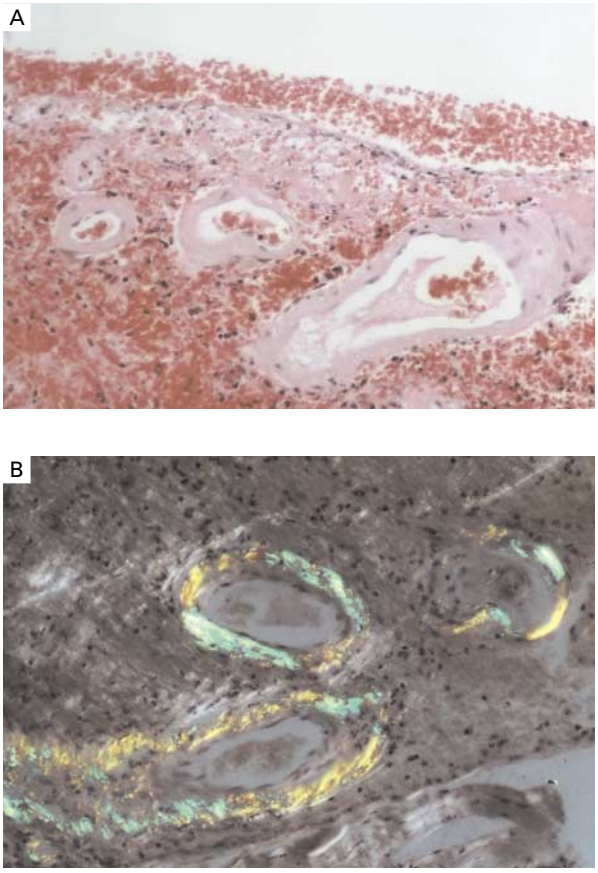

Figure 1. Surgical Specimens from the Matrix of a Hematoma Associated with Amyloid Angiopathy.

Panel A shows deposits of amyloid, an acellular eosinophilic material, within the vessel wall (hematoxylin and eosin, ×100). In Panel B, after staining with Congo red, the amyloid material within the vessel wall exhibits apple-green birefringence under polarized light (Congo red, ×100). Photomicrographs provided by Dr. Peter T. Ostrow, Department of Pathology, State University of New York, Buffalo.

cerebral arteries. Degenerative changes in the vessel wall induced by chronic hypertension reduce compliance and increase the likelihood of spontaneous rupture. In 1868, Charcot and Bouchard attributed bleeding to rupture at points of dilatation in the walls of small arterioles (microaneurysms).[32-34] These morphologic entities were later found to be subadventitial hemorrhages or extravascular clots resulting from endothelial damage by the hematoma.[34] Electron-microscopical studies suggest that most bleeding occurs at or near the bifurcation of affected arteries, where prominent degeneration of the media and smooth muscles can be seen.[32]

Progression of Hematoma

Initially, intracerebral hemorrhage was considered to be a monophasic event that stopped quickly as a result of clotting and tamponade by the surrounding regions. This impression is incorrect, as demonstrated by computed tomographic (CT) scans showing that hematomas expand over time (Fig. 3).[35,36] In a study of 103 patients, Brott et al.[35] found that the hematoma expanded in 26 percent of the patients within 1 hour after the initial CT scan and in another 12 percent within 20 hours. Kazui et al.[36] reported that the hematoma expanded in 41 of 204 patients (20 percent) with intracerebral hemorrhage, occurring in 36 percent of patients who presented within three hours after the onset of the hemorrhage and in 11 percent of those who presented more than three hours after the onset. This expansion has been attributed to continued bleeding from the primary source and to the mechanical disruption of surrounding vessels. Acute hypertension, a local coagulation deficit, or both[37] may be associated with expansion of the hematoma.[38,39]

Secondary Neuronal Injury after Intracerebral Hemorrhage

The presence of hematoma initiates edema and neuronal damage in surrounding parenchyma. Fluid begins to collect immediately in the region around the hematoma, and edema usually persists for up to five days,[40] although it has been observed for as long as two weeks after a stroke.[41] Early edema around the hematoma results from the release and accumulation of osmotically active serum proteins from the clot.[42] Vasogenic edema and cytotoxic edema subsequently follow owing to the disruption of the blood–brain barrier, the failure of the sodium pump, and the death of neurons.[43,44]

The delay in the breakdown of the blood–brain barrier and the development of cerebral edema after intracerebral hemorrhage suggest that there may be secondary mediators of both neural injury and edema. It had been thought that cerebral ischemia occurred as a result of mechanical compression in the region surrounding the hematoma,[45,46] but recent studies in animals and humans have not confirmed this.[42,47-49] It is currently thought that blood and plasma products mediate most secondary processes that are initiated after an intracerebral hemorrhage.[50-56] Neuronal death in the region around the hematoma is predominantly necrotic, with recent evidence suggesting the presence of programmed cell death (apoptosis) associated with nuclear factor-κB expression in neural-cell nuclei.[56]

CLINICAL FEATURES

Neurologic Status at Presentation

Patients with a large hematoma usually have a decreased level of consciousness[57] as a result of increased intracranial pressure and the direct compression or distortion of the thalamic and brain-stem reticular activating system.[58] Decreased central benzodiazepine-receptor binding on cortical neurons in the presence of small, deep lesions may also contribute to altered

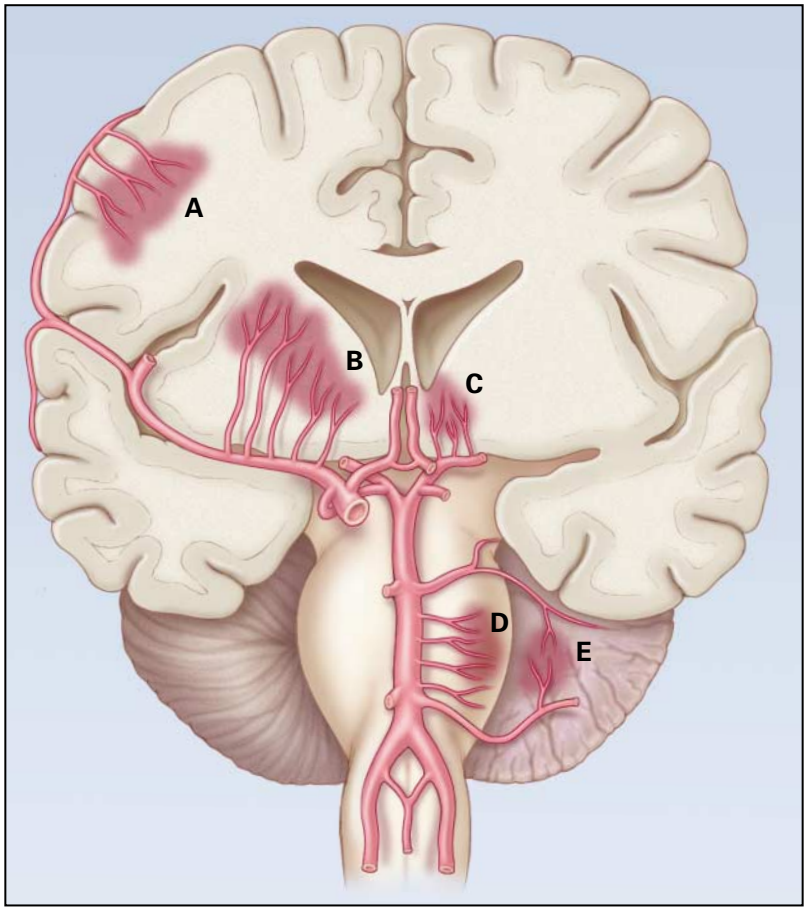

Figure 2. Most Common Sites and Sources of Intracerebral Hemorrhage.

Intracerebral hemorrhages most commonly involve cerebral lobes, originating from penetrating cortical branches of the anterior, middle, or posterior cerebral arteries (A); basal ganglia, originating from ascending lenticulostriate branches of the middle cerebral artery (B); the thalamus, originating from ascending thalmogeniculate branches of the posterior cerebral artery (C); the pons, originating from paramedian branches of the basilar artery (D); and the cerebellum, originating from penetrating branches of the posterior inferior, anterior inferior, or superior cerebellar arteries (E).

consciousness.[59] Patients with a supratentorial intracerebral hemorrhage involving the putamen, caudate, and thalamus have contralateral sensory-motor deficits of varying severity owing to the involvement of the internal capsule. Abnormalities indicating higher-level cortical dysfunction, including aphasia, neglect, gaze deviation, and hemianopia, may occur as a result of the disruption of connecting fibers in the subcortical white matter and functional suppression of overlying cortex, known as diaschisis.[60]

In patients with an infratentorial intracerebral hemorrhage, signs of brain-stem dysfunction include abnormalities of gaze, cranial-nerve abnormalities, and contralateral motor deficits.[61] Ataxia, nystagmus, and dysmetria are prominent when the intracerebral hemorrhage involves the cerebellum.[61] Common nonspecific symptoms include headache and vomiting due to increased intracranial pressure and meningismus resulting from blood in the ventricles.[57,62,63]

Secondary Deterioration

In one fourth of patients with intracerebral hemorrhage who are initially alert, a deterioration in the level of consciousness occurs within the first 24 hours after onset of the hemorrhage.[64,65] The presence of a large hematoma and ventricular blood increases the risk of subsequent deterioration and death.[64,65] Expansion of the hematoma is the most common cause of underlying neurologic deterioration within the first three hours after the onset of hemorrhage. Worsening cerebral edema is also implicated in neurologic deterioration that occurs within 24 to 48 hours after the onset of hemorrhage.[65] Infrequently, late deterioration is associated with progression of edema during the second and third weeks after the onset.[41]

Outcome

The mortality rate six months after spontaneous intracerebral hemorrhage ranges from 23 to 58 per-

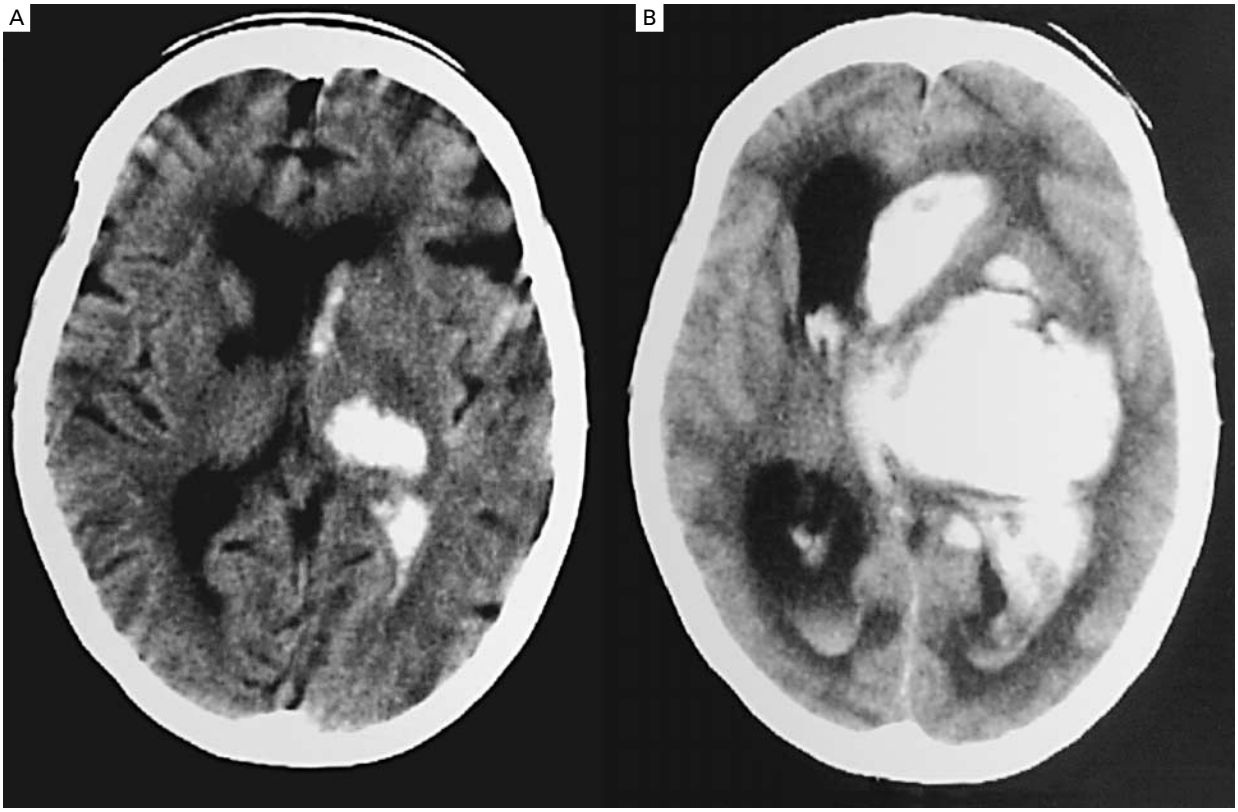

Figure 3. Rapid Expansion of Hematoma.
The first CT scan (Panel A) was obtained one hour after the patient presented and was followed by neurologic deterioration and expansion of the hematoma visible on the CT scan obtained six hours after presentation (Panel B).

cent.[66-68] A low score on the Glasgow Coma Scale, a large volume of the hematoma, and the presence of ventricular blood on the initial CT scan are factors that have been consistently identified as predictive of a high mortality rate.[64,66-68] Broderick et al.[66] found that the mortality rate at one month was best predicted by determining the initial score on the Glasgow Coma Scale and the initial volume of the hematoma. In their study, patients who initially had a score of less than 9 on the Glasgow Coma Scale and a hematoma volume of more than 60 ml had a mortality rate of 90 percent at one month, whereas patients with a score of 9 or greater and a hematoma volume of less than 30 ml had a mortality rate of 17 percent.

A rapid manual method to measure the volume of the hematoma on CT scans has been developed and validated. In this method, the estimated volume of the hematoma is half the product of A, B, and C, where A is the greatest diameter of the hemorrhage on the CT scan, B is the diameter perpendicular to A, and C is the number of slices showing hematoma multiplied by the slice thickness.[66]

DIAGNOSIS

Although the rapid onset of abnormalities and a decreased level of consciousness suggest the diagnosis of intracerebral hemorrhage (Fig. 4), distinguishing definitively between cerebral infarction and intracerebral hemorrhage requires imaging of the brain.[69] On the initial CT scan, the location and size of the hematoma, the presence of ventricular blood, and the occurrence of hydrocephalus should be noted. Selected patients should undergo conventional angiography to look for secondary causes of intracerebral hemorrhage, such as aneurysms, arteriovenous malformations, and vasculitis. Zhu et al.[70] reported abnormalities on angiography in 49 percent of patients with lobar hemorrhage and 65 percent of patients with isolated intraventricular hemorrhage. These authors also reported that 48 percent of the patients who were normotensive and 45 years of age or younger had abnormalities on angiography, whereas hypertensive patients who were older than 45 years of age had no underlying vascular abnormalities.

On the basis of this evidence, patients with lobar or

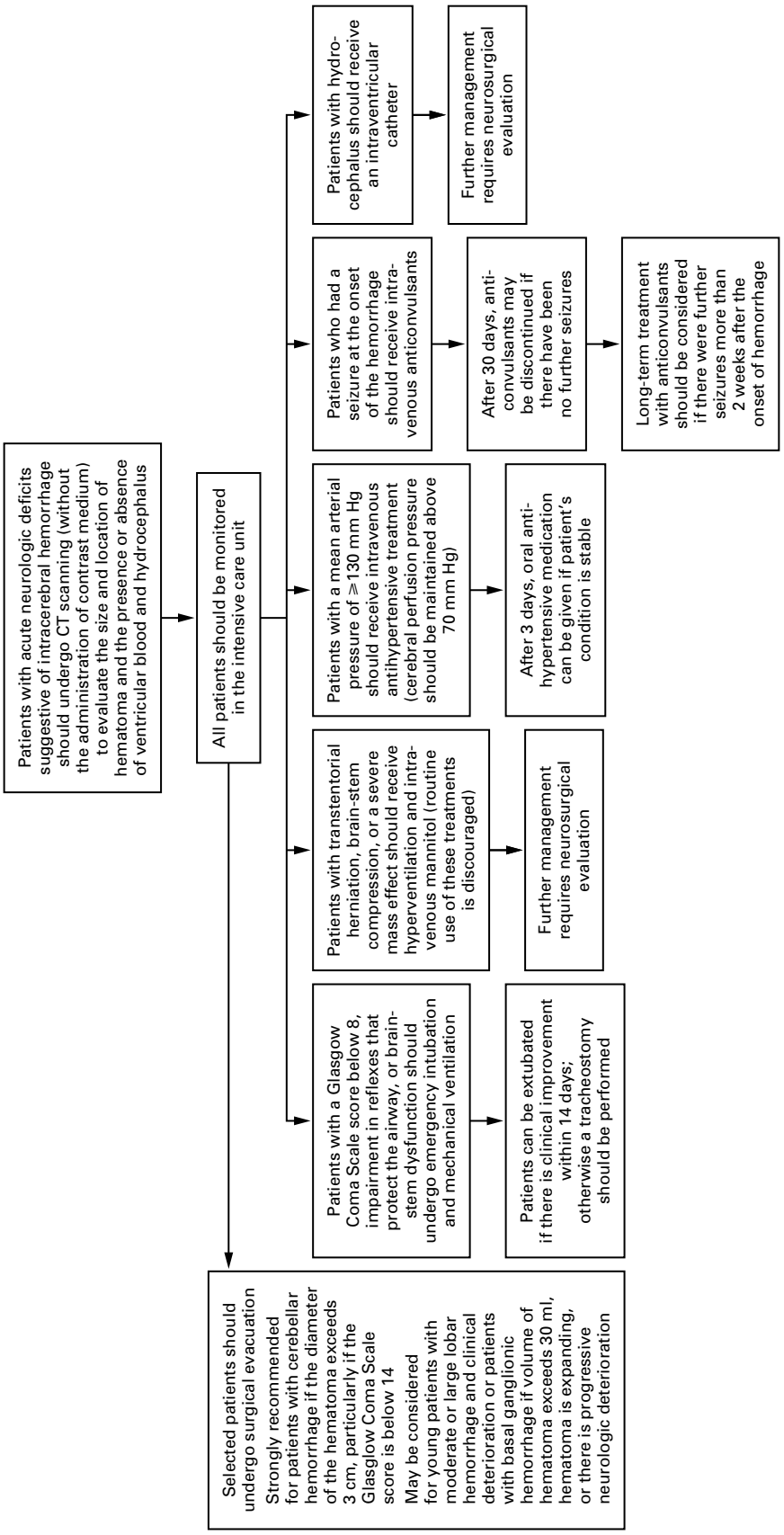

Figure 4. Algorithm for the Management of Intracerebral Hemorrhage.

primary intraventricular hemorrhage should undergo angiography regardless of age or the presence or absence of a history of hypertension. Patients with putaminal, thalamic, or cerebellar hemorrhage should undergo conventional angiography if they are normotensive and 45 years of age or younger. The guidelines of the American Heart Association[2] recommend angiography for all patients with no clear cause of hemorrhage who are candidates for surgery, particularly young patients without hypertension whose condition is clinically stable. The timing of conventional angiography depends on the patient's clinical condition and the urgency of surgery. Magnetic resonance imaging with gadolinium as a contrast medium and magnetic resonance angiography can also be used to identify secondary causes of intracerebral hemorrhage, although their sensitivity is not well established.[71] Conventional angiography should also be considered in patients who have subarachnoid blood associated with a parenchymal clot and in patients who have recurrent hemorrhages. In patients who have initially negative findings on imaging but who have a high likelihood of secondary intracerebral hemorrhage on the basis of clinical findings, angiography should perhaps be repeated two to four weeks after the resolution of the hematoma, when vascular anomalies may become visible.

MANAGEMENT

Evaluation and Management in the Emergency Room

A major challenge for physicians in the emergency room is when to intubate patients. Early intubation with the use of short-acting anesthetics is necessary in patients who have a decreased level of consciousness or impairment of reflexes that protect the airway (Fig. 4). A delay in protecting the airway can lead to secondary injury from aspiration, hypoxemia, and hypercapnia. Findings such as rapid deterioration, clinical evidence of transtentorial herniation, or hydrocephalus on CT scanning should mandate an urgent neurosurgical consultation. The use of hyperventilation and intravenous mannitol and the placement of an intraventricular catheter for the drainage of cerebrospinal fluid can preserve brain structures from mechanical and ischemic damage until surgical decompression can be performed. Finally, given the availability of thrombolytic therapy, early differentiation between cerebral infarction and intracerebral hemorrhage by CT scanning is imperative for the management of acute stroke.

Intensive Monitoring of Neurologic and Cardiovascular Status

The risk of neurologic deterioration and cardiovascular instability is highest during the first 24 hours after the onset of an intracerebral hemorrhage. Approximately 30 percent of patients with a supratentorial intracerebral hemorrhage and almost all patients with a brain-stem or cerebellar hemorrhage have a decreased level of consciousness and require intubation.[72] Therefore, we recommend monitoring of all patients in a dedicated intensive care unit for at least 24 hours after the clinical event. The patient's neurologic status should be assessed hourly with use of a standard evaluation and the Glasgow coma scale. Blood pressure can be adequately monitored with an automated cuff, whereas continuous monitoring of systemic arterial pressure should be considered in patients who require intravenous administration of antihypertensive medications and in patients whose neurologic status is deteriorating. Cardiovascular instability in association with increased intracranial pressure needs immediate attention to avoid the deleterious effects of hypertension or hypotension in a patient with limited autoregulatory capacity.

Mass Effect and Intracranial Hypertension

A mass effect resulting from the volume of the hematoma, the edematous tissue surrounding the hematoma, and obstructive hydrocephalus with subsequent herniation remains the chief secondary cause of death in the first few days after intracerebral hemorrhage. Because of the localized nature of the mass effect[73] and spatial compensation for local increase in volume afforded by ventricular and subarachnoid spaces, a marked, progressive elevation in the intracranial pressure is seen only in patients with a massive intracerebral hemorrhage.[74,75] Localized mechanical damage and even transtentorial herniation can be seen in the absence of a global increase in intracranial pressure.[74,75] In animals with experimentally induced intracerebral hemorrhage, the use of hyperventilation and osmotic agents improved cerebral blood flow and metabolism adversely affected by transtentorial herniation but had no effect in the presence of moderate intracranial hypertension alone.[76] A recent study in patients suggested that aggressive, timely reversal of transtentorial herniation through the use of hyperventilation and osmotic agents improved the long-term outcome.[77] Therefore, treatment with osmotic agents and hyperventilation is recommended in patients with impending cerebral herniation. Corticosteroids should be avoided, because randomized trials have failed to demonstrate their efficacy in patients with an intracerebral hemorrhage.[78,79] The experience with approaches such as administering high doses of barbiturates and hypertonic saline is limited, and these approaches should be investigated further.[80,81]

Management of Blood Pressure

Elevated blood pressure is common after intracerebral hemorrhage and is associated with expansion of the hematoma and a poor outcome.[82] It remains unclear whether elevated blood pressure predisposes patients to expansion of the hematoma or is a consequence of this event. Commonly, the elevated blood

pressure is secondary to uncontrolled chronic hypertension and a nonspecific response to stress.[47,83] Elevated blood pressure can also be a protective response (referred to as the Cushing–Kocher response) whose aim is to preserve cerebral perfusion, particularly in patients with evidence of brain-stem compression.[47]

There is considerable controversy regarding the initial treatment of blood pressure after an intracerebral hemorrhage. Most patients with an intracerebral hemorrhage have chronic hypertension, which leads to cerebral autoregulation that has been adapted to blood pressures that are higher than normal.[84] Furthermore, cerebral perfusion pressure and autoregulatory capacity may be compromised as a result of elevated intracranial pressure.[85] Two studies have demonstrated that a controlled, pharmacologically mediated reduction in blood pressure has no adverse effects on cerebral blood flow in humans or animals.[47,86] The current American Heart Association guidelines for the management of blood pressure in patients with an intracerebral hemorrhage are given in Figure 4.

Ventricular Blood and Hydrocephalus

The presence of blood in the ventricles is associated with a high mortality rate.[30,87] This effect may be related to the development of obstructive hydrocephalus[87] or a direct mass effect of the ventricular blood on periventricular structures, which is associated with global hypoperfusion of overlying cortex.[88] Ventricular blood also interferes with the normal functions of cerebrospinal fluid by inducing localized lactic acidosis.[87] External drainage of cerebrospinal fluid through ventricular catheters reduces intracranial pressure, but the sustained beneficial effect on hydrocephalus and neurologic status is counterbalanced by frequent clots in the catheter and infections.[89] To facilitate early and effective clearance of blood in the ventricles, recent efforts have been focused on the intraventricular administration of thrombolytic agents in patients who have ventricular blood in association with spontaneous intracerebral hemorrhage. A pilot study demonstrated that the intraventricular administration of urokinase every 12 hours until external drainage of cerebrospinal fluid was no longer required reduced the expected mortality rate at one month.[90]

Surgical Evacuation

The goals of the surgical evacuation of a hematoma are to reduce the mass effect, block the release of neuropathic products from the hematoma, and prevent prolonged interaction between the hematoma and normal tissue, which can initiate pathologic processes.[91] However, the benefit of evacuation of basal ganglionic, thalamic, and pontine hemorrhages through an open craniotomy is obscured by the neural damage incurred during the approach to the hematoma and by the recurrence of bleeding as a result of the loss of the tamponade effect of the surrounding tissue. A meta-analysis of three randomized, controlled trials of supratentorial hemorrhage reported that, as compared with the 126 patients who did not undergo surgery, the 123 patients with an intracerebral hemorrhage who underwent surgical evacuation through an open craniotomy had a higher rate of death or dependency at six months (83 percent vs. 70 percent).[92] Recent attempts at early craniotomy did not alter the outcome and were usually associated with an increased probability of recurrent bleeding.

Cerebellar hematomas are unique from a surgical perspective because they can be approached without causing substantial damage to higher cortical or primary motor pathways. Morbidity and mortality are related to compression of the brain stem and are decreased by timely decompression.[61,93] The best surgical results are in patients with a cerebellar intracerebral hemorrhage who have an initial score of less than 14 on the Glasgow Coma Scale or large hemorrhages (volume, 40 ml or more).[94] Patients with a good neurologic status (as evidenced by a Glasgow Coma Scale score of 14 or higher) and small hemorrhages (volume, less than 40 ml) appear to have a good likelihood of full recovery or only moderate disability with conservative management.[94] Early craniotomy is recommended in patients with a cerebellar hematoma because the rate of neurologic deterioration after cerebellar hemorrhage is very high and unpredictable. On the basis of available evidence, the recommendations for surgical evacuation are shown in Figure 4.

To prevent secondary pathologic processes and limit neural damage and the risk of recurrent bleeding associated with open craniotomy, studies are now focusing on early surgical evacuation with the use of stereotactic and endoscopic approaches. These approaches permit evacuation of the hematoma while causing minimal damage to overlying normal tissue (Fig. 5).[95] Zuccarello et al.[96] reported a small, randomized feasibility study evaluating the use of surgical evacuation, craniotomy, or stereotactic aspiration within 24 hours after the onset of symptoms in patients with an intracerebral hemorrhage. The likelihood of a good outcome was higher in patients who underwent surgery (56 percent) than in those who received medical treatment alone (36 percent). Auer et al.[95] randomly assigned 100 patients to undergo stereotactic-guided endoscopic evacuation within 48 hours after admission or to receive medical therapy alone. At six months, the outcome was better in the group assigned to endoscopic surgery: 40 percent of these patients had no deficits or only minimal deficits, as compared with 25 percent of the patients in the medical group.

Techniques to facilitate complete evacuation by liquifying the hematoma through the use of thrombolytic agents are under investigation.[97,98] A recent pilot study in which thrombolytic agents were instilled through an indwelling intracranial catheter into the matrix of the hematoma every six to eight hours with

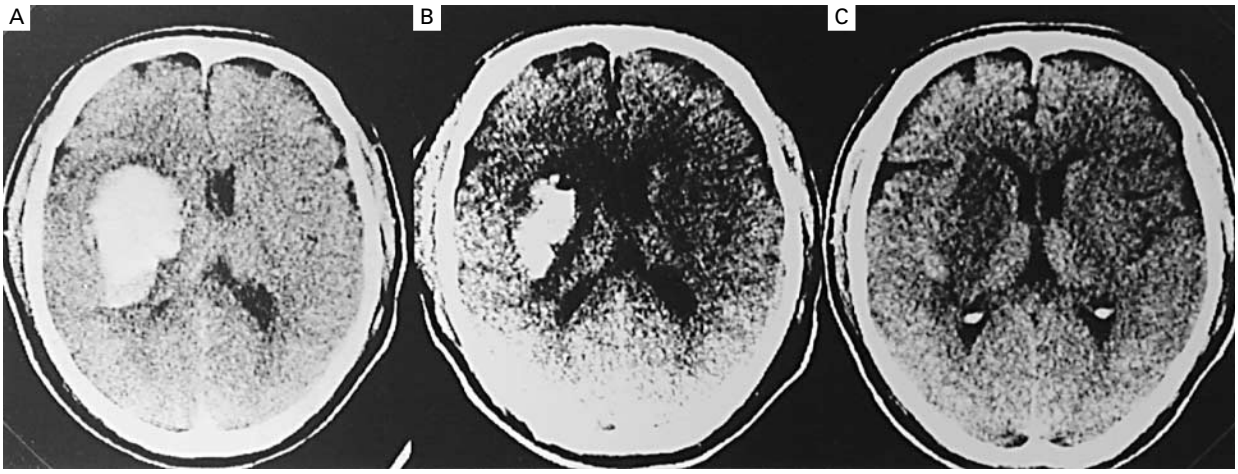

Figure 5. CT Scans of a Basal Ganglionic Hematoma before (Panel A) and after (Panels B and C) Stereotactic Removal.
In Panel A, the volume of the basal ganglionic hematoma was 60 ml preoperatively. Six infusions of urokinase (20,000 U each) were administered into the matrix of the hematoma every six to eight hours with concomitant aspiration. In Panel B, immediately after the aspiration of the hematoma, the hematoma is smaller and there is less displacement of surrounding tissue. Panel C shows the findings three days after the aspirations.

concomitant aspiration demonstrated a 50 percent reduction in the volume of the hematoma three days after evacuation, with a low rate of recurrent bleeding and death.[98]

Seizures and Recurrent Hemorrhage

Most seizures occur at the onset of intracerebral hemorrhage or within the first 24 hours.[99] Anticonvulsants can usually be discontinued after the first month in patients who have had no further seizures. Patients who have a seizure more than two weeks after the onset of an intracerebral hemorrhage are at higher risk for further seizures and may require long-term prophylactic treatment with anticonvulsants.[100]

Arakawa et al.[5] reported a rate of recurrent hemorrhage of 2 percent per year in 74 patients who had had a hypertension-induced intracerebral hemorrhage and who were followed for a mean of 2.8 years. The site of the subsequent intracerebral hemorrhage usually differed from that of the first hemorrhage. The rate of recurrence was 10 percent per patient-year in patients with an average diastolic blood pressure of more than 90 mm Hg during follow-up clinic visits and less than 1.5 percent in those with a lower diastolic blood pressure. The investigators concluded that an average diastolic blood pressure of more than 90 mm Hg during follow-up clinic visits was associated with an increased rate of recurrent bleeding, suggesting the importance of appropriate antihypertensive treatment.

FUTURE DIRECTIONS

New treatments need to be developed that prevent the deterioration of neurologic function after an intracerebral hemorrhage. Studies of genetic factors that may increase the risk of intracerebral hemorrhage should be pursued. For example, study of the association between genes for certain apolipoproteins and intracerebral hemorrhage may provide valuable insight into the pathogenesis of degenerative changes that lead to vessel rupture and, possibly, a means of preventing these changes. The development of therapies that reduce cerebral edema and neuronal damage may require a more complete understanding of the injury and of the sequence and mediators of pathophysiologic events that produce secondary injuries.

The proper approach to such issues as the treatment of blood pressure and the indications for surgical evacuation in patients with an intracerebral hemorrhage remains controversial. A randomized trial is required to determine the effect of the treatment of blood pressure on the expansion of hematomas. Surgical techniques that maximize the amount of hematoma that is removed, minimize damage to normal tissue, and inhibit postoperative bleeding need to be developed and evaluated in randomized trials. It is also important to recognize that there may be a window of time during which surgical evacuation is most effective with respect to the long-term outcome. Finally, the use of thrombolytic therapy to promote the resolution of ventricular blood clots appears to be promising; a randomized trial to establish the efficacy and safety of this approach is under way.[90]

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