Intracerebral Hemorrhage

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Citation

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Abstract

Intracerebral hemorrhage (ICH) is a common cause of stroke, accounting for between 5 and 10% of all strokes [1,2,3]. In a consecutive series of 938 stroke patients enrolled into the NINCDS Stroke Data Bank, primary ICH accounted for 10.7% of the cases [4]. The age-adjusted annual incidence rates for primary intracerebral hemorrhage range from 11 to 31 per 100,000 population in predominantly Caucasian population based-studies with a high rate of CT scanning [5]. The risk of intracerebral hemorrhage in blacks is 1.4 times the risk in whites [6]. The most common risk factors in the 403 black patients with ICH were pre-existing hypertension (77%), alcohol use (40%), and smoking (30%). Among the 91 non-hypertensive patients, 21 (23%) were diagnosed with hypertension after onset. Compared with women, men had a younger age of onset (54 versus 60 years; $p < .001$) and a higher frequency of alcohol use (54% versus 22%; $p < .001$) and smoking (39% versus 17%; $p < .001$). ICH secondary to hypertension (n = 311) and of undetermined etiology (n = 73) were the most common subtypes in blacks. Patients aged 65 years and older (compared with those aged 15 to 44 years; $p = .001$) and women (compared with men; $p = .02$) were more likely to be dependent at discharge11. ICH remains a significant cause of morbidity and mortality in this population.

Analyses of circadian variation in the onset of ICH have shown an increased incidence in the morning (6 A.M. to 12 noon), similar to ischemic stroke, but perhaps with a second peak in the afternoon. The results of seasonal influence on the occurrence of ICH are conflicting [7,8].

RISK FACTORS

Hypertension represents the main causative factor for ICH in the autopsy study of McCormick and Rosenfield [9]. The frequency of hypertension in a series of patients with ICHs varies widely from 40% to 89%, even in studies applying careful definitions of hypertension. Diagnostic bias towards the detection of larger hemorrhages, as well as differences in the prevalence of hypertension with time and in different populations, may well have influenced the results. Whereas chronic hypertension still appears to be the most important risk factor for ICH, studies suggest that its role in causing ICH is less dominant than previously thought 5.

Smoking and its relationship with ICH are not established. Fogelholm and Murros in a population-based case control-study did not find evidence of a positive association between cigarette smoking and risk of primary ICH [10].

Moderate drinking of alcohol increases risk of both intracerebral and subarachnoid hemorrhage in diverse populations. There is insufficient epidemiological evidence to conclude whether recent alcohol use affects risk of either ischemic or hemorrhagic stroke12.

Serum cholesterol level below the 10th percentile (sex-specific <4.62 mmol/L [178 mg/dL] in men), compared with higher cholesterol level, was associated with a significantly increased risk of intracerebral hemorrhage in men aged 65 years or older (relative risk, 2.7; 95% confidence interval, 1.4 to 5.0). An excess risk was also observed among elderly women at the lowest cholesterol range, but a chance finding could not be ruled out. No relationship was seen among men or women aged 40 to 64, and no statistical interaction of low serum cholesterol with hypertension was found in either sex. In these data, the association between low serum cholesterol level and intracerebral hemorrhage was confined to elderly men [14]. High serum total cholesterol decreased the risk of intracerebral hemorrhage but increased the risk of cerebral infarction. By contrast, low serum HDL cholesterol increased the risk of cerebral infarction but not of intracerebral hemorrhage [15].

CAUSES OF ICH

Chronic hypertension produces fibrinoid necrosis, lipohyalinosis, and medial degeneration, which make the vessels susceptible to rupture. ICH that originates in the

putamen, thalamus, pons or cerebellum is most likely linked with hypertension. ICH at these sites are often referred to as "hypertensive ICH" even in patients in whom the pre-stroke blood pressure level is unknown. However as mentioned above, recent studies suggest that the role of hypertension in causing ICH is less obvious than previously thought 5. The role of microaneurysms in causing ICH is debatable, indirect support for their role was provided by the anatomic distribution to sites preferentially affected by ICH in hypertensive patients [16]. However, microaneurysms were not documented at the actual sites of arterial rupture in Fisher's serial section studies of hypertensive ICHs [17].

TABLE 1: CAUSES OF ICH

Chronic hypertension

Cerebral amyloid angiopathy (CAA)

Acute changes in blood pressure and blood flow

Vascular malformations

Intracranial aneurysm

Bleeding diathesis

Sympathicomimetic agents and illegal drug abuse

Infectous vasculitis

Noninfectious vasculitis

Intracranial neoplasm

Moyamoya disease

Head trauma

Venous thrombosis

Cerebral endometriosis

Silastic dural substitute

Idiopathic hypereosinophilic syndrome

Zieve syndrome

Hemodialysis

Ventriculoperitoneal shunt

Ref 5 (p 1448)

Cerebral amyloid angiopathy (CAA) is characterized by deposition of amyloid in small and medium-sized arteries of the cortex an leptomeninges which is confined to the cerebral vessels only and it increases steadily with age. Lobar ICH, often recurrent, is the main consequence of CAA, and one of the most common causes of ICH in persons 70 years and older [18]. Sequential pathogenic events leading to hemorrhage are: (1) damage of the media and adventitia due to severe amyloid deposition results in dilatation of the cortical arteries, (2) the vascular dilatation progresses and is accompanied by thickening of the intima and disruption of the media and adventitia (microaneurysm formation), (3) plasma components invade the vascular wall (fibrinoid necrosis), and (4) finally, hemorrhage develops [19].

Abrupt, dramatic increase in blood pressure in normotensive patients has been documented to precipitate ICH. Their autoregulatory functions have not adjusted to high blood pressure in contrast to chronically hypertensive patients 5.

Arteriovenous malformations (AVMs) are important causes of non-hypertensive ICH, and tend to occur in relatively young patients20. Intracranial aneurysms characteristically cause subarachnoid hemorrhage, but may also bleed into the adjacent brain parenchyma and cause ICHs. Halpin et al [21] however, found that among ICH patients thought to have underlying lesions, 13% of hypertensive patients, 31% of patients with hematoma involving the basal ganglia, and 18% of those with posterior fossa ICHs all had underlying aneurysm or angiomas.

ICH is the most common and least treatable neurological complication of oral anticoagulants (OACs) in the elderly [22]. The onset of unusual headache, nausea, vomiting, confusion, ataxia, or dizziness in elderly patients receiving OACs warrants an urgent search for ICH. In patients taking OACs, approximately 40% of strokes are ICHs. Importantly, in OAC-associated ICH the bleeding evolves slowly, for 24 hours or more, in perhaps half of the patients. This is in contrast to spontaneous ICH in patients who are not anticoagulated, in whom the duration of bleeding is usually brief (approximately 10% show progressive enlargement in the first 24 hours) [23]. The mechanism(s) by which OACs accentuate the rate of ICH is unclear. It seems unlikely, given current concepts, that OACs induce vascular injury or inhibit vascular repair processes, leading to brain hemorrhage. OACs (and other antithrombotic agents) may cause spontaneous subclinical brain hemorrhages to grow to clinical importance. Small collections of hemosiderin are often found in elderly hypertensive patients at postmortem in relation to degenerative small-vessel vasculopathies [24,25].

Ideal candidates for OACs are patients with a high rate of ischemic stroke that can be substantially reduced by OACs. These patients should also be at low risk for development of traumatic ICH (falls, trauma). Unfortunately, risk factors for ischemic stroke and ICH overlap in many patients (e.g., advanced age, hypertension, prior stroke). Patients who are elderly (aged >70 years) with hypertension have an inherent risk for ICH that is multiplied by OACs to absolute rates approaching 1%/y. Lowering the target intensity (INR, 1.5 to 2.5) may be sensible for patients at high risk for ICH, although the efficacy of this range has not been established for stroke prevention and characterization of patients at high risk for ICH is incomplete. Whether and how lower intensities of anticoagulation (INR, <2.5), with or without aspirin, will shift the risk/benefit equation for stroke prevention is not presently clear and of obvious clinical importance23. ICH during heparin treatment is even less common. The risk factors for ICH during heparin treatment for acute cerebral infarction are large infarct size and uncontrolled hypertension.

Another common clinical problem is ICH in a patient with an indication for anticoagulation. Bertram et al [26] reported 15 patients with ICH that occurred under anticoagulation with phenprocoumon, with an international normalized ratio (INR) of 2.5-6.5 on admission. Absolute indications for anticoagulation were double, mitral, or aortic valve replacement, combined mitral valve failure with atrial fibrillation and atrial enlargement, internal carotid artery-jugular vein graft, frequently recurring deep vein thrombosis with risk of pulmonary embolism, and severe nontreatable ischemic heart disease. As soon as the diagnosis of ICH was established, INR normalization was attempted in all patients by administration of prothrombin complex, fresh frozen plasma, or vitamin K. After giving phenprocoumon antagonists (and neurosurgical therapy in four patients) heparin administration was started. Nine patients received full-dose intravenous and six low-dose subcutaneous heparin. The following observations were made: all patients with effective, full-dose heparin treatment with a 1.5- to 2-fold elevation in partial thromboplastin time after normalization of the INR were discharged without complication; three of four patients with only incomplete correction of the INR (> 1.35) experienced relevant rebleeding within 3 days (all patients with an INR higher than 1.5), two of whom were on full-dose heparin; three of seven patients with normalized INR and without significant PTT elevation developed severe cerebral embolism. Although this is based on a retrospective analysis, they support treatment with intravenous heparin (partial thromboplastin time 1.5-2 times baseline value) after normalization of the INR in patients with an ICH and an urgent need for anticoagulation.

Thrombolysis in acute ischemic stroke increases the risk of severe, life-threatening hemorrhagic complications by up to 10 times compared to controls. In experimental focal cerebral ischemia a significant loss of basal lamina components of the cerebral microvessels has been demonstrated. This loss in vessel wall integrity is associated with the development of petechial hemorrhage. The mechanisms for this microvascular damage may include plasmin-generated laminin degradation, matrix metalloproteinases activation, transmigration of leukocytes through the vessel wall, and other processes. Attenuation of the microvascular integrity loss with subsequent reduction in hemorrhage is theoretically possible by 1) an improvement in the definition of an individual time window of therapy (by means of imaging techniques), 2) a biochemical quantification of the basal lamina damage to avoid dangerous interventions, and 3) pharmacological strategies to protect the basal lamina during thrombolysis [27]. In a multiple logistic regression analysis based on data from several trials, four variables appeared to be predictive of ICH risk: advanced age (>65 years), low body weight (<70 kg), hypertension (systolic > 170 mmHg and/or diastolic > 95 mmHg), and alteplase (rt-PA) regimen.[28].

ICHs during treatment with acetylsalicylic acid ASA are less common than gastrointestinal bleeding, but are of special concern because they carry a much higher mortality. Although it appears to double the risk of hemorrhagic stroke, the risk is still small and outweighed by the reduction in ischemic strokes, at least in secondary prevention trials 5.

Sympathomimetics: amphetamines, pseudoephedrine, phenylpropranolamine (contained in many over-the-counter nasal decongestants and appetite suppressors), and cocaine (especially in its precipitate form known as crack) can induce ICH. Classically, the hemorrhage is lobar and occurs in a younger person. Development of ICH is associated with transiently elevated blood pressure in about 50% of cases, occurring in proximity (several hours) to recent drug use (whether first- time use or established pattern of drug use/abuse). Another supposed mechanism is hypersensitivity or direct toxic effect of the drug on cerebral blood vessels giving an arteritis-like vascular change characterized angiographically by beading that is reversible by

discontinuation of the drug abuse and use of steroids [29,30].

Bleeding into brain tumors is rare (5% to 6% in autopsy-based study) with the exception of pituitary adenomas, which may bleed in 16% of cases [31]. Glioblastoma multiforma is an example of primary malignant tumor, while the metastatic melanoma, choriocarcinoma, renal cell, and bronchogenic carcinoma all may cause ICH. Features suggesting ICH in brain tumor are; fundoscopic presence of papillaedema, CT findings of multiple metastatic lesions, large areas of edema surrounding the hematoma, postcontrast ring-like high-density area at the periphery of the hematoma, and atypical location of ICH. These findings need to be confirmed by MRI, MRA, angiography, and /or biopsy for further management.

CLINICAL PRESENTATION

Stroke as a sudden, non-conclusive, focal neurologic deficit is not difficult to diagnose but it is not easy to diagnose or to treat a stroke patient depending only on the clinical diagnosis. Before CT scan, there were many patients diagnosed clinically as ICH but were found to have infarction on autopsy.

GENERAL CLINICAL MANIFESTATIONS

ICH occurs characteristically during activity (rarely during sleep). It has been given its own name “apoplexy”. The prototype is an obese, plethoric, hypertensive, male who, “while sane and sound, fall senseless to the ground-impervious to shouts, shaking, and pinching-, breathes stentorously, and dies in a few hours” 1.

Manifestations of increased intra-cranial pressure (ICP) in a Mohr [32] study show headache is reported in about 36% and vomiting in about 44% of patients alert enough to report the symptoms. Although the absence of headache or vomiting does not rule out the diagnosis of ICH, presence of these symptoms is in favor of ICH or SAH as it is reported in less than 10% of occlusive strokes. Seizures are uncommon at the onset in 7% of cases but are found in 32% of lobar hemorrhages.

Hypertension is frequent (91% of cases) 32 and correlates with other physical signs indicative of hypertension such as left ventricular hypertrophy, and hypertensive retinopathy. The presence of subhyaloid hemorrhage is virtually diagnostic of SAH (ruptured aneurysm).

TOPOGRAPHIC LOCALIZATION OF ICH ON CLINICAL EXAMINATION (SEE PICTURES 1-5): PUTAMINAL HEMORRHAGE

The most common form of ICH is the putaminal hemorrhage. The classical presentation is described by the massive hemorrhages, with rapidly evolving unilateral weakness accompanied by sensory, visual, and behavioral changes. Headache (depends on the patient’s conscious level to complain of it) and vomiting are common within few hours from onset. Although the onset is abrupt, there is often a gradual worsening of both focal deficit and the level of consciousness in the following minutes or hours. In a fully developed syndrome, the neurological examination shows a dense flaccid hemiplegia with a hemisensory syndrome, homonymous hemianopia, conjugate deviation of the eyes toward the side of the lesion, and global aphasia in the dominant hemisphere hematomas, or hemi-inattention in non-dominant lesions. In the smallest putaminal hematomas the patient is alert with hemiparesis, contralateral hemisensory deficit, and has normal gaze. The full picture of the large hematomas can occur even when the hematoma remains small with lateral extension (in dominant hemisphere causing aphasia and hemi-inattention in the nondominant hemisphere). Prominent inattention and neglect syndromes are seen in cases of vertical extension of the putaminal hematomas in nondominant hemisphere [33,34].

Figure 1

Picture 1. A putaminal/intraventricular hemorrhage- this is post-TPA, but one can not tell this from the appearance alone.

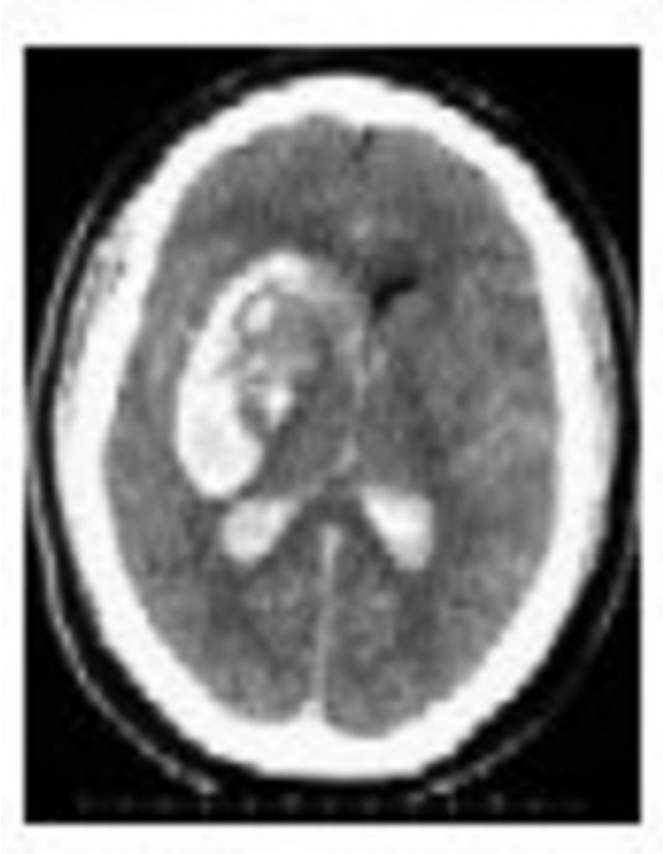
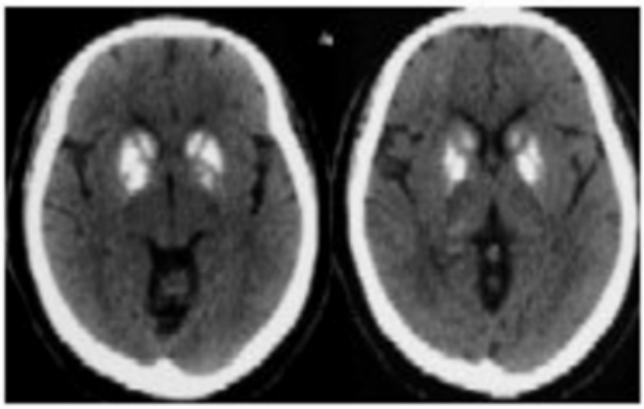


Figure 2

Picture 2. Note the symmetric calcifications without mass effect



CAUDATE HEMORRHAGE

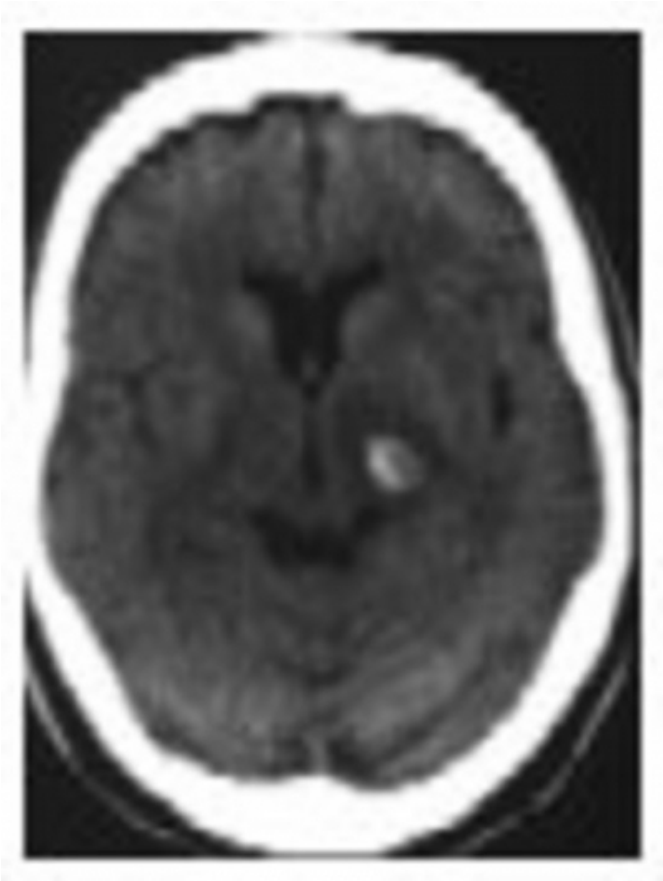
Caudate hemorrhage represents approximately 5 to 7% of cases of ICH. Clinical findings include gaze preference towards the side of the lesion, contralateral hemiparesis sometimes accompanied by transient hemisensory syndrome. Other findings include neck stiffness, disorientation and confusion occasionally accompanied by a prominent short-term memory defect. Headache, nausea, vomiting and neck stiffness regularly accompany caudate hemorrhage but are less common manifestations in putaminal hemorrhage. Disorder of language and neglect are not seen in hemorrhages confined to the caudate. As a result of extension into the frontal horn of the ipsilateral ventricle, approximately 75% of cases have been present with mild to moderate hydrocephalus of the body and temporal horns of the lateral ventricle [35].

THALAMIC HEMORRHAGE

Thalamic hemorrhage accounts for 10 to 15% of parenchymal hemorrhage. A typical presentation features a rapid onset of unilateral sensorimotor deficit, and vomiting, but low frequency of headache. The physical findings include hemiparesis or hemiplegia in nearly all cases, virtually all of them with an associated decrease or loss of all sensory modalities over the contralateral limbs, face, and trunk. The severity and distribution of the motor and sensory symptoms are similar to those of putaminal hemorrhage, therefore not serving as useful differential points [36]. Kumral et al [37] prospectively studied 100 patients with thalamic hemorrhage; all patients with posterolateral thalamic hemorrhage had severe sensorimotor deficit. Neuropsychological disturbances in patients with posterolateral thalamic hemorrhage were prominent, with primarily transcortical aphasia in those with left-sided lesions and hemineglect and anosognosia in those with right-sided lesions. Several variants of vertical gaze dysfunction skew ocular deviation, gaze preference toward the site of the lesion, and miotic pupils were frequent in posterolateral thalamic hemorrhage, particularly in large lesions. Patients with small and large anterolateral thalamic hemorrhage were characterized by severe motor and sensory deficits; language and oculomotor disturbances were also observed, although less frequently than in posterolateral hemorrhage. Sensorimotor deficits were observed in patients with medial thalamic hemorrhage (moderate in small hemorrhages and severe in large hemorrhages because of involvement of the adjacent internal capsule). Language disturbances in patients with left-sided lesions and neglect in patients with right-sided lesions were seen only in large medial thalamic hemorrhage. Dorsal thalamic hemorrhage was rare and characterized by mild and transient sensorimotor disturbances. Among patients with dorsal thalamic hemorrhages, only those with large lesions had oculomotor and neuropsychological disturbance.

Figure 3

Picture 3. Typical small thalamic bleed

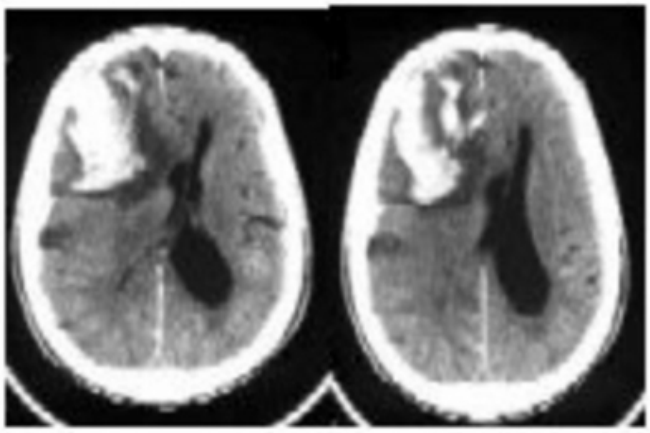


LOBAR (WHITE MATTER) HEMORRHAGE

Ropper and Davis [38] described 26 cases of spontaneous lobar hemorrhage. Occipital hemorrhage (11 cases) caused severe pain around the ipsilateral eye and dense hemianopia. Left temporal hemorrhage (7 cases) began with mild pain in or just anterior to the ear, fluent dysphasia with poor auditory comprehension but relatively good repetition, and a visual deficit subtending less than a hemianopia. Frontal hemorrhage (4 cases) caused a distinctive syndrome beginning with severe contralateral arm weakness, minimal leg and face weakness, and frontal headache. Parietal hemorrhage (3 cases) began with anterior temporal ("temple") headache and hemisensory deficit, sometimes involving the trunk to the midline. One patient had a right temporal hemorrhage. Spontaneous lobar hemorrhage and branch artery embolism in the same region produce similar clinical syndromes. Headache is a first and most prominent symptom. A rapid but not instantaneous onset over several minutes, when combined with one of the typical syndromes, suggests lobar hemorrhage rather than other types of stroke. Ancillary investigations (including CT scanning, angiography in 11 patients, and autopsy in 4) disclosed 2 patients with bleeding diatheses due to warfarin, 2 with arteriovenous malformations, and 1 with metastatic tumor. Only 8 of the 26 patients had chronic hypertension (blood pressure greater than 130/85 mm Hg), suggesting that hypertension is not a common etiological factor. In another study of 22 cases, most hematomas were found in the parietotemporal region. Common physical findings were hemiparesis, hemisensory syndrome, and visual field defects. Seizures occurred in 23% of the patients, and coma was infrequent at onset [39].

Figure 4

Picture 4. Typical lobar hemorrhage



CEREBELLAR HEMORRHAGE

Cerebellar hemorrhage appears with an average frequency of 10%. It may present with a spectrum of clinical manifestations, from a benign course with little to no neurologic deficit to a rapidly fatal course with hydrocephalus and brainstem compression. In patients with clinical deterioration, ventricular drainage and surgical evacuation of the clot may be life-saving [40]. Patients with medial ventral cerebellar peduncular hemorrhages presented with a characteristic syndrome of ipsilateral ataxia, lower motor neuron type facial weakness, and ipsilateral gaze paresis. The gaze paresis can not be overcome with a doll's head maneuver. The findings are explained by compression of the facial colliculus, with involvement of the sixth nerve nucleus and the middle cerebellar peduncle [41]. Three cases of cerebellar hemorrhage and 5 of cerebellar infarction, diagnosed by brain CT, were examined from the early phase of the onset. All cases were mild to moderate in severity. Dizziness and nausea were the most common symptoms and cerebellar and other CNS signs could be detected only for a short period in some of the cases. Although neuro-otological examinations especially gaze nystagmus, eye tracking and

positional nystagmus tests, were useful for diagnosing the central vestibular lesions, no definitive signs could be used to differentiate between cerebellar hemorrhage and infarction. Therefore, it is considered difficult in such mild cerebellar strokes to establish correct diagnosis by physical examinations alone [42]. Symptoms usually develop during day while the patient is active. Occasionally a single prodromal episode of dizziness or facial numbness may precede hemorrhage. The most common symptom is an inability to stand or walk. Vomiting, dizziness, occipital-occasionally in one side of the head, frontal or associated with neck and shoulder pain mimicking SAH and headache are very frequent symptoms while, dysarthria, tinnitus, and hiccups are less frequent. At least 75% of cases presented with two of the characteristic triad of appendicular ataxia, ipsilateral horizontal gaze palsy, and peripheral facial palsy [43].

Figure 5

Table (2)
Neurologic findings in cerebellar hemorrhage in non-comatose patients

Neurologic findings	No.	%
Appendicular ataxia	17/26	65
Truncal ataxia	11/17	65
Gait ataxia	11/14	78
Dysarthria	20/32	62
Gaze palsy	20/37	54
Cranial nerve findings		
Peripheral facial palsy	22/36	61
Nystagmus	18/35	51
Miosis	11/37	30
Decreased corneal reflex	10/33	30
Abducent palsy	10/36	28
Gag reflex loss	6/30	20
Skew deviation	4/33	12
Trochlear palsy	0/36	-
Hemiparesis	4/35	11
Extensor plantar response	23/36	64
Respiratory irregularity	6/28	21
Nuchal rigidity	14/35	40
Subhyaloid hemorrhage	0/34	-

Ref [43] p683 from*
* Ott KH, Kase CS, Ojemann RG, Mohr JP: Cerebellar hemorrhage: diagnosis and treatment. Arch Neurol 31:160, 1974.

BRAIN STEM HEMORRHAGE

Patients with brain stem lesion usually present with crossed-hemiparetic or hemiplegic syndromes of ipsilateral peripheral cranial nerve palsies with contralateral hemiparesis or hemiplegia. This classic picture however, occurs more frequently with arterial occlusion.

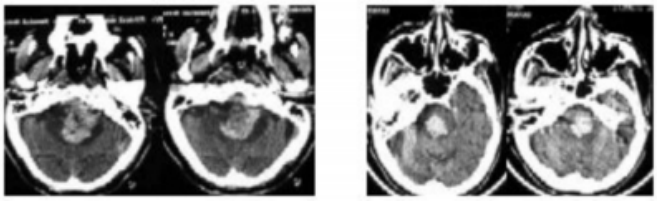
Spontaneous, nontraumatic mesencephalic (midbrain) hemorrhage is rare. In most instances the hemorrhage dissects down from the thalamus or putamen, or is part of a lesion originating in the cerebellum or pons, or arises from blood dyscrasias or AVMs. In its localized form, patients present with Weber syndrome (crossed third cranial nerve palsy and hemiparesis) 43.

Pontine hemorrhage represents approximately 6 % of ICHs (picture 5). In addition to its “classic” syndrome characterized by coma, quadriplegia, ocular fixation, absence of light reaction, pinpoint pupil (about 1mm in diameter) ocular bobbing, decerebrate posture, respiratory disturbance, tachycardia, hyperthermia and eventual demise, two more benign syndromes arising from hemorrhage confined to one side of the pons were also recognized. In one of these hemipontine syndromes, hematoma involved both the basis pontis and tegmentum and was associated with hemiparesis, brainstem signs, and preserved consciousness. In the other, hemorrhage was confined to the tegmentum and was associated with gaze paresis, motor sparing, and preserved consciousness. All patients suffering hemipontine hemorrhage survived. An impressive degree of functional recovery occurred in these survivors [44].

Medullary hemorrhage is even more rare than hemorrhage in the midbrain. The most frequent symptoms at onset are vertigo, sensory symptoms, and dysphagia. Presenting signs included palatal weakness, nystagmus, hypoglossal palsy, cerebellar ataxia, and limb weakness. Less common signs are facial palsy and Horner syndrome [45].

Figure 6

Picture 5. Two patients with pontine hemorrhages



INVESTIGATIONS

Before the introduction of CT scanning, the examination of the CSF was the most dependable method for the diagnosis of hemorrhage. The presence of blood in CSF or xanthochromic CSF indicates communication of the hematoma with the ventricular space but it is less frequent with small or lobar hematoma (less frequent communication with the ventricular system). In general, lumbar puncture is ill advised, for it may precipitate or aggravate an impending herniation. The white cell count in the peripheral blood may rise transiently to 15,000 - 20,000 /ml3. ESR rate is also elevated in some patients 1.

Computerized tomography (CT) followed with magnetic resonance imaging (MRI) several years later enabled first the direct visualization of extravascular blood and products of its degradation. The protein component of hemoglobin is over

90% responsible for the hyperdensity of CT image in the case of a hemorrhage, whereas paramagnetic properties of hemoglobin derivatives are responsible for signal changes in MRI. CT is only able to diagnose accurately an acute hemorrhage. The lesion becomes hypodense in 3 weeks and eventually forms a posthemorrhagic pseudocyst. Differentiation of a posthemorrhagic pseudocyst from old contusions, ischemic lesions or even astrocytomas may be difficult. CT has thus a "short memory" for hemorrhage. MRI can differentiate 5 stages of hemorrhage according to the time schedule: hyperacute, acute, subacute stage I, subacute stage II, and chronic. Sequelae of hemorrhage are detectable even years later. The development of intracranial hemorrhage in daily routine MR imaging is described and documented to serve as a guide of the model situation for the use of the physician [46].

The value of angiography in diagnosis of ICH has declined since the introduction of CT and MRI. Its main role at present is in the etiologic diagnosis of nonhypertensive forms of ICH, multiple ICHs, or those located in atypical sites (hemispheric white matter, head of caudate nucleus). Also looking for AVM, aneurysm, or tumor as the causes of hemorrhage. Even this role is steadily diminished with the improvement in noninvasive brain imaging 43.

COURSE AND PROGNOSIS

The prognostic value of clinical characteristics and CT scan findings in 50 patients of intracerebral hemorrhage (ICH) has been examined. Follow up has been done over a 6 month period. Each patient has been individually followed for 8 weeks. At the end of the follow up period 34% of the patients died, 36% were dependent on outside help for daily living, while 30% were capable of independent existence. Age of more than 60 yrs, Glasgow Coma Scale (GCS) Score of 6 or less at the time of admission, ICH volume greater than 30 ml, midline shift in CT scan of more than 3 mm and presence of intraventricular hemorrhage (IVH) and hydrocephalus all had an adverse impact on outcome. Young age, GCS score of more than 8, ICH volume of less than 20 ml, presence of lobar hemorrhage and absence of IVH/hydrocephalus were associated with relatively favorable outcome [47].

The most important predictor of the 28-day survival is the level of consciousness on admission, followed by first day MAP. Hypertension is the most important predictor of the first day MAP, followed by age, which had an inverse effect on the MAP level. At all levels of consciousness, high first day MAP (especially if > 145 mm Hg) worsened the 28-day survival rate [48].

GUIDELINES FOR THE MANAGEMENT OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE49

Initial Management in the Emergency Department

Initial management should first be directed toward the basics of airway, breathing, circulation, and detection of focal neurological deficits. In addition, particular attention should be given to detecting signs of external trauma. A complete examination should also include looking for complications such as pressure sores, compartment syndromes, and rhabdomyolysis, in patients with a prolonged depressed level of consciousness (patients "found down").

Airway and Oxygenation

Although intubation is not required for all patients, airway protection and adequate ventilation are critical. Patients who exhibit a decreasing level of consciousness or show signs of brain stem dysfunction are candidates for aggressive airway management. Imminent respiratory insufficiency rather than an arbitrary cutoff such as a specific Glasgow Coma Scale (GCS) score should guide intubation.

Medical Management: Randomized Trials

Four small randomized trials of medical therapy for ICH have been conducted: steroid versus placebo treatment (2 trials), hemodilution versus best medical therapy (1 trial), and glycerol versus placebo (1 trial). None of the 4 studies showed any significant benefit for the 3 therapies. In the study by Poungvarin et al, patients who were treated with steroids were more likely to develop infectious complications than those treated with placebo. Thus, the medical guidelines below are based on the reported experience of treatment of ICH in clinical series as well as general guidelines for treatment of any acutely ill patient in a neuro-intensive care unit.

BLOOD PRESSURE MANAGEMENT

The optimal level of a patient's blood pressure should be based on individual factors such as chronic hypertension, elevated intracranial pressure (ICP), age, presumed cause of hemorrhage, and interval since onset. In general, recommendations for treatment of elevated blood pressure in ICH are more aggressive than those for patients with ischemic stroke. The theoretical rationale for lowering blood

pressure is to decrease the risk of ongoing bleeding from ruptured small arteries and arterioles. A prospective observational study of growth in the volume of ICH did not demonstrate a relation between baseline blood pressure and subsequent growth of ICH, but frequent early use of hypertensive agents in this study may have obscured any relationship. Conversely, overaggressive treatment of blood pressure may decrease cerebral perfusion pressure and theoretically worsen brain injury, particularly in the setting of increased intracranial pressure. To balance these 2 theoretical rationales they recommend that blood pressure levels be maintained below a mean arterial pressure of 130 mm Hg in persons with a history of hypertension (level of evidence V, grade C recommendation). In patients with elevated ICP who have an ICP monitor, cerebral perfusion pressure (MAP–ICP) should be kept >70 mm Hg (level of evidence V, grade C recommendation). Mean arterial blood pressure >110 mm Hg should be avoided in the immediate period. If systolic arterial blood pressure falls below 90 mm Hg, pressors should be given. Nitroprusside, the most commonly used agent for severe elevation of blood pressure, is a vasodilatory agent that theoretically can increase cerebral blood flow and thereby intracranial pressure. This possible disadvantage has yet to be demonstrated in a clinical study.

Management of Increased ICP

ICP is considered a major contributor to mortality after ICH; thus, its control is essential. ICP may be managed through osmotherapy, controlled hyperventilation, surgery and other measures. A therapeutic goal for all treatment of elevated ICP is ICP <20 mm Hg and cerebral perfusion pressure (CPP) >70 mm Hg37. Optimal head position can be adjusted according to CPP values. Patients with suspected elevated ICP and deteriorating level of consciousness are candidates for invasive ICP monitoring. The GCS level that requires ICP monitoring should be based on rate of decline (of GCS) and other clinical factors such as CT evidence of mass effect and hydrocephalus. In general, ICP monitors should be placed in (but not limited to) patients with a GCS score of <9 and all patients whose condition is thought to be deteriorating due to elevated ICP (level of evidence V, grade C recommendation). The type of device depends on availability, experience, and situation. Intraventricular ICP monitors and intraparenchymal fiberoptic ICP devices are commonly used methods of monitoring ICP.

In addition to the mass effect of the hematoma, secondary hydrocephalus may contribute to elevated ICP. Ventricular drains should be used in patients with or at risk for hydrocephalus. Drainage can be initiated and terminated according to clinical performance and ICP values. Because of infectious complications, external drainage devices must be checked regularly, and duration of placement ideally should not exceed 7 days (level of evidence V, grade C recommendation). Use of anti-infectious prophylaxis is optional (level of evidence V, grade C recommendation). There is some recent evidence to support the use of intrathecal thrombolytics in the treatment of IVH, but this must be replicated in a larger manner.

The beneficial effect of sustained hyperventilation on ICP is unresolved and has not been systematically examined in this condition. In theory, reduction of ICP by hyperventilation ceases when the pH of cerebrospinal fluid (CSF) reaches equilibrium. In practice, this may not occur for many hours. Some authors believe that prolonged hyperventilation has a beneficial effect on brain water volume. As with osmotherapy, adverse rebound effects can occur if normal ventilation is resumed too quickly. When hyperventilation is deemed no longer necessary, gradual normalization of serum PCO2 should occur over a 24 to 48 hour period. In general, if hyperventilation is instituted for elevated ICP, PCO2 should be maintained between 30 and 35 mm Hg until ICP is controlled. In addition, most patients will require sedation with agents such as propofol, benzodiazepines, or morphine and treatment with intermittent muscular paralysis. If elevated ICP cannot be controlled, induced barbiturate coma or therapeutic hypothermia may be instituted. However, these should be viewed as a last ditch option and not part of a standardized algorithm in the treatment of elevated ICP in patients with ICH. Short-acting barbiturates such as thiopental are known to effectively reduce elevated ICP. The effect is presumably mediated through reduction of cerebral blood flow and volume. In addition to reducing the volume of the normal brain, barbiturates reduce brain swelling, perhaps as a result of mild systemic hypotension, and may act as free radical scavengers. Hypothermia may be neuroprotective and decreases ICP by lowering cerebral blood volume (by lowering metabolic demand).

The complications of both methods include pneumonia (from immobility and immune suppression), hypotension (most pronounced at the time of bolus barbiturate administration), and predisposition to infection. Systemic hypotension results from decreased venous tone, decreased baroreflex tone, and sympathetic activity. Cardiovascular side effects may be aggravated by concomitant dehydration

promoted by osmotherapy and diminished cardiac filling pressures. Maximal reduction in cerebral metabolism may be accompanied by electrocerebral silence (continuous EEG recording) and rises in jugular oxygen saturation.

Fluid Management

The goal of fluid management is euvolemia. Optimal central venous pressure (CVP) or pulmonary wedge pressure may vary from patient to patient. Fluid balance is calculated by measuring daily urine production and adding for insensible water loss (urine output plus 500 ml for insensible loss plus 300 ml per degree in febrile patients). Electrolytes (sodium, potassium, calcium, and magnesium) should be checked and substituted according to normal values. Acidosis and alkalosis should be corrected according to blood gas analysis.

Prevention of Seizures

Seizure activity can result in neuronal injury and worsening of an already critically ill patient and, therefore, must be treated aggressively. Additionally, nonconvulsive seizures may contribute to coma in10% of neuro-critical care patients. In patients with ICH, prophylactic antiepileptic therapy (preferably phenytoin with doses titrated according to drug levels [14 to 23 μg/ml]) may be considered for 1 month. This should be tapered and discontinued if no seizure activity occurs during treatment, although data supporting this therapy are lacking (level of evidence V, grade C recommendation).

Management of Body Temperature

Body temperature should be maintained at normal levels, unless deliberate hypothermia is attempted. Acetaminophen 650 mg or cooling blankets should be used to treat hyperthermia >38.5° C. Some authors recommend a more aggressive approach to hyperthermia. In febrile patients or those at risk for infection, appropriate cultures and smears (tracheal, blood, and urine) should be obtained and antibiotics given. If ventricular catheters are used, CSF analysis should be performed to detect signs of meningitis. If infection occurs, appropriate antibiotic therapy should follow.

Other Medical Management Issues

Many patients who are delirious or stuporous are agitated. Hyperactivity is distressing to patients, caregivers, and family and may lead to self-injury. If psychological support is insufficient, prudent use of minor and major tranquilizers is recommended. Short-acting benzodiazepines or propofol are preferred. Other drugs such as analgesics and neuroleptics can be added if necessary. Doses and regimen should be titrated to clinical needs.

Pulmonary embolism is a common threat during the recovery period, particularly for bedridden patients. Pneumatic devices and heparin (and related compounds) can decrease the risk of pulmonary embolism. Depending on the patient's clinical state, physical therapy, speech therapy, and occupational therapy should be initiated as soon as possible.

GUIDELINES FOR SURGICAL REMOVAL OF ICH

Patients with small hemorrhages (<10 cm3) or minimal neurological deficits should be treated medically because they generally do well with medical treatment alone (levels of evidence II through V, grade B recommendation). Patients with a GCS score <4 should also be treated medically because they uniformly die or have extremely poor functional outcome that cannot be improved by surgery (levels of evidence II through V, grade B recommendation).

Patients with cerebellar hemorrhage >3 cm in diameter who are neurologically deteriorating or who have brain stem compression and hydrocephalus from ventricular obstruction should have surgical removal of the hemorrhage as soon as possible (levels of evidence III through V, grade C recommendation). [51]

Stereotactic aspiration may be associated with better outcomes than standard craniotomy for moderate-sized cerebellar hemorrhages and at other sites, but this hypothesis has yet to be tested in a randomized study (no recommendation). [52] Young patients with large lobar hemorrhages (>50 cm3) who deteriorate during observation often undergo surgical removal of the hemorrhage. However, the efficacy of this approach is supported only by the small endoscopic study of Auer and colleagues3 (levels of evidence II through V, grade B recommendation). An ICH associated with a structural lesion such as an aneurysm or a vascular malformation may be removed if the patient has a chance for a good outcome and the structural vascular lesion is surgically accessible (levels of evidence III through V, grade C recommendation). Ultra-early removal of ICH by localized, minimally invasive surgical procedures is promising but untested (no recommendation).

In conclusion, therapy for ICH is largely supportive. Surgery has a definite role in cerebellar ICH and may play an

increasing role in supratentorial ICH. Medical management remains supportive and largely untested [49].

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