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Overview of Intracerebral Hemorrhage

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Abstract

Stroke is categorized into two major subtypes i.e., ischemic and hemorrhagic and is one of the major causes of morbidity and mortality worldwide. Primary intracerebral hemorrhage (ICH), i.e. spontaneous extravasation of blood into the brain parenchyma, begins very suddenly and is a medical catastrophe. The well-known risk factors for ICH are hypertension, heavy drinking of alcohol, and anticoagulant medication. Risk factors for early death include clinical and radiological severity of the bleeding. Moreover, intraventricular bleeding, use of anticoagulants, and high blood pressure on admission also predict early death after ICH. CT brain imaging is the immediate modality for establishing diagnosis and supplemented with MR imaging depending upon aetiology. Treatment of patients with ICH includes standard supportive care, medical management and surgical intervention.

Keywords : Stroke; Intra cerebral hemorrhage; Hypertension

Introduction

Stroke is categorized into two major subtypes i.e., ischemic and hemorrhagic and is one of the major causes of morbidity and mortality worldwide [1]. Primary intracerebral hemorrhage (ICH), is defined as bleeding that evolves within the tissue of the brain. It results from the rupture of small, penetrating vessels and is usually attributed to hypertension or amyloid angiopathy. After the onset, bleeding may continue and the hematoma grow for several hours, leading to progressive clinical deterioration of the patient's condition [2-4]. Computed tomography (CT) soon after the onset of symptoms is crucial for the diagnosis. Case fatality is high, as 35–52% of patients die within 30 days and half of the deaths occur in the first two days [5-7]. Up to 58% of survivors have been reported to be functionally independent at 1 year [8].

The incidence of ICH varies geographically, ranging from 10 to 20/100,000 persons per year [9,10]. ICH incidence in Finland seems to be somewhat higher, 21 to 31/100,000 persons/year [11-13]. The highest incidence has been reported in Japan, 48/100,000 persons/year. The well-known risk factors for ICH are hypertension, heavy drinking of alcohol, and anticoagulant medication [14,15]. Risk factors for early death include clinical and radiological severity of the bleeding. Low Glasgow Coma Scale (GCS) score (i.e. level of consciousness) and hematoma volume appear to be the most important predictors for early death after ICH [16]. Moreover, intraventricular bleeding, use of anticoagulants, and high blood pressure on admission also predict early death after ICH [5, 8, 14 and 17-19]. Treatment of patients with ICH has turned out to be complicated in many ways.

A. Symptoms and diagnosis of intracerebral haemorrhage

The clinical presentation of ICH usually starts with a focalneurological deficit followed by progression of symptoms over minutes to hours [20]. This symptomatic progression over hours is uncommon in patients with ischemic stroke. Another manifestation is a sudden decline in the level of consciousness. Increased blood pressure and impaired level of consciousness are common. Vomiting is more common in patients with ICH. Headache is more common with ICH than with ischemic stroke but less common than with subarachnoid hemorrhage [21]. Diagnosis is confirmed by brain imaging. Computed tomography (CT) and magnetic resonance imaging (MRI) show the presence of ICH equally well. CT has the advantage of demonstrating the intraventricular extension of the hemorrhage, while MRI shows better the underlying structures and perihematomal edema.

B. Subgroups of intracerebral hemorrhage

1. Primary intracerebral haemorrhage

The term 'spontaneous intracerebral hematoma' refers to non-traumatic bleeding into the brain parenchyma [1]. 'Primary intracerebral hemorrhage' means a spontaneous hematoma without any secondary cause, such as vascular abnormality or brain tumour, which have been ruled out by radiological or pathological investigations [14]. Primary intracerebral hemorrhage originates from bleeding of small arteries damaged by chronic hypertension, cerebral amyloid angiopathy (CAA), or other causative factors [14,22]. Almost two thirds of primary intracerebral hematomas are related to chronic hypertension [23]. In these cases the hematoma is typically located deep, in the basal ganglia, thalamus, or brain stem [1] figure 1. ICHs related to CAA, on the other hand, are mainly lobar or subcortical hematomas [22] Figure 2.

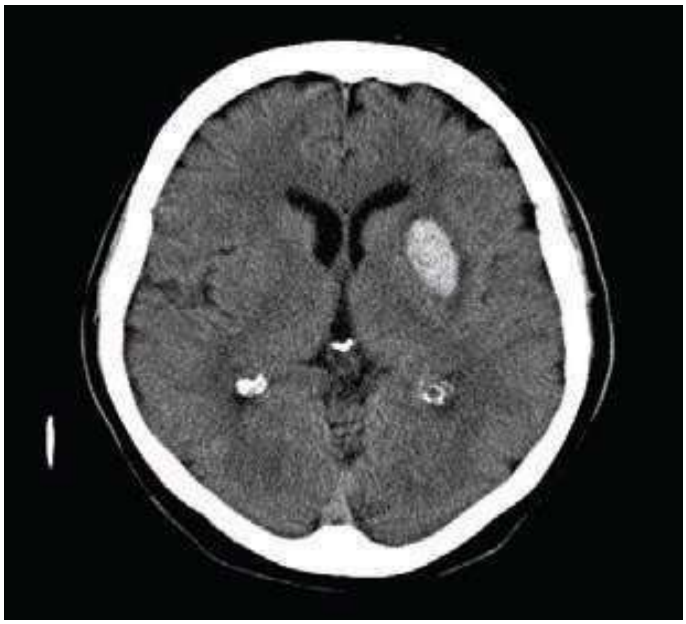

Figure 1: Left putaminal ICH in a 60-year-old female with a history of Hypertension.
(Source: Report of patient admitted in Department of Neurology, Narayana Medical College & Hospital, Nellore, A.P., India).

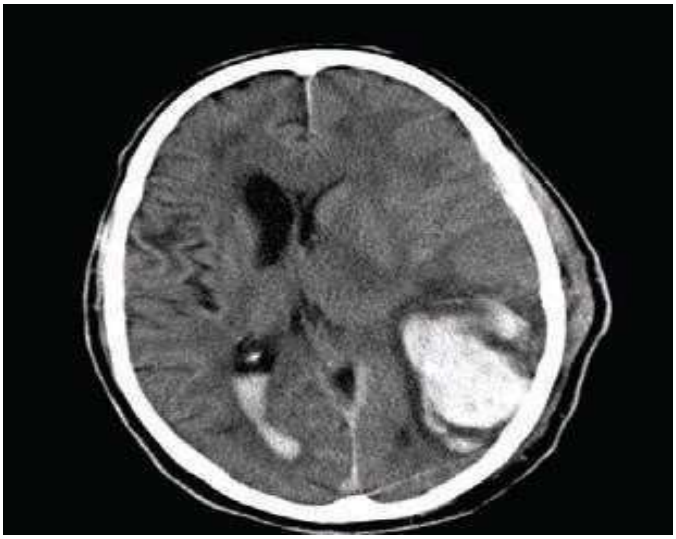

Figure 2: Left parietal hematoma in a 57-year-old man without a history of Hypertension
(Source: Report of patient admitted in Department of Neurology, Narayana Medical College & Hospital, Nellore, A.P., India).

2. Secondary intracerebral haemorrhage.

Only 12–18% of all ICH cases are classifiable as the secondary type of ICH [14]. The most important causes of secondary ICH are vascular abnormalities, which carry the risk of rebleeding. The secondary causes of ICH are represented in table 1.

Causes
Vascular or structural abnormality
Aneurysm
Arteriovenous malformation
Dural arteriovenous fistula
Cavernous hemangioma
Venous angioma
Moyamoya disease
Tumor
Coagulopathy
Hematological disease (leukaemia, thrombocytopenia)
Disseminated intravascular coagulation
Alcohol-induced coagulopathy
Hepatic failure
Other
CNS vasculitis
Cerebral venous thrombosis
Reperfusion after carotid endarterectomy
After thrombolysis

Table 1: Secondary causes of ICH
Source: Predictors of early deterioration and mortality in black Americans with spontaneous intracerebral hemorrhage. Stroke (1995) 26: 1764–1767.

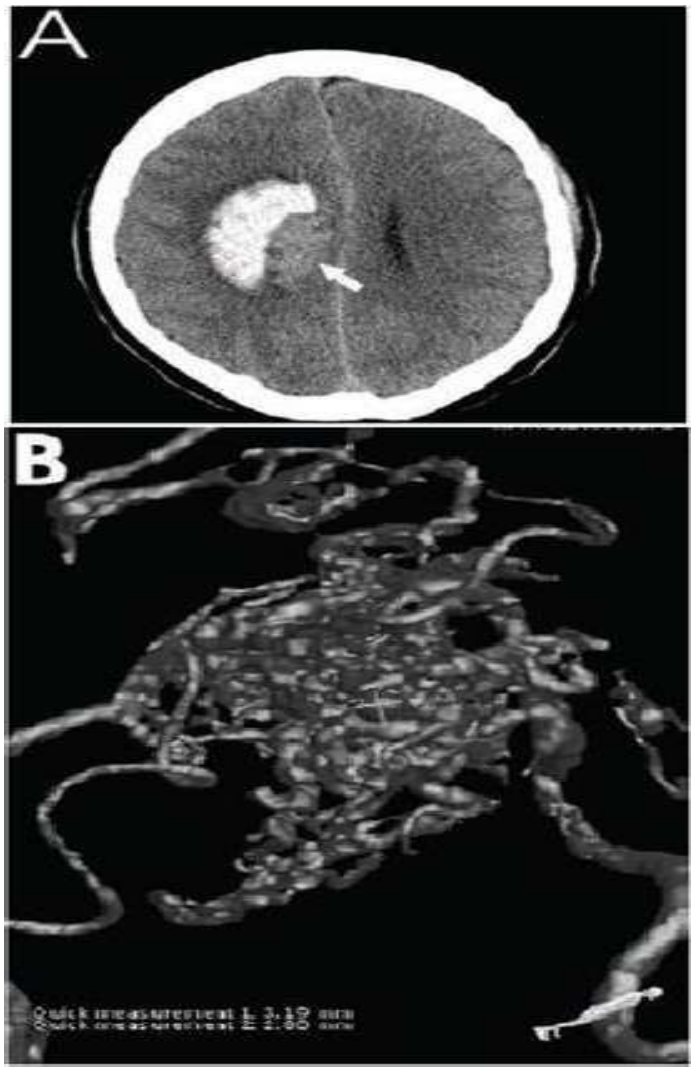

Figure 3: A. CT scan of right-side ICH caused by AVM in a 44-year-old male. AVM is visible even in the plain CT scan (white arrow). B. 3D-DSA of the aneurysm with a small secondary aneurysm. (Source: Report of patient admitted in Department of Neurology, Narayana Medical College & Hospital, Nellore, A.P., and India).

C. Risk factors of primary intracerebral hemorrhage

1. Untreated and treated hypertension

Hypertension is the most prevalent risk factor for ICH [23]. It is considered a major risk factor in half of all patients presenting with ICH and in 75% of those with deep hematomas [12,24-30]. The risk of ICH increases at higher blood pressure values [31]. Untreated hypertension has been found to be a highly prevalent risk factor for hemorrhagic stroke (ICH and subarachnoid hemorrhage combined) [29, 32].

2. Diabetes

Diabetes is a well-known risk factor for ischemic stroke [33, 34]. On the other hand, it is less clear whether there is an association between diabetes and ICH [35].

3. Amyloid angiopathy and genetic factors

Cerebral amyloid angiopathy (CAA) is a major cause of lobar media, which mainly affects cortical and leptomeningeal vessels, predisposing to ICH. CAA is caused by the deposition of β-amyloid protein on the vessel wall [14]. The prevalence of CAA rises with age, being approximately 60% among those over 90 years of age [36]. The diagnosis is clinically suspected in multiple lobar bleedings with no other obvious cause of ICH in patients 55 years of age or older [37].

4. Alcohol consumption and stimulant use

The relationship between alcohol intake and increased ICH risk has been identified in many case-control studies [26&38-43]. Short-term recent moderate or heavy binge alcohol intake within 24 hours or one week seems to be a more important risk factor for ICH than long-term habitual heavy drinking [26]. Amphetamine or cocaine use can provoke ICH. This uncommon etiology is mainly seen in young adult [44]. Cigarette smoking is a well-known predictor of ischemic stroke in both men and women, [45, 46]. but its role as a risk factor for ICH is less clear.

5 . Use of anticoagulants and platelet inhibitors

The risk for ICH in warfarin users has been reported to be 8 to 10-fold compared with nonusers [47, 48]. ICHs associated with oral anticoagulation account for a considerable proportion of all ICHs (6.9% according to Cucchiara *et al.* 2008), and mortality from such ICHs is very high, 50–67 % [15, 49].

6 . Other risk factors

Modern imaging methods, such as gradient-echo T2*-weighted MRI, can visualize blood breakdown products. This has led to the discovery of cerebral microbleeds [50]. Microbleeds are frequent findings in patients with ICH and may also predict ICH [51,52]. If patients with previous ischemic stroke have microbleeds and use antithrombotic and anticoagulant drugs, they may have a greater risk for ICH [53] compared with those who do not have microbleeds. Primary ICH can also develop in medical conditions that acutely raise blood pressure, such as eclampsia, acute glomerulonephritis, and pheochromocytoma [54, 56]. Strenuous physical activity has also been reported to be a risk factor for ICH [57, 58].

D. Short-term outcome after primary intracerebral hemorrhage

1. Predictors for short-term outcome

ICH is the most devastating subgroup of strokes with high mortality and morbidity. 35- 52% of patients are likely to die within the first month after the bleeding [5-7&12]. Half of the deaths occur in the first 2 days [5]. Of all patients with ICH, 20% are functionally independent at six months [7], and 58% of ICH survivors are functionally independent at 1 year [8]. The relative proportion of functionally independent patients increases over time because many severely handicapped patients die within the first year after ICH [12]. The well-known predictors for early death and poor functional outcome include the clinical and radiological severity of the bleeding. Level of consciousness and hematoma volume [5, 8, 14, 18 19] as well as the presence of intraventricular blood [18, 59] have repeatedly been reported to independently predict death within 30 days after the bleed. Age has not been systematically reported to influence short-term outcome. However, it has been reported [59] that very old age (≥ 80 years) significantly increases 30-day mortality. High mean arterial blood pressure (MABP) on admission has been repeatedly reported to be associated with early death and poor functional outcome after ICH [60-62]. This may be related to the "Cushing reflex"; blood pressure is elevated concomitantly with intracranial pressure to maintain a sufficient perfusion pressure in the brain [63]. A widely used ordinal prediction model for 30-day outcome was presented by Hemphill *et al.* 2001 (Table 2). The total ICH score is the sum of the points assigned to the characteristics mentioned in the Table 2 (0–6 points). Thirty-day mortality increases as the ICH score rises.

In the cohort of patients treated in California University Hospital, ICH scores of 1, 2, 3, and 4 associated with mortality rates of 13%, 26%, 72%, and 97%, respectively. None of the patients with an ICH score of 0 died, while all the patients with an ICH score of 5 died, and none scored 6 points.

Component	ICH Score Points
CGS	
4-Mar	2
12-May	1
13-15	0
ICH Volume, cm3	
≥ 30	1
< 30	0
IVH	
Yes	1
No	0
International locations	
Yes	1
No	0
Age,y	
≥80	1
<80	0
Total ICH Score	0-6

Table 2: Determinant of the practical ICH score (Hemphill et al. 2001).GCS score indicates GCS score on initial presentation (or after resuscitation); ICH volume, volume on initial CT calculated using ABC/2 method; and IVH, presence of any IVH on initial CT. (Source : The ICH Score A Simple, Reliable Grading Scale for Intracerebral Hemorrhage , Hemphill et al, 2002).

2. Cardiac diseases as predictors for outcome

In patients with ischemic stroke, previous cardiac diseases (cardiac failure, ischemic heart disease, or atrial fibrillation) have been reported to influence outcome after stroke, and cardiac complications are common [64]. One population-based study found cardiac disease (coronary artery disease or atrial fibrillation) to be an independent predictor for 30-day mortality [65]. Both antiplatelet agents and anticoagulants are commonly used in secondary prevention of cardiac disease. Consequently, the use of these agents may have emerged as a risk factor for early death after ICH due a proxy effect of a history of cardiac disease.

3. Hypertension and diabetes as predictors for poor outcome.

Although hypertension is the most important risk factor for ICH, pre-existing hypertension has not been reported to predict early death or poor functional outcome after ICH [13, 26, 65]. Diabetes has been reported to be an independent risk factor for early death in two studies [66, 67]. The mechanism of how diabetes increases the risk for early death is unclear, although hyperglycemia may cause brain edema and perihematomal cell death after ICH according to experimental studies [68].

E. Complications of primary intracerebral hemorrhage

1. Hematoma enlargement

In the past, ICH was believed to be a stable process with maximal volume at the onset. Enlargement of the primary ICH was first reported by Kelley *et al.* 1982 in a case series of 4 patients showing rapid hematoma enlargement between the admission CT scan and subsequent contrast-enhanced scans. Expansion usually progresses during the first 6 hours after the onset of stroke, and it is observed in only 5–12 % of patients scanned later than 6 hours after the onset [2, 3 & 23].

2. Cardiac complications

The risk for cardiopulmonary instability in patients with ICH is highest during the first 24 hours after the onset [14]. Increased intracranial pressure leads to severe hypertension and bradycardia, called Cushing responses [63].

3. Venous thromboembolism

Patients with ICH suffer from prolonged immobility due their impaired consciousness and/or paresis of the lower extremities.Warlow *et al.* 1975 showed that, if nothing is done to prevent deep venous thrombosis (DVT), 53% of stroke patients develop DVT and 15% develop pulmonary embolism (PE).

4. Hydrocephalus

Infratentorial ICH or extension of ICH to the ventricles may lead to obstructive hydrocephalus. Both intraventricular hemorrhage and hydrocephalus in patients with ICH are associated with high mortality [18, 69].

5. Surgical complications

External ventricular drainage carries risks for intracerebral hematoma, intraventricular hematoma, and infections [70]. The incidence of bacterial meningitis after the placement of drainage varies from 6 to 22% [70, 71].

F. Treatment of primary intracerebral hemorrhage

1. Conservative treatment

Conservative treatment of ICH covers all emergency and critical care procedures except operative treatment. In general, all patients with ICH should be admitted to a neurosurgical or neurological intensive care setting, because it reduces mortality [69].

2. Securing the airways

The onset of ICH is typically followed by a rapid decline of consciousness and progression of neurological symptoms. Loss of the normal reflexes to maintain an open airway develops, which increases the risk of aspiration, hypoxemia, and hypercapnia [72]. Sedatives (such as propofol) and non-depolarizing neuromuscular drugs (such as vecuronium) are used to facilitate the intubation procedure.

3. Controlling blood pressure

High admission MABP has been repeatedly reported to predict early death and poor outcome after ICH [60,62]. Blood pressure maintains the cerebral perfusion pressure (CPP), and overaggressive lowering of blood pressure may theoretically worsen cerebral perfusion in cases with high intracranial pressure (CPP = MABPICP). The recommendations of the European Stroke Initiative 2006 [15] and the American Stroke Association 2007 [73] for the management of high blood pressure are presented in Table 3.

The recommended medication for hypertension consists of intravenous 10 to 80 mg boluses of labetalol at every 10 minutes [74].

Groups	AHA recommendations Class IIb, level of evidence C			EUSI recommendations Class IV evidence	
	Very high pressure	Elevated ICP	Not elevated ICP	Hypertension	Normotensive
Treatment level	SBP > 200 or MABP > 150	SBP > 180 or MABP > 130	SBP > 180 or MAPB > 130	SBP > 180 and/or DBP > 105	SBP > 160 and/or DPB > 95
Target level	Aggressive reduction	keep CPP > 60 to 80	MABP ≤ 110	BP 170/100	BP 150/90

ICP = intracerebral pressure, SBP = systolic blood pressure, DBP = diastolic blood pressure, MABP = mean arterial blood pressure, BP = blood pressure, CPP = cerebral perfusion pressure. All values are in mmHg.

Table 3: Recommendations given by the American Heart Association (AHA) and the European Stroke Initiative (EUSI) for the treatment of acute high blood pressure in patients with IC

Source: The recommendations of the European Stroke Initiative 2006 (Steiner et al. 2006b) and the American Stroke Association 2007 (Broderick et al. 2007) for the management of high blood pressure.

4. Management of increased intracranial pressure

Emergency management of elevated intracranial pressure (ICP) includes head elevation, use of mannitol, and hyperventilation even before the installation of any ICP measurement devices. The management also includes sedation, phenobarbital therapy, hypothermia, and fluid infusion according to the cerebral perfusion pressure (CPP) guided therapy [50, 75-77]. Neurosurgical methods for lowering ICP include placement of an external ventricular catheter and decompressive craniectomy [78].

5. Reversal of anticoagulation

Anticoagulant treatment preceding the onset of ICH is related to high mortality and poor functional outcome compared to ICH without preceding anticoagulation [25,49,79]. Anticoagulation should be reversed immediately to prevent further deterioration, and warfarin users should have their International Normalized ratio (INR) value lowered below 1.4 immediately after the diagnosis of ICH [80]. This is done by using either fresh frozen plasma or prothrombin complex concentrate together with vitamin K. If the patient has used heparin or low molecular weight heparins (LMWH) before the onset of ICH, the effect of the medication should be reversed with protamine sulphate [81].

Conclusion

ICH is most commonly caused by hypertension, arteriovenous malformations, or head trauma. Intracerebral hemorrhage results in sudden, severe symptoms like headache, loss of consciousness, vomiting but headache may be absent (particularly in the elderly), and small hemorrhages may mimic ischemic stroke. CT brain imaging is the immediate modality for establishing diagnosis and supplemented with MR imaging depending upon aetiology. Treatment of patients with ICH includes standard supportive care, medical management and surgical intervention.

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