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Introductory Chapter: An Introduction to Hypertension-Related Intracerebral Hematomas

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1. Introduction

Of all cerebral strokes, hemorrhagic stroke forms approximately 15%, of which hypertensive intracranial hematomas (HIH) constitute the vast majority [1, 2]. Intracranial hemorrhage (ICH), contrary to popular belief, is not a ‘modern disease’ and is mentioned as ‘Cerebral Apoplexy’ in the writings of antiquity credited to Hippocrates [3]. ICH can be attributed to a number of underlying pathologies including amyloid angiopathy, cryptic vascular malformations, arteritis and hypertension [3]. Despite modern imaging such as computed tomography (CT) and magnetic resonance imaging (MRI), diagnostic uncertainty inhibits a serious study of the natural history and epidemiology of ICH [3]. ICH is predominantly of two types: primary ICH, when no underlying pathology is identifiable and secondary ICH, when hemorrhage occurs in a pre-existing lesion such as a tumor or arteriovenous malformation [2, 3].

ICH occurring spontaneously is often referred to as ‘Hypertensive’ in common medical parlance, and there is little doubt that elevated blood pressures promote the occurrence of ICH; although several environmental factors have been identified as risk factors, hypertension remains the single most relevant of them all [3]. A systematic review of literature has demonstrated that hypertension is one of the commonest and most prevalent risk factors associated with ICH [1, 4]. A 3.5-fold increase in the incidence of ICH is noted in hypertensive patients in comparison with normotensive patients [2]. Isolated systolic hypertension is found to correlate most strongly with ICH in contrast to diastolic hypertension and borderline isolated systolic hypertension [1]. The other factors found to have some relevance to the occurrence of ICH are cigarette smoking (increases risk of ICH by 4x to 5x), alcohol consumption, diabetes mellitus, use of oral contraceptives and male gender [1, 3]. There has also been an association between low mean serum cholesterol and the incidence of ICH, especially in the older individuals [3, 5]. HIH also has a racial predilection, being highest in Asian population and least in the Caucasians [3]. Of the myriad diseases being studied today, HIH is not only one of the many which is being

investigated so thoroughly that a clear understanding of the risk factors and their modifications has attributed to the plunging incidence of the disease [3].

2. Clinical presentation

Clinical symptomatology of the ICH is dependent on the dissection of the brain tissue by the expanding hematoma and mass effect, implying the importance of the location and size of the hematoma [6]. Location of ICH is usually in the deep nuclei of the brain: basal ganglia (40%), the thalamus (10–25%), the cerebellum (5–10%) and the pons (5%) [6]. Thalamic hematomas may further be subdivided into four different locations: anterolateral (21%), medial (15%), posterolateral (55%) and dorsal (9%) [7]. Lobar hematomas involving the neocortex account for 20% or less [6]. The hallmark of ICH is ‘Acute neurological deficit with rapid progression,’ in contrast to ischemic strokes [6]. Fluctuating neurological symptoms are extremely uncommon [6]. The general symptoms include raised intracranial pressure which manifests as headache (33–57%), nausea and vomiting (29–46%) and decrease in the level of consciousness (28–37%) [6]. At presentation, 4–20% of ICH patients are in a coma [6]. Meningeal irritation manifesting as neck stiffness and seizures (<10%) are other general symptoms of ICH [6]. Symptomatology related to the location of the hematoma varies. Cortical lobar hematomas in the dominant hemisphere can present with higher mental function symptoms such as aphasia, acalculia or motor apraxia [6]. Non-dominant hemispheric symptoms appear as left-side neglect, agnosia or visuospatial dysfunction [6]. Hematomas may present with symptomatology specific to the cerebral lobe involved such as abulic-apathetic behaviors with frontal lobe involvement and contralateral homonymous hemianopsia with occipital lobe involvement [6]. The involvement of the deep grey nuclei usually depends on the location and direction of the hematoma expansion, e.g., caudate nuclei hematomas may involve the anterior limb of the internal capsule involving predominantly frontothalamic and frontopontine fibers manifesting as prominent neurobehavioral changes, in contrast to putaminal hematomas which usually involve the posterior limb of the internal capsule and may present with contralateral hemiparesis or hemiplegia [6]. Caudate and thalamic aphasias may occur in the dominant hemisphere [6]. Cerebellar hematomas may demonstrate the typical ‘Cerebellar Syndrome,’ and pontine hematomas may present with dense quadriplegia or the typical ‘locked-in syndrome’ in addition to cranial nerve deficits [6].

2.1. Expansion of ICH

Expansion of ICH appears to be more common than initially thought. Over a third of patients may demonstrate the expansion of hematoma over the first 24 h [6]. A fivefold morbidity has been reported with the expansion of the ICH and a significant cause of death in these patients [8]. The radiographic criteria for hematoma expansion have been reported as an increase in hematoma volume by ≥ 12.5 cm or by ≥ 1.4 times [8]. Temporally, the highest probability of hematoma expansion is seen in the hyperacute stage (17% within the first 6 h) [8]. Hematoma enlargement after 24 h rarely occurs [8]. It stands to reason, therefore,

if a hyperacute CT scans reveal an ICH, repeat scans should be considered periodically. There have been speculations about the etiology of the expansion, viz. whether there occur repeated small hemorrhages or there is a continuous oozing [9]. Expansion of an ICH generally follows the general 'rule of thumb,' and the larger the hematoma at presentation, the more likely it is to expand [10].

Interestingly, hematoma expansion has been shown to be an independent determinant of morbidity and mortality in ICH [11]. For an increase of 10% in the size of the ICH, there appears to be a 5% increased hazard of death [12].

3. Pathophysiology and etiopathogenesis of ICH

It has been proven that ICH usually occurs in the area supplied by small perforating arterioles (50–700 μm in dia.) and the rupture occurs as a consequence of hypertension-related pathological changes which include fibrinoid necrosis, microaneurysm formation and lipohyalinosis [6]. It is conjectural that the pulse pressure may in fact be more important than the absolute blood pressure, since the turbulence generated would damage the vessel resulting in a rupture if collagen is inadequate especially in the presence of repetitive cycles of arteriolar dilatation [7]. The Charcôt-Bouchard aneurysm, which has been a controversy since its original description, is a fusiform dilatation of the thinning, vasculopathic arteriolar wall which virtually entirely consists of collagen [7]. The controversy has stemmed from the use of the term 'aneurysm' for the 'non-saccular,' 'fusiform' dilatation of the vessel walls [7]. These, then, morphologically, characterize a segmental disease, fusiform (dilatation by a factor of two or three, over lengths of 100–200 μm), which has been revealed by the use of alkaline phosphatase techniques and may be visualized in the pathological specimen of the hematoma as extensions of a vessel into an acute hematoma lined by a endothelial lining [7].

4. Management

The management is symptomatic and mainly supportive, and no definite treatment modality has proven to improve outcomes in ICH [6]. Mortality is high, generally ranging from 30 to 55% with a very high case fatality rate in the first 7 days [6]. The long-term prognosis for the survivors is not very encouraging with less than 30% of patients being independent at 3 months of the ICH ictus [6]. The goals of management therefore include prevention of further brain injury by deterring hematoma expansion, restricting edema and to attempt recruiting the brain's plasticity to improve the rehabilitation outcome [9]. Prehospital management is vital and primarily consists of ventilator and cardiovascular support and transporting the patient to the nearest available stroke unit [9, 13]. Management at the emergency room (ER) consists of a thorough neurological assessment, management of elevated blood pressures and neuroradiological evaluation and may entail emergency procedures such as insertion of an external ventricular drain, monitoring ICP and its management and reversal of coagulopathy [13]. Critical pathways should be formulated and followed at the

ER level [13]. Computed tomography and magnetic resonance imaging are both reasonable initial modalities of investigation, especially if the differentiation between infarction and hemorrhage is difficult clinically [13]. However, CT is considered the gold standard for the diagnosis of hemorrhage [13]. Intensive blood pressure lowering has been evaluated by several trials, and the majority of results reflect a proclivity toward rapid reduction to less than 140 mm Hg [10]. This seems clinically reasonable, generally well tolerated and appears to impact hematoma expansion in ICH [10].

4.1. Ultra-early hemostatic therapy for ICH

Ultra-early hemostatic therapy for ICH is recommended because an increase in the hematoma volume and expansion are associated with poorer outcome [12]. ICH has an increased incidence in patients on oral anticoagulants or antiplatelet drugs and those with coagulation factor deficiencies and platelet abnormalities [12]. Ultra-early hemostatic therapy is particularly indicated in these patients and includes appropriate intervention, such as platelet transfusions or administration of vitamin K, in addition to the other management options outlined above [12].

4.2. Surgical management

Early studies had failed to demonstrate any significant difference between conservative and surgical management of ICH [9]. There were also reports of poorer surgical outcome due to the trauma of surgery itself and a higher postoperative re-hemorrhage rate [7]. There have been over a dozen randomized controlled trials, addressing the issue of the surgical management of ICH [9]. The surgical approach to the hematoma depends on the location and the depth of the hematoma and eloquence of the brain involved among other considerations [9]. It has also been reported that surgery may be beneficial only if undertaken within 8 h of ictus, thus limiting the toxic effects of the blood components on the brain [14].

4.3. Recent advances and trials

The initial Surgical Trial in ICH (STICH) trial of over 1000 patients did not reveal any statistically significant benefit of surgery for supratentorial ICH except for hemorrhage within 1 cm of cortical surface [7]. The STICH II trial for lobar hematomas found a small (3.7%) absolute benefit in the surgical group, but it was riddled with controversy because of the inclusion of patients with a normal level of consciousness (i.e., clinically no evidence of raised ICP) [14]. The STICH II trial, however, did demonstrate significant benefit from surgery in the group that was considered a poor prognosis group (i.e., low GCS and a large hematoma volume) [14]. There have been several recent trials researching minimally invasive surgical techniques such as endoscopic or stereotactic aspiration with or without fibrinolytic agents [9]. 'Minimally Invasive Surgery and rtPA for Intracerebral Hemorrhage Evacuation' (MISTIE) is a series of clinical trials where minimally invasive evacuation of ICH and the use of either a thrombolytic agent [MISTIE II (2013) and MISTIE III (ongoing)] or a CT-guided endoscope (MISTIE-ICES) is under study [15]. Early results were favorable for the successful and early

removal of the ICH in addition to demonstrating a fall in the mortality rate and long-term qualitative outcome [15].

4.4. Recombinant activated factor VII (rFVIIa) therapy

Recombinant activated factor VII (rFVIIa) therapy, although a well-documented therapy in the Haemophilias, it has found limited application in the indiscriminate use in ICH and is associated with multiple thromboembolic complications including death [11]. It has, however, demonstrated a reduction in the growth of the ICH when administered within 4 h of the ictus. Perihematoma edema and secondary injury are the focus of attention and includes altering events at the molecular level, which would precipitate secondary injury in ICHs. These include iron-mediated toxicity and acute inflammation which is induced by the degradation products of hemoglobin [10]. Multiple modalities, such as the use of minocycline, hypothermia and albumin, have been advocated as possible neuroprotective agents in the prevention of secondary injury from inflammation in ICH [10]. Deferoxamine mesylate is investigated to counter the neurotoxic effects of iron resulting from hemolysis of the red blood cells [10]. Preclinical work with Pioglitazone has revealed that the transcription factor peroxisome proliferator-activated receptor gamma plays an essential role in enhancing phagocytosis with the dual role of restraining oxidative stress and inflammation [10].

5. Prognosis

There is a slightly more than 1% chance of a survivor of an ICH to endure either a new ICH or an ischemic stroke each year [9]. The three most important and reliable indicators of poor outcome after ICH are volume of the hematoma, level of consciousness and intraventricular hemorrhage (IVH), which is implicated most likely due to the involvement of more centrally located structures within the brain [9, 12].

6. Conclusion

Although, hemorrhagic stroke has been known since antiquity, it has been an extremely challenging medical condition to treat. One that has been investigated exhaustively, and future avenues of treatment will most likely combine several approaches not just at reducing the size of the hematoma and prevention of its expansion but also therapies aimed at mitigating the secondary insult. Further focus, understandably, would rest on grasping the molecular mechanisms of the pathogenesis and the innate immune responses and formulating remedies to combat these effects. This chapter has attempted a brief overview of the topic. Further sections will highlight many aspects of this neurological entity in depth, hopefully illuminating our understanding of this ubiquitous but challenging disorder.

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References

- [1] Sessa M. Intracerebral hemorrhage and hypertension. *Neurological Sciences*. 2008; **29**(S2):258-259
- [2] Ikram M, Wieberdink R, Koudstaal P. International epidemiology of intracerebral hemorrhage. *Current Atherosclerosis Reports*. 2012; **14**(4):300-306
- [3] Kase C, Caplan L. *Intracerebral Hemorrhage*. Boston: Butterworth-Heinemann; 1994
- [4] Ciccone A, Pozzi M, Motto C, Tiraboschi P, Sterzi R. Epidemiological, clinical, and therapeutic aspects of primary intracerebral hemorrhage. *Neurological Sciences*. 2008; **29**(S2):256-257
- [5] Valappil A, Chaudhary N, Girija A, Gopalakrishnan B, Praveenkumar R. Low cholesterol as a risk factor for primary intracerebral hemorrhage: A case-control study. *Annals of Indian Academy of Neurology*. 2012; **15**(1):19
- [6] Ko S, Choi H, Lee K. Clinical syndromes and management of intracerebral hemorrhage. *Current Atherosclerosis Reports*. 2012; **14**(4):307-313
- [7] Auer RN, Sutherland GR. Primary intracerebral hemorrhage: Pathophysiology. *Canadian Journal of Neurological Sciences*. 2005; **32**(Suppl 2):S3-S12
- [8] Kazui S, Naritomi H, Yamamoto H, Sawada T, Yamaguchi T. Enlargement of spontaneous intracerebral hemorrhage: Incidence and time course. *Stroke*. 1996; **27**(10):1783-1787
- [9] Rønning P, Sorteberg W, Nakstad P, Russell D, Helseth E. Aspects of intracerebral hematomas: An update. *Acta Neurologica Scandinavica*. 2008; **118**(6):347-361
- [10] Sonni S, Lioutas V, Selim M. New avenues for treatment of intracranial hemorrhage. *Current Treatment Options in Cardiovascular Medicine*. 2013; **16**(1):1-15
- [11] Mayer S, Brun N, Begtrup K, Broderick J, Davis S, Diringer M, et al. Efficacy and safety of recombinant activated factor VII for acute intracerebral hemorrhage. *New England Journal of Medicine*. 2008; **358**(20):2127-2137

- [12] Gulati D, Dua D, Torbey M. Hemostasis in intracranial hemorrhage. *Frontiers in Neurology*. 2017;**8**:80.
- [13] Morgenstern L, Hemphill J, Anderson C, Becker K, Broderick J, Connolly E, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2010;**41**(9):2108-2129
- [14] Uyttenboogaart M, Jacobs B. Surgery for cerebral haemorrhage—STICH II trial. *The Lancet*. 2013;**382**(9902):1401
- [15] WICH 2017. Brain Injury Outcomes [Internet]. 2017. Available from: <http://braininjury-outcomes.com> [Accessed: June 7, 2017]

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