

Clinical Management of Non-Traumatic Intracerebral Haemorrhage

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Introduction

Non-traumatic intracerebral hemorrhage is a feared entity when it presents to stroke physicians. It tends to have a higher mortality than ischemic stroke and it is the least known form of cerebrovascular event simply because little research has been undertaken in the past few decades. But the circumstances are changing with more focused studies completed in the last few years and some are on-going. This article will provide a very brief overview of the state of progress in the clinical management of non-traumatic intracerebral hemorrhage.

Because of the poor prognosis of this entity aggressive clinical measures need to be taken for its management as most of the morbidity and mortality is from haematoma expansion which occurs early in the presentation coupled with medical complications [1]. Haematoma expansion can be predicted by undertaking computed tomography (CT) angiogram of head in addition to non-contrasted CT of head [2]. The 'Spot Sign'-a feature of seeping of the contrast into the haematoma suggests haematoma expansion which reflects a poor functional outcome and increased mortality. The CT head angiography may also provide early diagnosis of underlying vascular malformation which would influence early management of intracerebral haemorrhage requiring surgical intervention to ablate the malformation and hence prevent progression of bleeding. Factors suggestive of underlying vascular malformation are age of patient under 65 years, female gender, non-smoker, lobar location of haemorrhage, intraventricular extension of the haemorrhage and most important absence of history of hypertension [3,4] (Figures 1 and 2). One of factors to bear in mind in intracerebral haemorrhage is cerebral venous thrombosis. Young female with or without use of combined oral contraceptive presenting with intracerebral hemorrhage should have CT venography or (MRV-magnetic resonance venography) to exclude venous thrombosis as the treatment for this condition necessitate use of anticoagulation [5]. For those without known predisposing factors for cerebral venous thrombosis on historical grounds then a search for malignancy needs to be undertaken. The work up of a patient with intracerebral hemorrhage is shown in Table 1.

It is important to recognize the role of anticoagulation and anti-platelet agents in the etiology of intracerebral hemorrhage. Less common is the presence of acquired and congenital coagulation factor deficiencies and intrinsic platelet abnormalities. Those on Vitamin K antagonist anticoagulation (mainly warfarin) with raised International Normalized Ratio (INR) of greater than 1.5 need administration of Vitamin K 5 to 10 mg intravenously slowly as well as giving them Prothrombin Complex Concentrate (PCC) intravenously to bring the INR to 1.3-1.5 [6,7]. The use of Recombinant Activated Factor VIIa (rFVIIa) does normalize INR rapidly but does not restore thrombin

generation effectively as PCC and hence this therapy is not recommended for use in Warfarin associated intracerebral haemorrhage [8,9]. In addition, the use of this agent leads more thromboembolic events [10] which obviously complicate the clinical situation.

The role of New Oral Anticoagulants (NOACs)-related intracerebral haemorrhage needs adequate study as the reversing agents developed so far have not been studied in intracranial haemorrhage. The NOACs in present use are Dabigatran, Rivaroxaban, Apixaban and Edoxaban. On the other hand, the use of anti-platelets like Aspirin and Clopidogrel present a difficult clinical challenge in ameliorating the intracerebral haemorrhage. A small study on antiplatelet-related intracranial haemorrhage using platelet transfusion provided promising results with reduction in haematoma expansion and better outcome of such patients [11]. However a larger study is on-going to determine this effect and hopefully should report its findings soon [12].

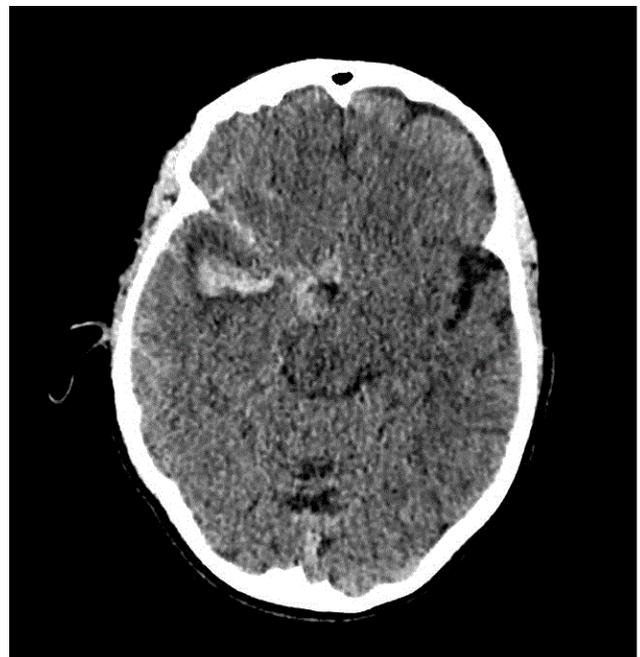
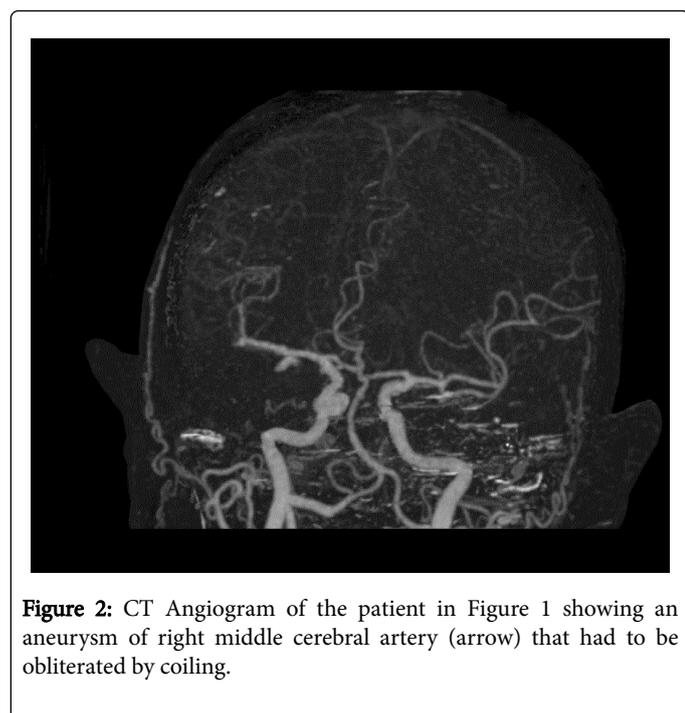


Figure 1: Non-contrasted CT head showing right hemisphere intracerebral hemorrhage with subarachnoid hemorrhage.

History	1) Time of onset of event
	2) Progression of symptoms
	3) Vascular risk factors: History of previous intracerebral haemorrhage, hypertension, diabetes mellitus, smoking
	4) Medications: Anticoagulant drugs, antiplatelets (e.g., Aspirin, Clopidogrel), anti-hypertensives, sympathomimetic drugs (e.g., Ephedrine, Phenylephrine)
	5) Recent head injury
	6) Illicit drugs such as Cocaine
	7) Seizures
	8) Liver disease associated with coagulopathy
	9) Haematologic disorders affecting platelets or other coagulation factors
Examination	Document the severity of neurologic deficit so that improvement or deterioration can be followed objectively
Investigations	1) Blood glucose, Prothrombin Time and Activated Partial Thromboplastin Time, toxicology, ECG, troponin, CT Head (non-contrasted) and consider CT angiography +/- venography

Table 1: Work up of patients with Intracerebral haemorrhage.



Past practices of leaving acute hypertension post-intracerebral hemorrhage is no longer advocated. This the most important advance in its clinical management. Systolic blood pressure tend to rise in this condition and reduction to levels of 140 mm of mercury is desirable as higher blood pressures are associated with haematoma expansion with neurological deterioration and ultimately increased mortality and dependency [13].

An important aspect in the clinical management of patients with intracerebral haemorrhage is meticulous attention to associated medical complications which include thromboembolism, hyperglycaemia, pneumonia, respiratory failure and sepsis from other

causes. These conditions contribute up to a half of proportion of deaths early in the clinical course of intracerebral haemorrhage. Interestingly the risk of thromboembolism is high in these patients especially women. CLOTS 3 trial [14] showed intermittent pneumatic compression reduced proximal deep vein thrombosis (DVT) while the early use of low molecular heparin, enoxaparin [15,16] found a reduction of pulmonary embolism and mortality but no difference in DVT or cerebral haematoma expansion. Thus any of these two modalities of thromboprophylaxis can be used in such patients.

Control of hyperglycaemia in the absence of history of diabetes mellitus is controversial and further studies are warranted to clarify levels to which glucose needs to be maintained in acute management of intracerebral haemorrhage [17,18]. Another complication is the onset of seizures which should be treated in a similar manner like in other situations but the use of prophylactic anti-convulsants is not warranted [19,20]. Pneumonia leading to respiratory failure and sepsis from other sources is an important complication and should be treated vigorously. It needs to be borne in mind that myocardial infarction leading to cardiac failure as well as arrhythmias are not uncommon in patients with intracerebral haemorrhage [21,22] and these cardiac conditions on their own increase mortality. Hence screening for these conditions by undertaking ECG, Chest X-ray and cardiac troponin is important in the overall assessment of such a patient.

Haemorrhage seeping into the ventricular system is a serious complication invariably leads to secondary hydrocephalus which requires prompt draining using a shunt. Clinical presentation would be with increasing headache and/or drowsiness. At present surgery in evacuation of small supratentorial cortical haematoma is not recommended [23-25] except when the haematoma compresses the nearby neural structures in brain stem or obstruction of 4th ventricle leading to hydrocephalus.

Prediction of the outcome in intracerebral haemorrhage within 24 hours of presentation is futile and it is only after aggressive management in the next 24 to 48 hours when the clinical picture stabilises that a meaningful assessment of the future outcome can be made. Recurrent haemorrhage is not uncommon in the next few years

if the patient survives the initial insult. Indicators for such recurrence are microbleeds seen in MRI head in the initial presentation, elderly patient, lobar localisation of bleed and on-going anticoagulation. However, for those whose indication for anticoagulation is strong then those with deep haemorrhage (non-lobar) can be cautiously anticoagulated. Those in atrial fibrillation and have sustained intracerebral haemorrhage and cannot be anticoagulated, then occlusion of left atrial appendage by a Watchman Device [26] can provide a reasonable way forward of addressing the issue of future thromboembolism.

Use of mannitol in intracerebral haemorrhage to counter the oedema and mass effect with the reduction of blood pressure has not been shown to produce significant benefit in terms of mortality or major disability [27].

Conclusion

Aggressive clinical management of non-traumatic intracerebral hemorrhage can be a rewarding experience when it leads to decreased morbidity and mortality. Obviously further studies are required to define the precise parameters of clinical interventions like blood glucose control, anti-platelet drug reversal and role of surgery.

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