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Coagulopathy Following Pediatric Head Injury and Its Importance In Predicting Outcome

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Abstract : Coagulopathy following pediatric head injury is not well known; in spite of its common occurrence following the injury and the fact that it may have a major prognostic role in the predicting the outcome of these children. The authors discuss the incidence, pathophysiology and management of coagulopathy in children with head injuries in light of the available literature and its usefulness in predicting outcome following head injury.

Keywords: Pediatric head injury, coagulopathy, outcome

Introduction

After the first year of life, death in children is mainly the result of head injury caused by accidents[1]. Although children have a higher survival rate than adults following head injury, children less than four years are prone to more long-term cognitive deficits[2], and identifying patient characteristics associated with poor outcome after head injury may result in better management of these variables. Abnormal coagulation is present irrespective of the severity of head injury and appears to be mild and transient after mild head injury, but may be severe in children with severe head injury and may lead to DIC[3-7]. We reviewed the literature on coagulopathy following head injury to have an understanding and overview of the recent advances of this important condition, and its usefulness in pediatric neurosurgical practice.

EPIDEMIOLOGY

Each year more than 20,000 children die from head injury in the United States and head injury is the leading cause of death and morbidity in children between 1 and 14 years, accounting for up to 70% of all pediatric trauma deaths[1]. Though data is not available for India, it is thought to parallel the western data. The incidence of abnormal coagulation parameters, suggestive of DIC varies from 20% to 50%, with the incidence of clinically evident DIC varying from 1-24% in different studies[8-11]. This large variation is probably a reflection on the lack of consensuses in defining DIC, and the percentage of patients having milder forms of coagulopathy is obviously much higher.

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PRESENTATION

Patients are usually asymptomatic for the coagulopathy and the only evidence may be the presence of thrombocytopenia secondary to local platelet consumption, anemia or in its most severe form DIC. Intracranially, coagulopathy may make itself visible as intracerebral, subdural (Fig 1), extradural or scalp hematoma(s) or may manifest as excessive bleeding and 'oozing' during surgery. It is Important to maintain a high index of suspicion and have a coagulation 'screen' performed in all cases.

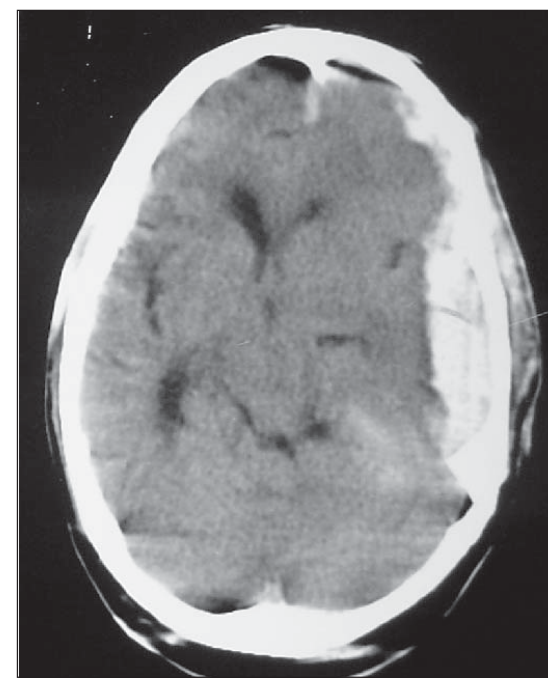

FIGURE 1. Plain CT head of a 14 year old child who developed subdural bleed after 48 hours of injury and who was found to have a deranged coagulation profile (The initial CT at 12 hours of injury was normal)

PATHOPHYSIOLOGY

It is uncertain whether coagulopathy occurs as a marker of severe brain trauma, or, in fact contributes to secondary brain injury. Evidence exists for thrombin activation rather than primary fibrinolysis as the basis for the coagulopathy in head injured patients. Goodnight et al[12] were the first to suggest this relationship and subsequently other investigators used more specific markers of thrombin activation (fibrinopeptide Bb 15-42, D-dimer, thrombin/antithrombin complex and prothrombin fragment F 1+2) to investigate the pathophysiology and severity of coagulopathy in head trauma[7]. However, it is commonly believed that the tissue factor released from damaged brain parenchymal cells binds to factor VII, causing activated coagulation and prolongation of the prothrombin time (PT). The tissue factor-factor VII complex activates factor X and prothrombin, occasionally leading to DIC with consequent hemorrhage. Apart from DIC, other coagulation abnormalities like thrombocytopenia and platelet function disorders have been reported to occur commonly following head injury[13].

LABORATORY INVESTIGATIONS

Investigating coagulopathy is the Achilles heel of management of pediatric head injury. As the tests are not very sensitive, only gross assumptions may be possible. Also, head injury being a dynamic state, there is need for repeated sampling which may not be practical in this fragile population. The six basic tests are:

1. Prothrombin time (PT)
2. Activated partial thromboplastin time (APTT)
3. Thrombin clotting time (TT)
4. Fibrinogen assay
5. Platelet count
6. Fibrin degradation product assay (FDP)

An abnormal PT implies a derangement of the extrinsic coagulation pathway, whereas an abnormal APTT denotes a dysfunction of the intrinsic pathway. DIC usually causes prolongation of PT, APTT and TT accompanied by low platelet count and elevation of FDP levels, the exact cut-off values for which are still subject to controversy[14,15].

TREATMENT

In case the clinical picture or laboratory tests are suggestive of coagulopathy, the management should consist of elimination of precipitating factors, replacement of depleted clotting factors and prevention of thrombi formation. Usually, however, practical considerations (e.g. impending herniation due to epidural hematoma) preclude management along these lines and frequently the results of only simple bedside tests such bleeding and clotting times may be available to the surgeon prior to surgery. In such cases, it would be prudent to operate under cover of replacement therapy, in order to save time. Controversy exists regarding the optimal management of children who are asymptomatic and do not require surgery. Some authors prefer a wait and watch policy with the reasoning that biochemical coagulopathy only mimics DIC, being usually self-limiting, and it may not be cost-effective to treat all patients with costly coagulation factors. It is also not clear whether aggressive therapy would be rewarded with improved outcomes[16]. However, others recommend that replacement therapy should be started even before coagulation results are available[12,17,18].

The mainstay of therapy for coagulopathy is adequate replacement of the depleted coagulation factors with fresh frozen plasma and platelet concentrate. In case fresh frozen plasma is not available or fibrinogen levels are extremely low, cryoprecipitate can be used. Cryoprecipitate is a rich source of fibrinogen and Factor VIII, whereas fresh frozen plasma is rich in Factor V only. Advice should certainly be sought from an experienced haematologist as to the replacement of these blood factors, and the replacement should be titrated depending on the existing levels of these factors. Platelets may not be required unless the count is below 75,000 per cubic mm, although if the patient requires neurosurgical intervention, the count should be kept at 100,000. As a general rule, platelets are administered at a rate of one concentrate pack per 10 kg weight, and 50 mg/kg of fibrinogen should be given for replacement purposes[19].

This approach, however, has a number of drawbacks, when used in the pediatric patient. Fresh frozen plasma requires time to type and crossmatch, to thaw and administer, and management of coagulopathy may require multiple doses of FFP, which impose a significant volume load on a child in whom cerebral edema may develop. Recently, recombinant factor VIIa (rFVIIa) has been used in such cases with excellent results[3]. The dose of rFVIIa is 90 to 120 mg/kg given as a single bolus dose[3]. However, due to its prohibitive cost of approximately $800 per mg, its use is limited to selected centers. Most authors do not advise the administration of procoagulant medications such as epsilon amino-caproic acid (EACA) as they may cause unchecked thrombosis to occur, given the overall coagulation activation following head injury. Moreover, these drugs may precipitate renal failure by

preventing lysis of fibrin in glomerular capillaries[19]. Despite the fact that heparin has been used in DIC, its use should be avoided and in cases of active bleed, heparin should probably not be used except as a last resort. Although no controlled studies are available in this regard, it is generally agreed that head-injured children have some degree of disruption of the vascular tree, and further intracranial hemorrhage can be disastrous and needs to be avoided.

OUTCOME AND PROGNOSIS

It has been shown by numerous studies that the presence of coagulopathy in head-injured children is of definite prognostic value. The severity of coagulopathy correlates with the extent of brain injury as well as the consciousness status of these patients[8-12,20,21]. Prospective studies have shown that presence of coagulopathy is an independent prognostic factor in head injury and even a single abnormality in the PT or APTT within the first day of admission is significantly related to the mortality. Kumura et al have shown APTT value to be the single most important predictor of survival, even more than GCS[8]. Jaap van der Sandle et al reported on 150 patients with head injury among whom 60 had deranged coagulation[11]. They felt that FDP levels related most accurately with the extent of damage and outcome and in some cases, the FDP levels were better indicators of prognosis than GCS[11,22]. Another study has shown fibrinogen levels to be the most important predictive factor for survival in children with head injury[23]. Clearly, larger, controlled studies are sorely needed to demystify this controversy surrounding the prognostic markers.

CONCLUSIONS

From the preceding review, it appears that coagulopathy after head injury may be a more common phenomenon than is routinely recognized. The mechanisms may vary, but the abundance of tissue thromboplastin in the brain is certainly an important factor that triggers the coagulation cascade, with the resultant fibrinolysis. The coagulopathy itself is usually self-limiting, and only a few patients are symptomatic for this. Despite this, reliable evaluation of basic coagulation parameters should be performed as early as possible and therapy should be urgently initiated in presence of active bleeding or the need for a neurosurgical procedure. All the same, any patient with abnormal coagulation parameters should be carefully monitored, and though there does not seem to be any indication for administration of other pro-coagulant or anti-coagulant agents such as EACA or heparin at present. A new drug (rf VIIa) has shown promise, which may help in improving the outcome in such patients. Although PT, APTT, FDP and fibrinogen levels have all found to be independent predictors of outcome, larger, randomized trials are necessary in order to have more definitive results.

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