The haematological investigation of suspected Non Accidental Injury

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Abstract

Most children suspected of Non Accidental Injury (NAI) will undergo a number of haematological investigations to exclude coagulation defects. Investigations should be dependent on the clinical presentation but often there can be an over or under-requesting of haematological investigations. The correct interpretation of results is reliant on an understanding of both the physiological processes involved in coagulation in children of different ages and of the laboratory testing of the coagulation systems. Age-specific, population-based studies of bruising and bleeding patterns in normal children, NAI children and children with congenital bleeding disorders may be helpful in limiting the number of investigations undertaken for suspected NAI. Investigation of suspected Non Accidental Injury requires a multidisciplinary approach; close liaison between the haematology laboratory and the requesting clinician is integral to this approach. This article describes the use of a staged approach to laboratory investigation.

Keywords Bruising and bleeding in children; coagulation factors; coagulation physiology; haemostatic investigation; Non Accidental Injury

Introduction

Almost all children who have a suspected non-accidental injury (NAI) will undergo haematological investigation so that an underlying bleeding disorder can be excluded, either as causative or contributory to the injury. Inadequate investigation or incorrect interpretation of test results may either fail to diagnose a bleeding disorder in a child suspected to have a NAI or misdiagnose a bleeding disorder in a child who has suffered NAI. Either way, the repercussions for the child, their family, involved clinicians and other members of the safeguarding team are significant.

Haematology requests by clinicians for the investigation of NAI can be variable, and may range from basic tests of haemostasis to requests for multiple clotting factor assays and tests of platelet function. Much discussion has taken place over the last decade about the most appropriate approach to the testing of haemostasis in NAI, with a number of publications presenting a "personal practice" of haematologists who have had a long-standing interest in this problem as well as practical experience of the medico-legal aspects of the haematology of NAI. Even amongst these authors there have been some differences in practice. The need for a more consensual approach has been recognized and recently addressed by the Royal College of Paediatrics and Child Health (RCPCH).

A suggested scheme for the haematological investigation of suspected NAI was agreed by a group of expert paediatric 'coagulationists' and safeguarding paediatricians and has been included in the College's Child Protection Companion Handbook. This scheme is described and discussed in this paper; the American Academy of Pediatrics has also recently published guidance on the evaluation for bleeding disorders in suspected child abuse.

Approach to haematology investigation

Ideally a child with a suspected NAI would have the same diagnostic processes applied to them as any child presenting with a history of bleeding or bruising. The diagnosis of a congenital bleeding disorder is based on a triad of clinical history, family history and laboratory investigation. Most children with suspected NAI will have a short clinical history of bleeding or bruising and the presentation will vary from a single bruise to a life-threatening intracranial haemorrhage. It would be entirely inappropriate to investigate these two extremes of presentation in the same way, and investigations should rather be tailored to the specific circumstances of the presentation. However, in practice this does not necessarily occur, with for example our own laboratory being asked to perform "extended clotting screens", random clotting factor assays or "NAI screening tests".

There can sometimes be minimal contact between the requesting clinical team and the haematologist. Age and family history are important considerations. Whilst a family history of a congenital bleeding disorder may be helpful in guiding clinicians, it should be noted that up to 50% of newly diagnosed haemophiliacs have no preceding family history of this disorder. Many children with suspected NAI are babies or infants and have therefore had limited haemostatic challenges compared with older children.

The aim of the initial haematology investigation of NAI should be to exclude significant bleeding disorders capable of causing the presenting symptoms. It should be noted that acquired bleeding disorders are much more common than congenital bleeding disorders; all congenital bleeding disorders fulfil the orphanet definition of Rare Disorders. For example, haemophilia A occurs in 1:10,000 of the population and the homozygous "rare bleeding disorders" vary in frequency from 1 to 2 per million of the (UK) population. To put this in context, there are 1719 UK patients with haemophilia A and 369 with haemophilia B who are under the age of 18 years, whilst only 9341 patients of all ages are registered with one of the rarer bleeding disorders (just 694 of whom required treatment of their condition between April 2015 and March 2016 as documented in the UKHCDO 2016 Returns).

Physiology of haemostasis

An understanding of the physiology of haemostasis is essential when investigating a possible bleeding disorder. This is

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particularly true for suspected NAI, which often involves babies and infants whose haemostatic mechanisms will differ from older children and for who the correct interpretation of results against age-related normal ranges is of paramount importance.

The end product of coagulation is a stable blood clot, made up of clumps of activated, aggregated platelets enmeshed in fibrin. Fibrin is the end result of the activation of the coagulation pathways, involving the transformation of inactive coagulation factors to their active forms, which was first described some four decades ago independently by Macfarlane and Ratnoff in the classic coagulation cascade models. These coagulation pathways comprise extrinsic, intrinsic and common pathways that lead to the formation of thrombin, which then cleaves fibrinogen to form fibrin [see Figure 1]. The initial phase of coagulation is driven by tissue factor complexing with circulating factor VIIa, this complex then activating factor X and so generating thrombin. In addition to cleaving fibrinogen, thrombin also activates FVIII and FV, which in turn enable tenase and prothrombinase complexes to be formed and thereby propagate coagulation. These events take place on the surface of platelets, which provide necessary phospholipid.

Much has since been discovered (and continues to be discovered) about the processes involved in haemostasis and the relationships that exist between the coagulation, anticoagulation, fibrinolytic and inflammatory systems, as well as the intricacies of platelet physiology and the molecular basis for bleeding disorders. Despite these advances, this simple coagulation cascade model still remains helpful in determining both the investigation and interpretation of bleeding disorders.

Investigation of haemostasis

Who should and who should not have investigation?

The RCPCH's Child Protection Companion recommends that coagulation investigations are generally **not** indicated when the only bruising is clearly the result of a slap or blow with an instrument. Investigations are recommended for any child with unusual bruising or bleeding out of proportion to the injury sustained, including infants with subdural and/or retinal haemorrhage and also when there are any indications in the history or examination of a bleeding disorder. In practice however, it would appear that virtually all children with suspected NAI will undergo at least first line investigations of haemostasis. This is discussed in more detail below.

The haematological investigation of NAI will include a number of basic (first-line) coagulation tests. Abnormalities on such testing would be an indication to consider more specific investigation of the coagulation pathways.

i) First Line Coagulation Tests

- Full blood count and blood film (will confirm thrombocytopenia, anaemia, abnormal platelet morphology, as well as giving an indication of the possibility of a primary haematological disorder such as acute leukaemia or aplastic anaemia).
- Coagulation Screen. This usually consists of a Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT) and Fibrinogen assay. Results are interpreted against the investigating laboratory's age-related normal ranges.

The possible causes of abnormal first line clotting tests are summarized in Table 1.

The following statements are important in the interpretation of the first line coagulation tests.

- Vitamin K deficiency will prolong the PT and APTT: it is important to ensure the child is vitamin K replete particularly if the suspected NAI involves a neonate.
- Any prolongation of the PT or APTT requires repeat testing of the child's plasma to which an equal volume of normal plasma has been added (50:50 mix). Factor deficiencies will be corrected by the addition of normal plasma to the test plasma, resulting in normalization of the PT and APTT; a lack of correction is caused by inhibitors to

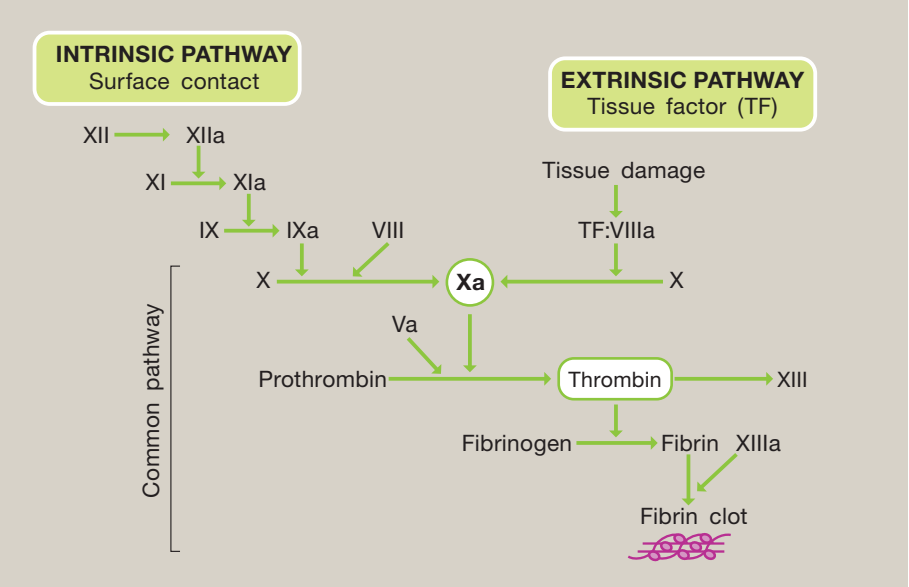

Figure 1 Coagulation cascades.

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