Significance of platelet function diagnostics for clarification of suspected battered child syndrome

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Summary
Summary: The manifestation of an unclear bleeding tendency in childhood calls for an extended coagulation work-up, particularly when a battered child syndrome is suspected and typical concomitant injuries are absent. The chosen diagnostic tests should be able to detect the presence of relatively common coagulation defects such as von Willebrand syndrome or hemophilia, but also rare diseases such as inherited thrombocytopathies. The PFA-100® test does not help to provide a definite diagnosis especially in cases of mild inherited thrombocytopathies, since in most cases the PFA-100® test results are normal. For this purpose, specific platelet function testing is needed. However, the methods are only available in some coagulation laboratories. Also, other limitations need to be taken into consideration such as pre-analytical problems and difficulties in the interpretation of test results especially in infants.

We present two cases that were diagnosed with an aspirin-like defect as an inherited thrombocytopathy, even though their PFA-100 closure times were within the normal range. Based on pathological findings in the platelet aggregometry test, this diagnosis could be made.

In case of unclear bleeding tendency particularly in infancy and early childhood, a child abuse should also be considered (6, 8, 17). An extended coagulation work-up is required if
  • the morphology of bleedings is not clearly suspicious for a battered child syndrome and
  • in the absence of typical concomitant injuries, e.g. bone fractures.

An interdisciplinary coordination between the forensic doctor and the paediatric haemostaseologist for assessment of bleeding symptoms, the parents’ explanations for the clinical findings and the critical evaluation of the results of an extended coagulation work-up are essential in cases of pronounced and threatening bleedings.

The necessity of performing platelet function tests in the presence of unclear bleeding symptoms that are suspicious for child abuse is shown by two case reports presented here. In both cases, an inherited thrombocytopathy was diagnosed by platelet aggregometry.

Case 1

A boy (age: 7 weeks) was presented by his mother to the emergency department with a soft tissue bleeding in the face and buttocks area and immediately admitted to our hospital. The bleeding pattern was suspicious for physical abuse by the child’s father who had cared for the boy alone overnight prior to admission to the hospital.

The clinical examination and diagnostic imaging showed no signs for fresh or older accompanying injuries in the absence of intracerebral and retinal bleedings. The ex-
tended coagulation work-up included the global coagulation tests and determination of von Willebrand factor associated parameters showing no abnormal findings. Because of the seemingly unique situation and the relatively large amounts of blood required for performing aggregometric tests, they were at first postponed.

Four weeks later, the patient was presented by his mother to the coagulation outpatient clinic where blood was taken for platelet function testing by aggregometry. A marked thrombocytopathy with absent platelet aggregation to several agonists (adenosine diphosphate, arachidonic acid and collagen) was found and initially the diagnosis of Glanzmann's thrombasthenia was suspected. Upon repeated testing, this diagnosis could not be confirmed and subsequent coagulation studies in the family revealed the presence of an aspirin-like defect in the patient, his father and brother, inherited as an autosomal-dominant thrombocytopathy.

The criminal investigations against the child’s father that had been initialized in the interim were stopped immediately after the first results of the platelet aggregation studies in the child were presented.

Case 2
A female infant (age: 2 months) was admitted to an external children’s hospital with multiple haematomas in the face and trunk area under the suspicion of child abuse.

A comprehensive diagnostic imaging was performed, which revealed no evidence for the presence of acute or previous injuries. An exploratory coagulation work-up, which only included the determination of the global plasmatic coagulation tests (PT, aPTT) and the blood counts showing normal results. Before discharge from the hospital, a follow-up appointment in our coagulation outpatient clinic was organized in order to perform an extended coagulation work-up including platelet function diagnostics.

At that time they were accompanied by a midwife, who on initiative by the youth welfare office had taken care of the family since they were already known to have difficult social circumstances. The family’s midwife confirmed the presence of a skin bleeding tendency in the child but she also pointed to a rough handling especially by the father in the daily care of the infant stressing the insufficient care condition. Despite the fact that the platelet function testing clearly showed the presence of an aspirin-like defect in the infant and her father, the infant was later placed in a foster family as the parents lost custody due to a combination of physical abuse and child neglect.

Discussion
Small haematomas are frequently observed in children starting at the end of the first year of life due to the motor development and with it the increased incidence of small traumas. Such soft tissue bleedings are typically located in prominent areas of the body such as in the areas of
- forehead,
- pretibial,
- elbow and
- dorsal forearms.

Atypical bleedings (6, 8) are localized on
- chest,
- back,
- neck,
- genitals,
- dorsal sides of thighs and
- ventral sides of forearms.

The co-existence of child abuse and a bleeding disorder must always be taken into consideration as it is illustrated by our second case.

Fig. 1
Aggregation and adenosine triphosphate (ATP) release in citrated whole blood induced by arachidonic acid (final concentration: 0.5 mmol/l)

a) normal aggregation (upper curves) and ATP release (lower curve)

b) typical for an aspirin-like defect: absence of aggregation and of ATP release
Before performing coagulation diagnostics the evaluation of a detailed bleeding history of the child and the family members is of particular importance (11). It should be taken into consideration that the global plasmatic coagulation tests (PT, aPTT) and the determination of blood cell count does not rule out the presence of a mild form of von Willebrand disease as the most common inherited coagulation disorder, factor XIII deficiency and thrombocytopenia (3, 12, 13).

Therefore, the extended coagulation work-up must be able to also detect rare bleeding disorders such as hereditary thrombocytopenies (13).

For this purpose, platelet function tests are required, even though they exhibit certain limitations (9, 10, 16) such as restricted availability in specialized coagulation laboratories, lack of standardized reference ranges especially in newborns and toddlers, test-dependent requirements for large volumes of freshly drawn venous blood.

Because relatively large amounts of blood are needed for extensive coagulation tests, applying a diagnostic algorithm based on previous test results might be useful with blood sampling (10). From our point of view, a stepwise procedure for coagulation testing is recommended if the patient is hospitalized, but not in an outpatient setting where the patient has been sent from a paediatrician or an external hospital with suspected child abuse for an extended coagulation diagnostics. Due to the lack of clear reference ranges – especially in neonates and infants – the interpretation of some individual findings of some coagulation studies can be considerably difficult in very young children. Moreover, the limited availability of coagulation tests in specialized laboratories and some pre-analytical problems such as decreased clotting factor activities due to a long sample transport to external laboratories must be also taken into account. However, in the interest of the child but also the parents every effort should be made to clarify the etiology of bleedings not clearly evident but suspicious for child abuse.

In case some coagulation tests are not available in the hospital's laboratory, the child should be sent to a paediatric coagulation outpatient clinic close to home to complete the diagnostics as soon as possible. In our case 2, this procedure led to the diagnosis of an inherited thrombocytopeny. In this context, it should be mentioned that the overall approach was not optimal for case 1, because the platelet function tests were out a few weeks after the hospitalization in the outpatient clinic, when criminal charges had already been initiated against the child’s father.

Case 1 has led us to change the approach in prioritizing coagulation tests in our hospital if child abuse is suspected.

In both cases a hereditary thrombocytopeny was diagnosed by aggregometry as an established method of platelet function testing in children and adults (7).

The S2-guideline of the German Society for Social Pediatrics and Adolescent Medicine on Child abuse and child neglect published by AWMF (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften) in 2008 recommends as basic laboratory tests for detection of primary haemostasis defects solely the determination of the "in vitro bleeding time (PFA-100)" (1). It should be mentioned that the Platelet Function Analyzer (PFA-100) is a screening test of primary haemostasis and that the test results not only depend on the platelet function but also on the platelet count, the presence and function of the von Willebrand factor as well as on the haematocrit (4).

According to the recently published AWMF S2k-guideline on diagnosis of inherited thrombocytopenies and other literature data, the PFA-100 test is not suitable to exclude a platelet function defect definitely (2, 5, 14). This particularly applies to entities that are associated with a mild bleeding tendency such as the aspirin-like defect. In this context, it should be mentioned that in both cases described, the PFA-100 test showed normal findings.

A one-time testing of platelet function is only sufficient for the exclusion of a relevant thrombocytopeny but not for the definitive diagnosis of such a rare disease. Almost all platelet function tests represent failure-prone methods, which are affected for example by long sample transports and the patient’s medication.

Therefore, repeated testing in another blood sample is important to reproduce pathological test results as well as investigating first grade relatives, especially the parents, in order to reach a definite diagnosis of an inherited platelet function disorder.

This proceeding was adopted in the two cases described, providing the diagnosis of an aspirin-like defect (ALD). The ALD represents an autosomal dominant inherited platelet function disorder with clinical and laboratory findings similar to the intake of acetylsalicylic acid such as aspirin (15). The bleeding tendency is usually mild with recurrent epistaxis, easy bruising and menorrhagia as the most common clinical signs. The typical laboratory findings show the absence or a markedly reduced arachidonic acid-induced aggregation (Fig. 1).

Conclusions

In case of an unclear bleeding tendency in childhood suspicious but not clearly evident for child abuse and without typical concomitant injuries the presence of an inherited coagulation disorder has to be considered, too. In these cases platelet function testing should be part of a stepwise comprehensive coagulation diagnostics where at first the more common bleeding disorders such as von Willebrand disease and haemophilia are excluded.

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Conflict of interest
The authors declare that they have no conflict of interest.

References

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