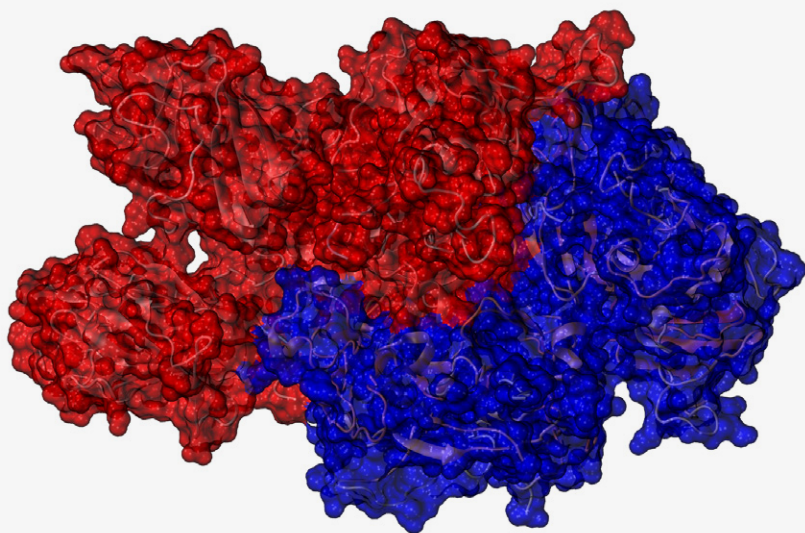


When an elephant hides
another one

May 2021



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Title figure:

Factor VIII (source: www.de.wikipedia.org)

CASE REPORT

This male infant was referred to our neonatal intensive care unit (NICU) on day of life (DOL) 26 because of flaccid paralysis of the lower limbs.

The infant had been born at 41 1/7 weeks of gestation to a 37-year-old G2/P1 mother by normal vaginal delivery. Pregnancy had been uneventful, except for the history of gestational hypothyroidism requiring hormone substitution. The newborn was eutrophic (birth weight of 3830 g) and adapted well. There were no maternal or fetal risk factors, and mother and infant were discharged home within 48 hours of delivery. The family medical history was also unremarkable.

On DOL 26, the baby was referred to the emergency department of a regional hospital because of absent movements of the legs for a couple of hours. The parents also described constant dribbling of urine and occasional leakage of stool. They also had observed a localized progressive swelling on the child's back, first noted by a midwife 2 days prior to admission.

The patient's past medical history revealed that the baby had been admitted to a regional level II neonatal unit for RSV bronchiolitis on DOL15. Three days later, he developed a fever and worsening of his clinical condition. At this point, a standard sepsis work-up was performed, including a lumbar puncture (LP), described as non-traumatic, along with blood and urine cultures, which all remained sterile. During the following

days, his clinical condition improved, but progressive normocytic normochromic anemia (hemoglobin decreasing from 166 g/L to 105 g/L over 3 days) was noted and considered to be mixed in origin (inflammatory state, repeated blood sampling, dilution following fluid administration). He was discharged home one week later on DOL 22. At this time, his physical examination was recorded as normal.

On DOL 26, physical examination in the emergency department of the regional hospital confirmed signs of spinal cord compression with 1) massive abdominal distension, 2) absence of movements of the legs, 3) absent and diminished withdrawal reflex on the right and left foot, respectively, 4) absence of tendon reflexes on the right, with only the patellar reflex present on the left, and 5) the absence of plantar grasping and toe extension on the left. There was also diminished sensitivity in the perineal region, signs of bowel and bladder dysfunction (incontinence), and the anal sphincter tone was lax. In addition, a rather soft paraspinal swelling measuring 10 × 3 cm, extending to the left paravertebral area, was noted (Fig. 1).



Fig. 1

*Left-sided paravertebral swelling on DOL 26
(10 cm × 2 cm × 3 cm).*

A babygram revealed signs of coprostasis (Fig. 2). The ultrasound examination revealed a hematoma measuring $10 \times 2 \times 3$ cm in the paravertebral left musculature, as well as urinary retention (200 ml) and coprostasis of the entire colon. The hematoma was non-homogeneous, suggesting variable ages.

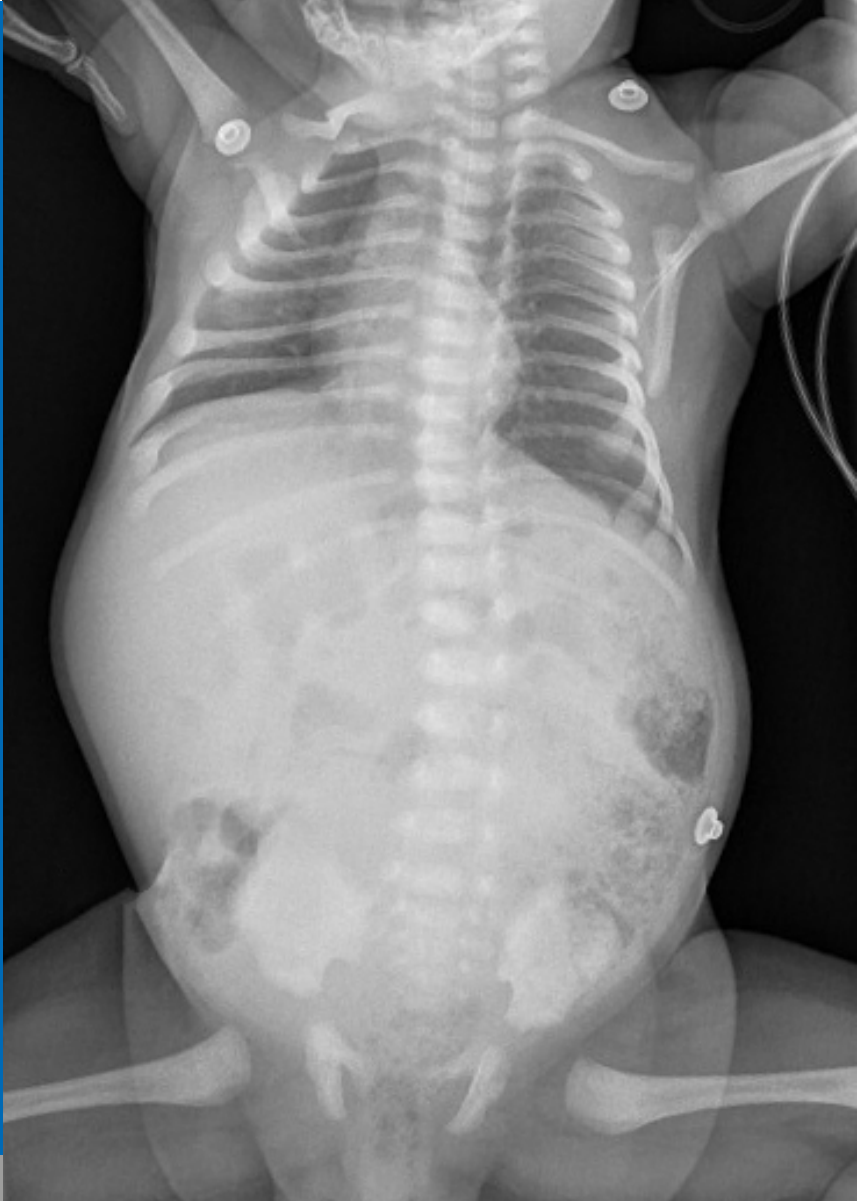


Fig. 2

Babygram showing abdominal distension and coprostasis; in addition, slight deviation of the spine is noted.

Laboratory analysis revealed a more pronounced anemia (hemoglobin 90 g/l). IV access was obtained, and both a bladder catheter and a nasogastric tube were inserted. He received a bolus of crystalloid solution (10 ml/kg) and a single dose of intravenous vitamin K. He was then transferred to our level III NICU for further investigations and management of the spinal cord compression.

The patient was hemodynamically stable during transfer and emergency magnetic resonance imaging (MRI) was performed immediately following admission, before coagulation studies were obtained. MRI showed extensive spinal cord compression by an acute epidural hematoma with a hyperacute component, extending over 16 cm from T3 to S5. In addition, there was a very small intramedullary hemorrhage at the level of L1 (Fig. 3). The paravertebral hematoma was also described and measured 1.5 × 2 × 12 cm.

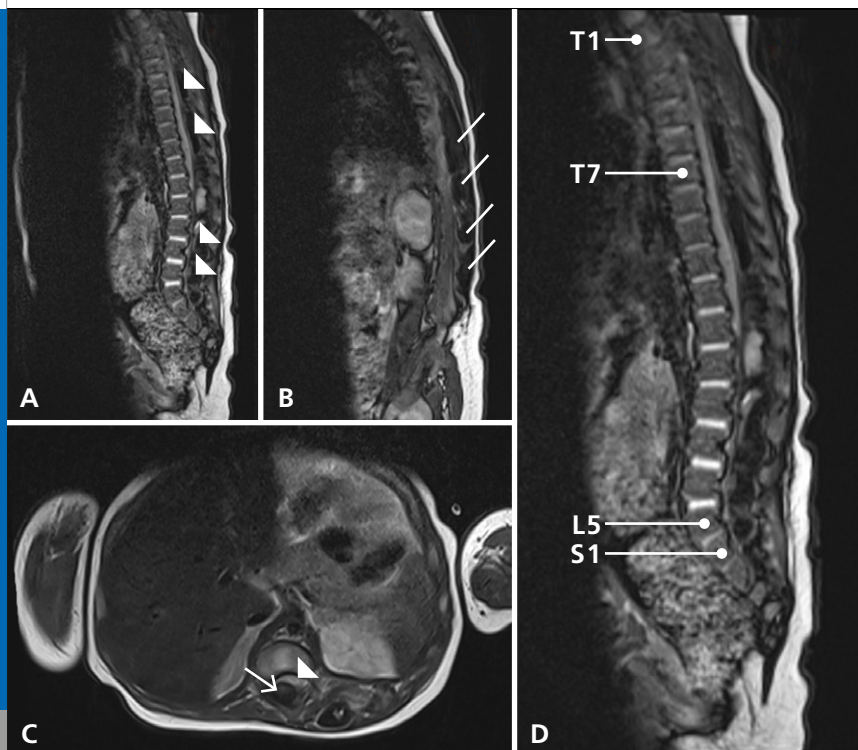


Fig. 3

A) Sagittal view of the spine (T2-weighted images), showing the extensive epidural hematoma with mass effect (white arrowheads); B) Parasagittal view of the spine (T2-weighted) showing the paravertebral hematoma (white lines); C) Axial view (T2-weighted image) showing the epidural hematoma (white arrow) with compression of the lumbar medulla (white arrowhead); D) Vertebral column anatomy with marks.

Coagulation tests were obtained at the end of scanning, approximately 2.5 hours after admission. Activated partial thromboplastin time (aPTT) was prolonged with 107 s (normal range 33 – 47 s for term infants). The other coagulation parameters were normal (prothrombin time (PT) of 110 %, fibrinogen level of 3.0 g/l) and the platelet count was 381 g/l. These results suggested a problem with the intrinsic coagulation pathways, including a deficiency of coagulation factors VIII, IX, XI and/or XII. Blood and fresh frozen plasma were given with little effect on coagulation. Analyses finally revealed severe factor VIII deficiency (less than 1 %) consistent with the diagnosis of severe hemophilia A. Replacement therapy with plasmatic clotting factor VIII was given from hour 7.5 to 10 after admission to stop the bleeding. Finally, a cerebral ultrasound examination showed mild ventriculomegaly, probably secondary to disturbed cerebrospinal fluid circulation.

Only 14 hours after admission, with normalized coagulation tests, the patient underwent surgical decompression of the spinal cord. Due to strong adherence between the hematoma and the spinal cord, the incision was extended from T4 to L4 (Fig. 4). At the end of the procedure, the baby received two blood transfusions for a hemoglobin value of 87 g/L.



Fig. 4

*Post-operative aspect of the patient's back:
scar extending from T4 to L4.*

Replacement therapy was administered during the post-operative period to maintain an adequate FVIII level to avoid re-bleeding and enable healing. It was gradually reduced until 23 days after surgery. A post-operative MRI of the spine and brain (5 days after surgery) documented resolution of ventriculomegaly, normal brain parenchyma, and the epidural hematoma was no longer visible (Fig. 5).

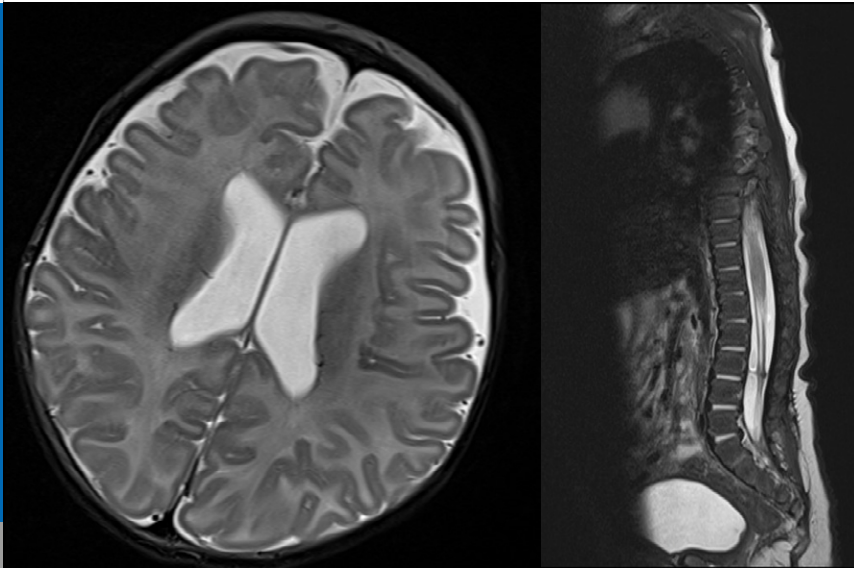


Fig. 5

A) Axial view of the brain (T2-weighted image): mild ventricular dilatation and increased extraaxial CSF spaces; B) Sagittal view of the spine (T2-weighted): no residual blood but probable synechia at the level of L3, likely representing the initial site of lumbar puncture or residual hematoma.

Following the surgical procedure, the patient's neurological status slowly improved with progressive proximal to distal recovery of the mobility of the left leg followed by the right leg. Twelve months later, despite the inability to move the right foot and reduced general movements of right lower limb, he was able to stand up when supported by bilateral orthoses.

Unfortunately, the patient developed a neurogenic bladder (albeit with normal kidney function). Indeed, urodynamic assessment revealed normal bladder volume, poor compliance, inability to void but no signs of increased bladder pressures. Intermittent catheterization of the bladder (5 times a day) is still needed and performed by the parents at the age of 12 months.

DISCUSSION

We report an unusual bleeding complication after LP in the first weeks of life in a newborn with previously undiagnosed severe hemophilia A.

The majority of bleeding complications in the neonatal period are due to acquired hemostatic problems (such as thrombocytopenia or coagulation factor deficiency) secondary to, mostly transient, underlying disorders (e.g., infection, asphyxia with liver dysfunction) or medications taken by the mother at the time of delivery (e.g., anticonvulsants, vitamin K antagonists) (1–3).

Inherited bleeding disorders, including hemophilia, are rare, with only 418 cases documented in Switzerland in the World Federation of Hemophilia (WFH) report of October 2018 (4); cases may not become clinically apparent during the first weeks of life. Hemophilia A and B are hereditary X-linked disorders, and are due to de novo mutations in around one third of cases. Hemophilia A, the most common form, affects approximately 1 in 10'000 males, and is due to a deficiency of factor VIII. Hemophilia B is due to a factor IX deficiency and affects approximately 1 in 30'000 males. The severity of hemophilia A is classified according to plasma factor VIII activity level: severe (less than 1%), moderate (1 – 5 %) and mild (5 to 40 %) hemophilia (5).

During the first month of life, the most common finding pointing to the diagnosis of an inherited hematologic disorder is a positive family history, or spontaneous or unusual bleeding episodes (6). Iatrogenic causes of bleeding revealing a coagulation problem are almost equally common before and after the first month of life (6). Of note, circumcision is the leading iatrogenic cause during the first month of life (especially in the USA where circumcision is a routine procedure), followed by venipuncture bleeds and other invasive procedures (7).

Spinal bleeding in hemophilic patients is a very rare complication reported only in 2/1'410 pediatric cases by De Terzanos Pinto et al. (9) and 6/2'500 cases by Eyster ME et al. (10). These bleeding episodes occurred either spontaneously, following trauma, or remained undefined in some cases (8). Anecdotal reports exist on spinal epidural hematoma following LP in hemophilic pediatric patients. A spinal epidural hematoma, which presented with paraplegia after LP in an infant aged 3 months with previously undiagnosed hemophilia A (16), has also been described. To the best of our knowledge, ours is the first reported case of symptomatic spinal epidural hematoma following LP in a newborn with previously undiagnosed hemophilia A (14).

LP is usually not associated with major bleeding complications. While clotting tests are regularly performed

before LP in adult patients, this is not the case in pediatric patients (coagulation studies are only obtained in the presence of a positive family or personal bleeding history). Although the processes of primary hemostasis with the production of an initial platelet plug at the bleeding site is effective in patients with severe hemophilia A, due to the deficiency of FVIII, these patients are unable to generate the burst of thrombin on the platelet surface necessary to stabilize the initial plug into a fibrin clot (Fig. 6). Therefore, delayed bleeding may occur several hours or even days later due to inefficient secondary hemostasis (17).

The clinical presentation of spinal epidural hematoma may vary, ranging from acute onset of pain followed by neurological deficits to a more delayed course without clear evidence of clinical signs or symptoms (8). In our case, the diagnosis was delayed given the subtle and relatively slow clinical course over several days; unfortunately, only the recognition of neurological deficits led to further investigations.

Correction of the underlying coagulation disorder and substitution of the missing coagulation factor VIII represent the main part of the treatment of epidural hematomas (18). However, controversy exists regarding the role and timing of surgical interventions. Some advocate the importance of surgical removal of symptomatic hematomas (11), while other reports describe good outcomes with conservative therapy

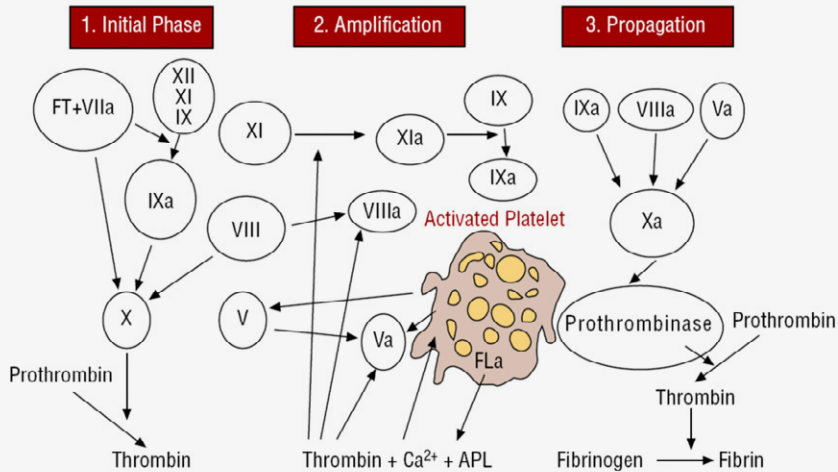


Fig. 6

Phases of coagulation (Source: Pérez-Gomez F et al. The new coagulation cascade and its possible influence on the delicate balance between thrombosis and hemorrhage. Rev Esp Cardiol 2007;60(12):1217–9).

(12). In our case, the neurosurgical team adopted the algorithm proposed by Varela Rois et al., advocating decompressive laminectomy (5).

In summary, our patient had a very rare presentation of hemophilia A. In the absence of a positive family history, the diagnosis was made because of an unusual and severe bleeding complication following LP leading to compression of the spinal cord. Prompt initiation of the replacement therapy, initially using FFP followed by factor VIII as soon as the diagnosis was confirmed, stopped the bleeding. Neurosurgeons thereafter opted to evacuate the compressive hematoma. The outcome is quite favorable, and the infant has regained mobility of the lower limbs; however, long-term multidisciplinary support and follow-up will be required.

See also: COTM 08/2009:

When bleeding does not stop after capillary blood sampling for the newborn screening test

See also: COTM 11/2003:

Hemophilia A: presentation with neonatal circulatory collapse

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