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VITAMIN K DEFICIENCY BLEEDING IN INFANTS - CASE REPORT

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K ვიტამინის დეფიციტით განვითარებული ჰემორაგიული დაავადება ახალშობილებში - კლინიკური შემთხვევა

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რეზიუმე

K ვიტამინის რუტინული ადმინისტრირების აუცილებლობა დასტურდება მთელი რიგი კლინიკური კვლევებით, რომლებიც წარმოებდა 1960-1990წწ. აღნიშნული კვლევის შედეგებით ავტორები ამტკიცებენ K ვიტამინის ადმინისტრირებით კოაგულაციური მაჩვენებლების მნიშვნელოვან გაუმჯობესებას პლაცებოსთან შედარებით. ნეონატალურ პერიოდში K ვიტამინის ადმინისტრირების შედეგად K ვიტამინის დეფიციტის ფონზე განვითარებული ჰემორაგიული დაავადებების კლინიკური შემთხვევების წილი მნიშვნელოვნად შემცირდა, რასაც ადასტურებს ჩატარებული ობსერვაციული კვლევები. მნიშვნელოვანია იმ ფაქტის გაანალიზება, რომ K ვიტამინის დეფიციტის გამო განვითარებული ჰემორაგიული დაავადება გვიან ნეონატალურ ან ახალშობილობის პერიოდში შესაძლოა მაინც განვითარდეს პერორალურად ან ინტრამუსკულურად ნეონატალურ პერიოდში მიწოდებული K ვიტამინისგან დამოუკიდებლად. აღნიშნულს განვიხილავთ ჩვენი კლინიკური შემთხვევის მაგალითზე.

Vitamin K deficiency is common in the newborn, and if vitamin K is not replaced, the infant is at risk for vitamin K deficiency bleeding (VKDB), in the past called a hemorrhagic disease of the newborn. Hemorrhagic disease of the newborn (HDN) was first described in the literature as an entity by Townsend in the late 1800s, although bleeding in the newborn had been described in detail long before that time [1]. The modern era of understanding the importance of vitamin K began with Dam and Doisy being awarded the Nobel Prize in 1943 for their work on identifying and isolating the new vitamin. This report described HDN as a “hemorrhagic disorder of the first time of life caused by a deficiency of vitamin K and characterized by deficiency of prothrombin, proconvertin [Factor VII] and probably other factors”.

Clinical features — VKDB is characterized by cutaneous bruising or bleeding from mucosal surfaces, the gastrointestinal tract, umbilicus or circumcision site, and/or intracranial hemorrhage (ICH). With the etiology of HDN identified, the disorder is now known as vitamin K deficiency bleeding (VKDB). This disorder is characterized by its time of presentation, namely early-onset, classic, or late-onset [4]. Early-onset VKDB begins within the first 24 hours of age. It usually occurs in mothers who are taking medications that affect vitamin K metabolism. It is associated with ICH (intracranial hemorrhage) in approximately 25 percent of affected infants. Classic VKDB occurs between 2 days and 1 week of life and is largely prevented by administration of vitamin K at birth. Late-onset VKDB occurs between 1 week and 6 months of age, with a peak incidence between 2 and 8 weeks [10]. There is a high frequency of ICH in affected infants (eg, 50 percent in some series), and associated central nervous system symptoms such as vomiting or seizures may be the primary presenting symptoms [24]. Late-onset VKDB appears generally and exclusively by breastfed infants with no vitamin K prophylaxis at birth. It may also be associated with liver dysfunction secondary to neonatal hepatitis, bile duct atresia [11], or intestinal malabsorption. Late-onset VKDB most commonly presents with evidence of intracranial bleeding in 30% to 60% of cases. Until now the efficacy of eliminating late VKDB through early postnatal application of IM Vitamin K has not been proved by any randomized studies. Vitamin K in eliminating late VKDB [12], however, there are several large national surveillance studies that have examined rates of late VKDB since the introduction

of vitamin K prophylaxis in Japan, Germany, Great Britain, and Thailand. All of these studies have shown significant reductions in late-onset VKDB in the population [13-16]. The high incidence of mortality and morbidity, along with its virtual elimination with prophylactic vitamin K, has made it a focus of public health interventions around the world.

Case Report - According to parents, the Baby has been ill for two days. They mentioned symptoms like high temperature, irritation, agitation. For this reason, the child was admitted to the regional hospital, where doctors registered seizures, rigidity, tensed fontaneles. After that the child was transfered to our clinic. Immediately by admitting we began monitoring vital parameters: Ps-152, RR-48, T 36.4C°, T/A 84/37. General condition was very severe, caused by Hemmorrhage perhaps induced from Later Hemmorrhagic disease of newborns. **Neurological Status**: Grimace, generally very sick appearance with moaning, Ptosis on the right side and half-closed left eye, inability of adjusting the gaze, anisocoria: D>S, rigidity of neck muscles, hypertonus and tremor of limbs, very tensed und bulged pulsating fontanelles. Skin evidently pale, subcutaneous tissue mediocre developed, reduced turgor and elasticity. Temperature normal. Sinus rhythm, peripherial puls weakly palpable, cold extremities, capillary refill time 3s, non-invasive arterial pressure normal according to age parameters, auscultatory of heart - muffled heart sound. Auscultatory of lungs - on the both side vesical breathing, Percussion resonant. Sunken abdomen, liver - 3 cm under the rib cage, smooth, Spleen on the edge of costal arch. Visually urinary and reproductive systems without pathologies, kidneys non-palpable. **Computer tomography**: in the right frontal lobe oval formed inhomogeneous structure, with indistinct outlines, hyperdense and central viscous liquid density mass. Dorsally - lightly hyperdense, with admixture of blood-density. Extensive perifocal edema and its effect on surrounding structures with shifting midline structures to the left by about 2,4cm. Lateral venticles are asymmetrical, on the right side are anterior horn and body compressed, it appears in the form of narrow line. Small amount of blood in posterior horn. The left lateral ventricle is deformed and slightly dilated. Basal cisterns and convexity subarachnoid spaces are compressed. The structures of posterior fossa are well differentiated, Stem without compression. Stem cisterna is moderate. Dislocation of cerebellar tonsils in parietal foramen was not found. Bones of skullcap and the skull base without destruction. Paranasal sinuses and mastoid cells are pneumatized. All of this makes us think of Later Hemorrhagic disease of newborns. It was urgently needed to determine hemostasis parametres (INR). Severe Coagulopathy was probably caused due Vitamin K defficincy, that´s why it was applied. Anaemia was also diagnosed and transfusion of one unit of blood with the same group and resus-factor was inducted. Without any complications. Following the **treatment** the coagulogram showed: PT 20.90 sec; PT % 42.90 %; INR 2.01; APTT 47.90 sec; TT 17.40 sec; Fibrinogen 3.94 g/l; According to the neurosurgical consultation, immediate operation was necessary to save the child s life. There was conducted brain ventricle or intracranial cyst shunting (implantation of Ommaya Reservoir in cystous bulk formation in the brain), cyst intra-operative draining, to exclude compression of healthy brain structures.

The patient was treated with ery. mass and AGP transfusion. On 19.03.2023, a control CT study was conducted, which showed image of cerebral edema and spontaneous intracerebral hemorrhage, also compression on brain structures and brain deviation to the left up to 2cm. The patient needed operation to get rid off compression on brain, evacuation of intracerebral hematoma and extirpation of intracranial damage. Repeated surgical intervention was performed: Removal of compression on the brain, intracerebral hematoma evacuation, AASB30 Partial extirpation of intracranial lesions AASB10. Compared to the previous study, on repeated post-operative CT scan of the brain was revealed postoperative Status of brain due to right-sided frontal-occipital bone decompression trepanation. Subkutanes drainage tube is seen, with a small amount of blood and air density areas. Viscous fluid density region with blood-density-like admixtures in the frontal area is evacuated. Basally appears a relatively small area with a similar structure - presence of residual mass is suspected. Detailed assessment with existing research is difficult. An average amount of post-operative blood and air density areas is seen. On the right side frontal lobe white substance is swollen. The deviation of intermediate structures is reduced up to 9.5 mm to the left. Lateral ventricles are relatively free. Compression on the right anterior horn and body is reduced. The volume of blood in the posterior horn is unchanged. Convexital subarachnoid spaces are compressed - CT image of intracranial hypertension is expressed. Posterior fossa structures are well-

differentiated, the stem does not experience compression. In order to stabilize the patient, it was recommended to continue treatment with medication and further observation in dynamics. To correct anemia on 20.03.2023 was ery. mass transfusion without complications inducted. Postoperative changes are noted on the right side of the brain scan on March 20, 2023. In the frontal lobe are shown noticeable amounts of unevenly distributed Hemorrhagic component. Most of the frontal-scalp-temporal lobe on the rightside is represented by edema of reduced density - with ischemia-like changes. The intermediate structures are 6-7 mm deviated to the left. A small amount of blood is seen into the posterior horns of the lateral ventricles. The condition remains severe, neurologically: right-sided anisocoria. It is difficult to assess the complete status because of analgesie and sedation. Urgent Extended decompressive craniotomy-AASK80, Extirpation of intracranial lesions AASB00 were planned. During the operation extirpated yellow-colored tissue of colloid consistency with bloodclots were sent to histological examination.

The post-operative wound of the right frontal-scalp area was treated with antiseptics and wrapped aseptically. Subcutaneous drainage is removed. Fontanel is soft, pulsating. On 20.03.23 held control CT scan of the brain was shown: still present Swelling-infiltrative changes in the right hemisphere. In the previous study existing hemorrhagic component is evacuated. It is noted in the left hemisphere ischemic changes. Treatment will continue as prescribed; the patient is under the supervision of neurosurgery. 25/03/2023 The post-operative bone defect is soft on palpation, Fontanel slightly drooping, soft. From the wound is Liquor draining. Therefore, following the rules of aseptic-antiseptic, additional stitches were applied. It was treated with antiseptics and wrapped aseptically. There were no complications. 27/03/2023 The condition of the patient remains serious, although without worsening dynamics. Patient is on controlled breathing; midazolam infusion was stopped. An incomplete opening of the eyes. The eyeballs are turned to the right, he does not fix his gaze, crying grimace, the trepanation hole is soft, the prolapse of the mass can be felt, Liquorrhoea has stopped. Signs of spastic quadriplegia are expressed. He has spontaneous breathing, regular cough and swallowing reflexes can be caused. The temperature is within normal limits. The rhythm is sinus, the pulse on the periphery is weaker than the average filling, limbs are cool. Cap. filling 3 sec. By auscultation, the tones are rhythmic, clean. Breathing is equal on both sides; no pathologic sound is heard Oxygenation/ventilation is within acceptable limits. During aspiration of tube is obtained a small amount of white secretion. The abdomen is moderately distended, soft, liver and the spleen are without dynamics. Diuresis is adequate to receiving fluids. 20.03.2023 by cytological examination of operative material: moderate erythrocytes, a small amount of lymphocytes and A single neutrophil are seen, no other type of cell population to be registered in material. Micromorphology of operational material was also made. Hemorrhagic masses/hematoma fragments and acellular, structureless fragments with a small amount of glial tissue are revealed in the examined histopreparat.

Conclusion: The picture corresponds more to arterio-venous malformation with hematoma. As of 03/28/2023, the patient's condition still remains critical. He is breathing spontaneously, does not require assisting oxygen therapy. Ventilation/oxygenation parameters within the acceptable norm. Neurological status: eyes open incompletely, eyeballs turned to the right, pupils round, equal. He does not fix his gaze, cries with a high voice, has sucking and swallowing reflexes, trepanation hole is soft, the prolapse of the mass can be felt, the liquid flow is stopped. Signs of spastic quadriplegia are expressed skin and mucus clean, pale, limbs warm. Cap. Filling time 2 sec. The temperature is within normal limits. Pulse on the periphery of a weaker than average fullness and tension. Dulled heart tons, rhythmic. Hemodynamics is stable. Breathing is carried out on both sides equally, with auscultation dry wheezing. Abdomen is moderately bloated, soft, liver and spleen without dynamics. Diuresis is adequate. Feeding is given with a p/o pacifier. Receives the given amount without problems. The patient's condition improved with the treatment, is on spontaneous breathing, does not require assisted oxygen therapy. Ventilation/oxygenation parameters within the acceptable norm. Neurological status: eyes open incompletely, eyeballs turned to the right, pupils round, equal. He does not fix his gaze, he cries with a high-pitched sound, the trepanation hole is soft, the prolapse of the mass can be felt, Liquorrhoea is not manifested. Signs of spastic quadriplegia are expressed. skin and mucus clean, pale, limbs warm. Cap. Filling time 2 sec. The pulse is rhythmic, with medium fullness and tension on the periphery. Dulled Heart tons. Breathing is carried out equally on both sides, by auscultation dry wheezing. Takes food with p/o pacifier, receives the given volume. belly is soft.

In terms of parenchymal organs, the condition is unchanged. Diuresis is to received fluid adequate. The patient is transferred for further treatment and monitoring in the pediatric department.

Major disease(s) 162.9 Intracranial hemorrhage (non-traumatic), unspecified D69.9 Haemorrhagic condition, Unspecified + Complication(s). G93.6 Cerebral edema, G93.5 Compression of brain, R90.0 Intracranial volumetric damage J96.0 Acute respiratory failure D64.9 Anemia, unspecified*

Discussion. According to studies ischemic and hemorrhagic stroke incidence rates in Pediatric, including neonatal as well as later childhood stroke, range from 3 to 25 per 100 000 children in developed countries. Where newborns have the highest risk ratio: 1:4000 live births. Stroke is a clinical syndrome. There is a risk of Vitamin K deficiency in newborn infants because their immature liver does not efficiently utilize vitamin K. In addition, they tend to have low vitamin K stores because of the low vitamin K content of breast milk, a sterile gut, and poor placental transfer of vitamin K. In infants, the plasma concentrations of all vitamin K-dependent factors are approximately 20 percent of the adult values. Within a month after birth, the levels rise to within normal limits [20]. The risk of developing VKDB is further increased by maternal ingestion during pregnancy of warfarin or other coumarin-like anticoagulants, certain antibiotics (ie, cephalosporins), and some anticonvulsants [21]. The possibility of VKDB should be considered in an infant presenting during the first six months of life with bleeding, bruising, lethargy, or fussiness, especially if they are exclusively breastfed or did not receive vitamin K prophylaxis at birth. If there is a strong clinical suspicion of VKDB (eg, clinically apparent bleeding and known refusal of vitamin K prophylaxis), the infant should be treated immediately, even before test results are available. Evaluation should include laboratory testing of prothrombin time (PT) and international normalized ratio (INR), both of which are prolonged in vitamin K deficiency. Infants with abnormal results or neurologic symptoms should have urgent neuroimaging to detect brain hemorrhage. A complete blood count with platelets and fibrinogen should also be performed to exclude other causes of bleeding. All newborn infants are given vitamin K shortly after birth to prevent VKDB. The administration of Vitamin K1 (phytonadione) is practiced as a single-shot weight-adjusted dose of intramuscularly (IM) injection within six hours of birth.

Conclusion. A presumptive diagnosis of VKDB should be made in an infant presenting with bleeding or neurologic symptoms and either prolonged PT or INR, or a history of not receiving vitamin K prophylaxis at birth. Such infants should be treated immediately with parenteral vitamin K (phytonadione), 1 to 2 mg intravenously or subcutaneously. The vitamin K dose should normalize the coagulation profile within two to three hours [21,26]. For severe bleeding episodes, fresh frozen plasma or prothrombin complex concentration may be used together with vitamin K. Following measures are necessary for neonates with intracerebral hemorrhage [1]: Correction of markedly low platelet counts; Replacement of deficient coagulation factors for neonates who have coagulation factor deficiency; Ventricular drainage for those who develop hydrocephalus, followed by shunting if hydrocephalus persists.

Note that all neonates should receive prophylactic administration of vitamin K1 (0.5 to 1 mg by intramuscular injection) as part of routine management to prevent vitamin K deficient bleeding A presumptive diagnosis of vitamin K deficient bleeding can be made in an infant presenting with bleeding or neurologic symptoms and either a prolonged prothrombin time (PT) or international normalized ratio (INR), or a history of not receiving vitamin K prophylaxis at birth. Such infants should be treated immediately with parenteral vitamin K, 1 to 2 mg intravenously or subcutaneously. For severe bleeding episodes, fresh frozen plasma or prothrombin complex concentration may be administered in addition to vitamin K. Surgical evacuation of intracerebral brain hemorrhage can reduce elevated intracranial pressure, but it is not clear whether this intervention improves outcome [1]. In a population-based registry study of 86 infants with neonatal hemorrhagic stroke, there were three deaths (4 percent), which all occurred beyond the neonatal period. With follow-up available for 50 cases at a median of 37 months, poor neurologic outcome was observed in 42 percent [7]. Impairments included sensorimotor deficits, language and epilepsy. There was no recurrence of hemorrhagic stroke. Interventions beyond the neonatal period included ventriculoperitoneal shunt placement, epilepsy surgery, and arteriovenous malformation

embolization. More favorable outcomes were reported in a prospective cohort study of 26 neonates with spontaneous hemorrhagic stroke (parenchymal and intraventricular) With follow-up available at two years for 20 children, full recovery occurred in 45 percent, mild deficits in 30 percent, moderate deficits in 5 percent, and death in 20 percent.

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SUMMARY

The proof that routine vitamin K administration works and is efficient was given by several small clinical trials held in the 1960s to 1990s. Through these trials was demonstrated that compared with cases with placebo vitamin K improves child's biochemical indices of coagulation status. Besides these trials other observational studies and clinical experiences over decades support the efficacy of vitamin K in this setting and it was also shown that rates of VKDB declined dramatically after widespread using of this practice. But it is important not to forget that VKDB may still appear in neonates with liver disease despite application of IM or oral vitamin K.

Keywords: Vitamin K deficiency, Hemorrhagic disease, Newborn.