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Hemorrhage in the skin of a newborn

Draft clinical recommendations for discussion by neonatologists and pediatricians

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ABSTRACT

The hemostasis system of newborns is called “developmental hemostasis” and plays an important role in the adaptation of a newborn child to the conditions of the extrauterine environment. Hemorrhages in newborns occur both when individual parts of the hemostasis system (vessels, platelets, coagulation factors) are damaged, and when they are combined. The incidence of cutaneous hemorrhagic syndrome of newborns ranges from 15.0 to 24.9% in neonatal departments of obstetric institutions. According to the type of hemostatic disorders, cutaneous hemorrhagic syndrome is divided into microcirculatory, hematomic and mixed types. The etiopathogenetic classification identifies platelet disorders (qualitative and quantitative) and blood clotting disorders that may be associated with the formation of hematomas and bruises, a combination of these two factors is possible. Cutaneous hemorrhagic syndrome can occur as an isolated one or be accompanied by other manifestations of hemorrhagic syndrome, such as gastrointestinal bleeding, intracranial hemorrhages, retinal bleeding, adrenal hemorrhages, etc. When examining a child with a skin hemorrhage, it is necessary to conduct a thorough examination, collect a hereditary and perinatal anamnesis, perform a general blood test and coagulogram, neurosonography and ultrasound examination of the abdominal cavity, kidneys and adrenal glands to exclude internal bleeding, conduct an oculist examination to exclude retinal hemorrhages. Local treatment of hemorrhages in the skin is not carried out, if disorders of the hemostasis system are detected, then correction of these disorders is carried out, which led to the development of cutaneous hemorrhagic syndrome.

Keywords: skin hemorrhage, newborns, cutaneous hemorrhagic syndrome of newborns, disorders of the hemostasis system of newborns, petechiae

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Кровоизлияние в кожу у новорожденного

Проект клинических рекомендаций для обсуждения специалистами неонатологами и педиатрами

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РЕЗЮМЕ

Система гемостаза новорожденных носит название «гемостаз развития» и играет важную роль в адаптации новорожденного ребенка к условиям внеутробной среды. Кровоизлияния у новорожденных возникают как при повреждении отдельных звеньев системы гемостаза (сосудов, тромбоцитов, факторов коагуляции), так и при их сочетании. Частота кожного геморрагического синдрома новорожденных составляет от 15,0 до 24,9% в отделениях новорожденных родовспомогательных учреждений. Кожный геморрагический синдром по типу нарушений гемостаза подразделяется на микроциркуляторный, гематомный и смешанный типы. Этиопатогенетическая классификация выделяет нарушения со стороны тромбоцитов (качественные и количественные) и нарушения свертываемости крови, которые могут быть связаны с образованием гематом и кровоподтеков, возможно сочетание этих двух факторов. Кожный геморрагический синдром может протекать как изолированный или сопровождаться другими проявлениями геморрагического синдрома, такими как желудочно-кишечные кровотечения, внутричерепные кровоизлияния, ретинальные кровотечения, кровоизлияния в надпочечники и др. При обследовании ребенка с кровоизлиянием в кожу необходимо провести тщательный осмотр, собрать наследственный и перинатальный анамнезы, выполнить общий анализ крови и коагулограмму, нейросонографию и ультразвуковое исследование органов брюшной полости, почек и надпочечников для исключения внутренних кровотечений, провести осмотр окулиста для исключения ретинальных кровоизлияний. Местное лечение кровоизлияний в кожу не проводится. Если выявлены расстройства системы гемостаза, то проводится коррекция этих нарушений, которые привели к развитию кожного геморрагического синдрома.

Ключевые слова: кровоизлияние в кожу, новорожденные, кожный геморрагический синдром новорожденных, нарушения системы гемостаза новорожденных, петехии

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DEFINITION

Hemorrhage in the skin of a newborn is a clinical and hematological syndrome characterized by the occurrence of hemorrhages into the skin and subcutaneous tissue due to disorders in the hemostatic system.

ETIOLOGY AND PATHOGENESIS

The hemostatic system of newborns is referred to as «developmental hemostasis» and plays a significant role in the adaptation of the newborn infant to the conditions of the extrauterine environment. Hemorrhages in newborns occur both as a result of damage to individual components of the hemostatic system (vessels, platelets, coagulation factors) and in cases of their combined disorders [1, 4, 5]. Damage to the vascular component of hemostasis with the development of cutaneous hemorrhagic syndrome occurs during traumatic deliveries, when the umbilical cord is wrapped around the neck (leading to increased pressure in the veins of the scalp), and during pressure fluctuations that occur during the passage of the chest through the birth canal [15]. Disorders of the cellular component of hemostasis lead to the development of petechiae and ecchymoses on the skin and occur with the development of thrombocytopenia and thrombocytopathy. Thrombocytopenia develops as a result of increased platelet destruction or reduced platelet production, and a combination of these two mechanisms is also possible [20]. Thrombocytopathy (disorder of platelet functional activity) is characteristic of all newborns during the first 10–14 days of life and may be exacerbated by perinatal diseases and the use of medicinal products with platelet-inhibiting properties. Thrombocytopenia and thrombocytopathy can be either acquired or hereditary/congenital. Disorders of coagulation hemostasis lead to the development of superficial hematomas and pronounced subcutaneous tissue ecchymoses, and may accompany a number of perinatal conditions (asphyxia, intrauterine infections, sepsis, vitamin K deficiency, etc.) or be hereditary in nature (hemophilia A, hemophilia B, von Willebrand disease, etc.). Involvement of all components of the hemostasis system in the pathological process occurs with the development of disseminated intravascular coagulation (DIC) syndrome, resulting in the simultaneous appearance of all morphological elements of cutaneous bleeding [4, 5, 9, 12, 18].

EPIDEMIOLOGY

Cutaneous hemorrhagic syndrome is diagnosed in 15.0–24.9% of infants managed in departments for neonatal physiology and pathology, presenting predominantly as petechial rash on the face and upper torso, which is considered a consequence of rapid or prolonged labor [5, 6]. In neonatal intensive care units (NICU), petechial rash is observed in 10.2–31.2% of newborns and ecchymoses in 4.2–22.2% [2, 5]. Cutaneous hemorrhagic syndrome may occur in isolation (45.5%) or be accompanied by other hemorrhagic manifestations (54.5%) — including subaponeurotic and intracranial hemorrhages, gastrointestinal bleeding, retinal hemorrhages, and adrenal hemorrhages. Isolated cutaneous hemorrhagic syndrome manifests at birth in 48.5% of cases, during the early neonatal period in 25.7%, and during the late neonatal period in 25.7%. Cutaneous hemorrhagic syndrome combined with other bleeding manifestations is diagnosed at birth in 56.1% of cases, in the early neonatal period in 24.3%, and in the late neonatal period in 19.6% [6].

FEATURES OF DISEASE CODING ACCORDING TO THE INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS (ICD-10)

P54.0 Hemorrhage into the skin of the newborn. This code is assigned when hemorrhagic elements in the form of petechiae, ecchymoses, bruises, or superficial hematoma are present on the newborn's skin, provided that diseases causing cutaneous hemorrhagic syndrome have been excluded. Code P54.0 provides for the registration of only four manifestations of cutaneous bleeding: petechiae, ecchymoses, bruises, and superficial hematomas.

Comment. *If hemorrhage into the skin is part of the symptom complex of a newborn disease that has its own ICD-10 code (e.g., congenital or transient thrombocytopenia, hemophilia, DIC syndrome, hemorrhagic disease of the newborn, birth trauma, congenital cytomegalovirus infection, sepsis), then hemorrhage into the skin is not coded as a separate diagnosis. In such cases, the type of hemorrhagic manifestations on the skin and subcutaneous tissue and the degree of severity of the clinical manifestations of cutaneous hemorrhagic syndrome are specified when justifying the corresponding diagnosis.*

CLASSIFICATION

Classification of cutaneous hemorrhagic syndrome by type of hemostatic disorder

The microcirculatory (petechial-spotty / bruising) type is characterized by painless, non-tense superficial hemorrhages into the skin and mucous membranes that do not compress surrounding tissues or cause their destruction — presenting as petechiae and bruises. Bleeding occurs with minimal trauma to microvessels, for example, at sites of blood pressure cuff application, sensor placement, or removal of adhesive tape [1].

The hematoma type of bleeding is characterized by massive, deep, tense, and typically painful intradermal hemorrhages and hemorrhages into the subcutaneous tissue, including subgaleal hemorrhage with ecchymoses in the neck area. Spontaneous, post-traumatic, and postoperative hemorrhages are observed, most of which are distinctly delayed in nature, occurring several hours after trauma, intramuscular injections, or other skin punctures [1].

The mixed (microcirculatory-hematoma) type is not merely a simple combination of features of the microcirculatory and hematoma types of bleeding, but rather a specific and interconnected aggregation of them. The classic manifestation of this type of bleeding is DIC syndrome [1].

Etiopathogenetic classification [10]

Platelet component disorders, specifically both quantitative and qualitative platelet abnormalities, are associated with bleeding manifestations, including petechiae and ecchymoses.

Qualitative disorders (thrombocytopathies) include Glanzmann thrombasthenia, Bernard–Soulier syndrome, platelet storage pool defects, and other platelet function deficiencies.

Quantitative disorders (thrombocytopenias)

Quantitative disorders include the following.

A. ***Congenital thrombocytopenias*** with reduced platelet production: amegakaryocytic thrombocytopenia, thrombocytopenia with absent radius (TAR) syndrome, amegakaryocytic thrombocytopenia without limb anomalies, Wiskott–Aldrich syndrome, Chediak–Higashi syndrome, May–Hegglin anomaly, Alport syndrome, and Bernard–Soulier syndrome; infiltrative bone marrow disorders, including congenital leukemia, congenital neuroblastoma, Letterer–Siwe disease, and osteopetrosis.

B. ***Increased platelet destruction:*** DIC associated with systemic infection or severe birth asphyxia; localized thromboses (e.g., renal vein thrombosis); necrotizing enterocolitis; maternal eclampsia; Kasabach–Merritt syndrome; systemic infections (bacterial, viral, fungal, and protozoal, both congenital and acquired); immune-mediated thrombocytopenias (neonatal alloimmune thrombocytopenia and neonatal autoimmune thrombocytopenia); and von Willebrand disease (type IIB).

C. ***Combined reduced production and increased destruction of platelets: i***nfection (congenital TORCH syndrome or acquired bacterial sepsis) and erythroblastosis fetalis.

D. ***Other causes:*** exchange transfusion, extracorporeal membrane oxygenation, and polycythemia.

Coagulation disorders that may be associated with the formation of hematomas and ecchymoses

Coagulation disorders associated with the formation of hematomas and ecchymoses include the following.

A. ***Hereditary coagulation factor deficiencies:*** X-linked recessive disorders (hemophilia A and B); autosomal dominant disorders (von Willebrand disease); and autosomal recessive disorders (deficiencies of factors XI, VII, V, X, II, XIII, and fibrinogen).

B. ***Acquired coagulation factor deficiencies:*** vitamin K deficiency; sepsis/necrotizing enterocolitis; renal vein thrombosis; severe liver disease; and maternal use of medications (vitamin K antagonists, salicylic acid and its derivatives, barbiturates and their derivatives, and hydantoin derivatives).

Combined platelet and coagulation system disorders — simultaneous presence of petechiae, ecchymoses, bruises, and hematomas:

a) disseminated intravascular coagulation;

b) liver dysfunction.

CLINICAL MANIFESTATIONS

Cutaneous hemorrhagic syndrome may be isolated or combined, primary or secondary, factors that determine its clinical presentation.

In patients with cutaneous hemorrhages, the clinical picture may consist of isolated cutaneous hemorrhagic syndrome (petechiae, ecchymoses, bruises, and hematomas) or may be accompanied by other hemorrhagic manifestations involving the platelet or coagulation arms of hemostasis. These manifestations do not always present with clinical signs of internal organ involvement. Non-massive, moderate hemorrhages at various sites (intraventricular hemorrhage, retinal hemorrhage, adrenal hemorrhage, subcapsular hepatic hematoma, among others) may follow an asymptomatic course. When an infant presents solely with bleeding symptoms, the underlying cause is most likely a hemostatic disorder or vitamin K deficiency (primary hemorrhagic syndrome). Conversely, when the infant exhibits “non-hemorrhagic” symptoms and signs of neonatal conditions — such as birth trauma, intrauterine infection, birth asphyxia, sepsis, severe hemolytic disease of the newborn, among others — the hemorrhagic syndrome may represent a manifestation or complication of an underlying neonatal disease (secondary hemorrhagic syndrome), warranting individualized clinical evaluation [6].

During follow-up of an infant with cutaneous hemorrhages, jaundice may develop due to hemolysis of red blood cells at the sites of hemorrhage, and hyperbilirubinemia may reach levels requiring phototherapy [6].

During follow-up, anemia may also develop; in such cases, further evaluation is warranted to exclude inter-

nal bleeding, which may remain clinically silent for a period of time (intraventricular hemorrhage, adrenal hemorrhage, subcapsular hepatic hematoma, intestinal bleeding, among others) [6].

DIAGNOSIS

Diagnostic criteria

Hemorrhages into the skin serve as a marker of hemostatic system impairment. Such infants require careful examination and evaluation to determine whether the manifestations of cutaneous bleeding represent a compensatory adaptive response of the neonatal hemostatic system to extrauterine life in the setting of the neonatal thrombophilic phenotype, whether they are the initial presentation of an inherited hemostatic disorder, or whether they reflect an underlying neonatal disease, including immune-mediated thrombocytopenias.

History and presenting complaints

- Obtaining a family and perinatal history is recommended to identify possible hemostatic abnormalities associated with the development of cutaneous hemorrhagic syndrome [3–5, 7, 10, 11, 17, 21, 24]. **Strength of recommendation: B (quality of evidence: 3).**

Comments.

Hereditary risk factors for hemostatic abnormalities associated with the development of cutaneous hemorrhagic syndrome include:

1. *A family history of increased bleeding tendency, manifested by easy bruising, epistaxis or gingival bleeding, menorrhagia, or prolonged bleeding from minor cuts.*
2. *The presence of relatives with confirmed hemostatic disorders.*

Prenatal risk factors for hemostatic abnormalities associated with the development of cutaneous hemorrhagic syndrome include:

1. *Maternal factors — hypertensive disorders, eclampsia, diabetes mellitus, medication use, infections, production of autoimmune or alloimmune antiplatelet antibodies, and HELLP syndrome.*
2. *Placental factors — placental abruption, chronic placental insufficiency, and placental vessel thrombosis.*

Intrapartum risk factors for hemostatic abnormalities associated with the development of cutaneous hemorrhagic syndrome include: *rapid or precipitous labor; labor abnormalities; malpresentation; asynclitic head engagement; deflexed head positions; low transverse station of the sagittal suture; forceps delivery and vacuum extraction; improper execution of obstetric maneuvers; induction/hyperstimulation of labor; and breech presentation.*

Neonatal risk factors for hemostatic abnormalities associated with the development of cutaneous hemorrhagic syndrome include: *asphyxia, birth trauma, small or large for gestational age, sepsis, necrotizing enterocolitis, polycythemia, cold injury, severe hyperbilirubinemia, severe hemolytic disease of the newborn, perinatal infections, renal vessel thrombosis and other thrombotic conditions, and use of medications that cause thrombocytopenia, thrombocytopathy, or hypocoagulation.*

Physical examination

- In a newborn with signs of cutaneous bleeding, a therapeutic visual examination is recommended [4, 5, 9, 21, 22]. **Strength of recommendation: B (quality of evidence: 3).**

Comments. *Therapeutic visual examination includes assessment for bleeding manifestations of the microcirculatory and hematoma types: examination of the skin to identify petechiae and ecchymoses, with attention to the cervical and inguinal folds and axillary region; examination of the neck and postauricular areas, where ecchymoses associated with subgaleal hemorrhage may be visualized; inspection of intramuscular injection sites (vitamin K administration) and the hepatitis B vaccination site, with palpation for induration; comparative measurement of thigh circumferences bilaterally, as intermuscular hematomas may occur in hemophilia, with blood gradually tracking into the subcutaneous tissue and ecchymoses appearing on a delayed basis. Examination of the mucous membranes — the conjunctivae, oral mucosa, and vaginal vestibule — should be performed to detect petechiae. Attention should be paid to bloody discharge from the nose, umbilical stump, or vagina, as well as blood-stained fluid obtained via gastric tube or endotracheal tube, noting the color (pink, brown, red) and amount of discharge. Neurological assessment should focus on signs that may indirectly indicate intracranial hemorrhage: separation of cranial sutures in subarachnoid hemorrhage (SAH) and ocular findings in SAH and intraventricular hemorrhage (IVH). Examination of the diaper contents should note the presence of blood streaks or blood in the stool, as well as a pink tint or blood clots in the urine.*

During follow-up examination, attention should be paid to the development of signs of posthemorrhagic anemia, which may indicate that the cutaneous hemorrhagic syndrome is part of a combined presentation. Jaundice may appear after 24–48 hours or later (as hemorrhages resolve).

Laboratory diagnostic tests

- In a newborn with cutaneous hemorrhages, a complete blood count with platelet and reticulocyte counts, with follow-up monitoring, is recommended

to detect thrombocytopenia, anemia due to blood loss, and hematologic signs of infectious disease [4, 5, 9, 16, 19, 25]. **Strength of recommendation: B (quality of evidence: 3).**

- In a newborn with pronounced cutaneous hemorrhages, coagulation studies (a screening assessment of the hemostatic system) are recommended if examination reveals one or more hematomas, one or more ecchymoses, or multiple petechiae and ecchymoses extending to the trunk and limbs beyond the presenting part. Coagulation studies should include measurement of fibrinogen levels, activated partial thromboplastin time, prothrombin time, and international normalized ratio to rule out coagulation disorders, including hemorrhagic disease of the newborn [4, 5, 9, 16, 19, 23, 25]. For differential diagnosis of hemorrhagic disease of the newborn, vitamin K1 (phytomenadione 1% emulsion) should be used. **Strength of recommendation: B (quality of evidence: 3).**

Instrumental diagnostic tests

- For all newborns with cutaneous hemorrhagic syndrome of any severity, neurosonography is recommended to assess for intracranial hemorrhage [4–6, 9, 10, 18, 21]. **Strength of recommendation: B (quality of evidence: 3).**
- For all newborns with multiple manifestations of cutaneous hemorrhagic syndrome, comprehensive abdominal ultrasound, including evaluation of the kidneys and adrenal glands, is recommended to rule out internal bleeding [4–6, 9, 10, 18, 21, 23]. **Strength of recommendation: B (quality of evidence: 3).**
- For newborns with cutaneous hemorrhagic syndrome involving the face combined with hemorrhages on the conjunctiva or sclera, ophthalmology consultation is recommended to rule out retinal hemorrhages [4, 5, 8, 13, 14]. **Strength of recommendation: B (quality of evidence: 3).**

TREATMENT

Treatment is required not for the cutaneous hemorrhages themselves, but for the hemostatic disorders that led to the development of cutaneous hemorrhagic syndrome. Therefore, treatment should be targeted according to the nature of the hemostatic abnormalities.

PREVENTION AND FOLLOW-UP, MEDICAL INDICATIONS AND CONTRAINDICATIONS FOR THE USE

In cases of pronounced isolated cutaneous hemorrhagic syndrome of the petechial-bruising type with normal aPTT and PT, hematology consultation is indicated to rule out thrombocytopathies. Assessment of platelet functional activity is advisable after 2 weeks of age, as a physiological reduction in platelet functional activity is observed in newborns during the first 2 weeks of life.

ORGANIZATION OF MEDICAL CARE

Evaluation of newborns with cutaneous hemorrhagic syndrome is performed in an inpatient setting.

Indications for hospitalization include:

1) the presence of pronounced cutaneous hemorrhagic syndrome (hematomas, ecchymoses, abundant petechial-bruising rash on the non-presenting part);
2) severe thrombocytopenia regardless of the severity of cutaneous hemorrhagic syndrome;
3) transfer to a higher-level facility (after stabilization of the condition, if necessary) for further evaluation and treatment when the facility where the infant was born lacks the capacity to perform the necessary diagnostic tests, consultations, and treatment.

Indications for discharge from the healthcare facility include:

1) satisfactory condition;
2) stabilization of the infant's condition with no progression of hemorrhagic elements on the skin;
3) no other contraindications to discharge.

CONCLUSION

Hemorrhage into the skin of the newborn is a common condition of the neonatal period, affecting up to 25% of newborns. Careful evaluation of cutaneous hemorrhagic manifestations is essential, as they may arise either from transient birth-related events or as a consequence of severe congenital or hereditary diseases. Any manifestations of cutaneous hemorrhagic syndrome warrant a basic coagulation workup. Based on the identified abnormalities in the platelet or coagulation arms of hemostasis, a diagnostic workup should be performed to identify the underlying condition responsible for the cutaneous bleeding.

ADDITIONAL INFORMATION

Author contribution. All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

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