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LANGERHANS CELL HISTIOCYTOSIS (A CLINICAL CASE)

Langerhans cell histiocytosis (LCH) is a rare myeloid disorder with a variable clinical presentation, based on the activation of the MEK-ERK signaling pathway in dendritic cell precursors. The localization of pathological lesions varies: the most common sites include the skeleton, skin, posterior pituitary gland, lymph nodes, liver, spleen, bone marrow, lungs, and central nervous system [2].

This article presents a clinical case of Langerhans cell histiocytosis in a newborn delivered at the Perinatal Center of the M.E. Nikolaev Republican Hospital No. 1-NCM. At birth, the child exhibited characteristic skin lesions in the form of a bumpy, dark cherry-colored rash on the scalp, fingers, and toes, with some areas showing light inclusions and a firm texture. Over time, with treatment, the pustules and vesicles ruptured, forming ulcers, crusts, and hemorrhages. The stages of diagnosis, including histological and immunohistochemical studies (CD1a+, Langerin+, S100+), differential diagnosis, and a comprehensive treatment approach, are described in detail. Special attention is given to the challenges of diagnosing newborns and the importance of interdisciplinary collaboration.

Keywords: Langerhans cell histiocytosis, newborns, skin manifestations, diagnosis, treatment, histological examination.

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Introduction. Langerhans cell histiocytosis is a heterogeneous disease characterized by the accumulation of dendritic cells resembling epidermal Langerhans cells in various organs. The disease can affect any organ or system in the human body, but most commonly involves the skeleton (80% of cases), skin (33%), and pituitary gland (25%). Other affected organs include the liver, spleen, hematopoietic system, and lungs (15% each), lymph nodes (5-10%), and the central nervous system, excluding the pituitary gland (2-4%) [3].

Epidemiological data indicate that LCH occurs at a rate of 3-10 cases per 1 million children annually. The male-to-female ratio is 2:1, with the peak incidence occurring in early childhood [4]. Early-onset LCH (before the age of 2) is associated with a high risk of developing multisystem forms, whereas monosystemic and monofocal forms are more commonly identified in children over 5 years old [1].

The causes of Langerhans cell histiocytosis remain unknown. No convincing evidence has been found to support genetic predisposition or infectious etiology. The pathogenesis of LCH is not fully understood. In 50-60% of patients, a somatic V600E mutation in the BRAF gene is detected, leading to activation of the MAPK/ERK signaling pathway [4,9]. In recent years, mutations in the MAP2K1, ARAF, and other components of this pathway have also been described [1, 7].

The clinical course of the disease varies from localized forms with benign progression and spontaneous recovery to disseminated forms with aggressive progression and fatal outcomes. Aggressive forms often present with malaise, weight loss, and developmental delays. Osteolytic bone lesions are observed in 80% of cases, lung involvement in 12-23%, and liver or spleen involvement in 15-50% [2, 5]. Skin lesions occur in 30-45% of cases, ranking second in prevalence after skeletal involvement. Lymph node involvement is the rarest symptom. In newborns and infants, skin lesions may be the only sign of LCH [3,1,8]. The rash can appear on the trunk, scalp, and other areas. Patients with skin, bone, or lymph node involvement classified as "risk-free organs" typically have a good prognosis and require minimal treatment. However, patients with "risk organ" involvement (liver, spleen, lungs, bone marrow) have a poorer overall prognosis. CNS involvement, vertebral or facial bones, or lesions in the anterior or middle cranial fossa also indicate an unfavorable prognosis for recovery. LCH in the orbit, mastoid, or temporal region is classified as a "CNS risk" due to the increased likelihood of diabetes insipidus, other endocrine abnormalities, or brain parenchymal lesions [5,9].

Since Langerhans cell histiocytosis can affect any organ or system, it should be considered in cases of clinical manifestations involving the skin, bones, lungs, liver, or CNS. The diagnosis is clinicopathological and should only be made in an appropriate clinical setting to avoid misdiagnosis due to the presence of normal reactive Langerhans cells, particularly in regional lymph nodes. In addition to clinical and radiological signs, the diagnosis must always be based on histological and immunophenotypic examination of affected tissue, which should be taken from the most accessible but representative lesion [3].

The goal of LCH treatment is to suppress the activity and proliferation of histiocytes, lymphocytes, and macrophages

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causing the disease. Treatment for "risk-free organ" LCH generally yields good results. Aggressive forms require immunosuppressive agents, radiation therapy, and other methods. New insights into LCH mechanisms open prospects for targeted therapy [7].

The prognosis depends primarily on initial "risk organ" involvement (especially bone marrow, liver, and lungs) with impaired function [6]. Timely diagnosis enables effective treatment, significantly improving the prognosis. Current experience shows that LCH with isolated skin involvement in newborns, when treated promptly, has a favorable course [7].

Objective: To describe a clinical case of Langerhans cell histiocytosis in a newborn.

Materials and Methods: A retrospective analysis of the medical records of a patient from the Department of Neonatal and Premature Pathology No. 2 of the Perinatal Center of the M.E. Nikolaev Republican Hospital No. 1-NCM was conducted. Data from clinical observations, laboratory tests, instrumental diagnostics, histological and immunohistochemical studies, and telemedicine consultations were used.

Clinical Case. A newborn boy, from the 6th pregnancy (first half – toxicosis, second half – anemia), 4th delivery. Gestational age: 38.6 weeks. Birth weight: 3750 g, length: 54 cm. Apgar score: 7/8.

At birth, the condition was severe due to grade 2 respiratory failure, signs of intrauterine infection, and pronounced skin syndrome. No resuscitation was required in the delivery room. The cry was loud but short, with groaning. The skin of the scalp, fingers, toes, and palms showed nodular, bumpy, dark cherry-colored rashes with some light inclusions and a firm texture. The face was cyanotic due to hemorrhages. Breathing involved accessory muscles, with retraction of the lower intercostal spaces and lower chest aperture. Auscultation revealed weakened breath sounds and transmitted wet rales. Heart sounds were clear and rhythmic. The abdomen was soft, liver +2 cm, spleen not enlarged. No stool or urination. External genitalia were male. Anus in the typical location.

The child was transferred from the delivery room to the neonatal intensive care unit (NICU) in a transport incubator on spontaneous breathing, connected to a ventilator in NCPAP mode with parameters: T.High – 0.4 sec, FiO2 – 25%, PEEP – 4.6 cm H2O. Conscious, responsive to manipulations with motor activity and crying. Pain score on N-PASS: 2. Head in birth configuration, face symmetrical. Eyelid edema present, photomotor reflex intact. Anterior fontanelle 1.0 x 1.0 cm, level with skull bones, non-bulging, non-pulsating, non-tense. Posterior fontanelle 0.5 x 0.5 cm. Sutures closed. No seizures. Neonatal reflexes present. Muscle tone physiological. No musculoskeletal abnormalities. Visible mucous membranes pink and moist. Nodular cherry-colored lesions present on all skin areas, including the scalp, some with firm-elastic infiltrates, elevated above the skin surface. Eyes clear. Acrocyanosis. Generalized edema. Umbilical vein catheterization was performed for intravenous therapy and blood sampling. Breathing on assisted ventilation, auscultation revealed air-oxygen flow noise transmitted throughout lung fields, weakened, with transmitted rales. Moderate retraction of the lower intercostal spaces. Respiratory failure score on the Silverman scale: 3.

Hemodynamics relatively stable. Heart sounds clear, rhythmic, systolic murmur. Radial and femoral pulses palpable, satisfactory filling. Capillary refill time: 3 sec on the sternum, 4 sec on extremities. Feeding with PreNaN formula and colostrum via gastric tube, bolus every 3 hours starting at 12 hours. Abdomen soft, non-distended, accessible to palpation. Occasional bowel sounds. Liver +1.5-2.0 cm below the costal margin, edge elastic. Spleen not enlarged. Anus in the typical location. No stool at the time of examination. External genitalia male. Urination free into the diaper. Preliminary diagnosis:

Primary diagnosis: P22.0 Neonatal respiratory distress syndrome: NRDS. P39.2 Intra-amniotic fetal infection, not elsewhere classified. Complication: Grade 2 neonatal respiratory failure.

Blood tests showed decreased hemoglobin (148 g/L), lymphocytopenia (16.7%). Biochemical analysis revealed hyperbilirubinemia (46.14 μmol/L). Urinalysis was normal. PCR for intrauterine infections negative. Echocardiography showed a patent ductus arteriosus (0.42 cm), an aneurysm of the secundum atrial septum with shunts (0.25 cm and 0.14 cm), signs of grade 1 pulmonary hypertension. Tricuspid valve regurgitation grade 1-2. Pulmonary artery dilation. Slight right ventricular enlargement. EF 70.1%. Chest and abdominal X-rays revealed hypoventilation and uneven intestinal pneumatization. Given the clinical picture and instrumental findings, ampicillin/sulbactam – 75 mg/kg/day, 0.37 mL twice daily IV, and local treatment of ruptured lesions with 1% potassium permanganate solution were prescribed.

On day 1, the child was transferred to the Department of Neonatal and Premature Pathology No. 2 (DNPP No. 2). Temperature 36.9°C. HR 122 bpm. RR 65 bpm. SaO2 100%. Oxygen support: NCPAP, O2 flow 1 L/min. Condition severe due to grade 1 respiratory failure and infection. Conscious. Loud cry, responsive to manipulations with painful crying and motor activity. Head in birth configuration, face symmetrical. Proportional build. Neonatal reflexes present. Anterior fontanelle 1.0 x 1.0 cm, non-tense. Posterior fontanelle 0.5 x 0.5 cm. Sutures closed. No seizures. Muscle tone in arms and legs physiological. Full hip abduction. Feeding via gastric tube with NaN1 + colostrum. Skin pale pink, face cyanotic, moist, pustules with purulent-hemorrhagic contents present on the scalp, face, behind the ears, fingers, axillae, and groin, some with firm-elastic infiltrates, elevated up to 0.8 cm in diameter, some ruptured with eroded surfaces. Visible mucous membranes clean, pink. Conjunctivae calm. Generalized edema. Peripheral lymph nodes not enlarged. Auscultation: breath sounds weakened, no rales. Percussion: lung sound. Heart sounds rhythmic, clear, systolic murmur at the apex. Femoral pulses palpable bilaterally, satisfactory filling. Abdomen soft, non-tender. Bowel sounds present. Umbilical stump dry, clean. Liver +1.0 cm. Spleen not enlarged. Meconium stool. Urine output monitored. Treatment continued as per orders.

Day 3: Skin pink with jaundice, petechiae on the forehead. Multiple ruptured lesions with crusting on the body and scalp; firm hemorrhagic lesions persist on the index fingers, left axilla, right shoulder, left little toe, and lower lip mucosa with serous-purulent discharge. No new eruptions.

Day 6: A consultation was held with neonatologists, a pulmonologist, and an allergist-immunologist. Further examinations were recommended, including consultations with a dermatovenereologist, geneticist, and tests for Krec, Trec, ANA, anti-denatured DNA, and complement C4.

Additional consultations: Ophthalmologist retinal angiopathy. Head ultrasound moderate periventricular hyperechogenicity. Abdominal and cervical spine ultrasound no abnormalities. Thymus ultrasound enlarged thymus with diffuse parenchymal changes resembling calcifications.

Skin pale, petechiae on the forehead fading. Multiple ruptured lesions with necrosis and hemorrhages on the body, scalp, and shoulders; firm hemorrhagic lesions persist on the left little toe and

lower lip mucosa as an ulcer with serous-purulent discharge. No new eruptions.

Lab results: CRP elevated to 15 mg/L. Staphylococcus saprophyticus and Enterococcus faecalis isolated from umbilical blood; Enterococcus faecalis (10^3 CFU) and E. coli (10^4 CFU) from skin. Coagulogram showed moderate hypocoagulation, prolonged prothrombin time. [Per cardiologist-rheumatologist recommendation, a chest CT was performed: lung volume preserved. Uneven lung aeration. Multiple foci of consolidation in both lungs, some with cavitation. Bronchial lumens narrow. No pleural effusion. No enlarged intrathoracic lymph nodes. Thymus heterogeneous, with hyperdense and hypodense inclusions, enlarged. Transverse thymus size: 6.4 cm, coefficient 0.87. Conclusion: CT findings consistent with bilateral polysegmental destructive pneumonia. Thymomegaly grade 3.] Given CRP elevation to 15 mg/L, ampicillin/sulbactam was increased to 150 mg/kg/day IV in 3 divided doses. Hemostatic therapy: sodium etamsylate 12.5% 10 mg/kg, 0.3 mL IV 4 times; menadione sodium bisulfite 1% 0.3 mL IM once. Immunomodulatory therapy: Viferon-1 150,000 IU twice daily rectally. Local treatment: 1% potassium permanganate solution for ruptured lesions.

Day 9: Second consultation with neonatologists, pulmonologist, and allergist-immunologist. Recommendations: PCR urine for fungi to rule out fungal pneumonia; microscopy for fungi (urine, throat, stool); stool for opportunistic flora; consultations with a surgeon and geneticist; referral for telemedicine consultation to the "Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology, and Immunology" and the "V.I. Kulakov National Medical Research Center for Obstetrics, Gynecology, and Perinatology."

Microscopy: isolated fungi in throat swab, none in stool or urine. CRP elevated to 33.54 mg/L. COVID-19 ELISA negative. Consulted by a surgeon, dermatovenereologist, and geneticist. Dermatovenereologist's diagnosis: Pyoderma. Geneticist's diagnosis: Unspecified congenital infectious disease. Pyoderma. Congenital immunodeficiency not excluded.

Gentamicin was added at 7.5 mg/kg/day in 2 divided doses (2.5 mg/kg 3 times daily). Antifungal therapy per clinical guidelines "Invasive Candidiasis in Newborns": fluconazole (Diflucan) 6 mg/kg/72 h IV.

Day 12: Telemedicine consultation with specialists from the "V.I. Kulakov National Medical Research Center for Obstetrics, Gynecology, and Perinatology." Given the characteristic skin lesions from birth, their distribution, and clinical progression, Langerhans cell histiocytosis Hashimoto-Pritzker syndrome could not be ruled out. Further differential diagnosis was recommended. Treatment: switch antibiotics to vancomycin + sulperazon; use only aqueous disinfectants for skin lesions; treat erosions with "Sudocrem," "Bepanthen ointment," or zinc ointment.

Following the consultation, a clinical pharmacologist at the M.E. Nikolaev Republican Hospital No. 1-NCM recommended against vancomycin due to severe intrauterine pneumonia, high CRP (33.54 mg/L), and isolation of Staphylococcus saprophyticus and Enterococcus faecalis resistant to clindamycin, cefoxitin, moxifloxacin, and ciprofloxacin. Cefoperazone/sulbactam was prescribed per empirical antibiotic therapy protocol at 40 mg/kg/day in 2 divided doses with IV test dose. Gentamicin continued at 7.5 mg/kg/day in 2 divided doses (2.5 mg/kg 3 times daily). Sodium etamsylate was discontinued due to normalized coagulogram. Antifungal therapy with fluconazole and local skin treatment continued.

Day 14: Skin pale pink. Multiple pale red-pink papules and nodules in regression with crusting on the face, scalp, trunk, and limbs, treated with fucorcin. Single ulcer on the lower lip mucosa in epithealization phase. No new eruptions; significant skin improvement. Healing lesions behind the ears, buttocks, and calves.

Day 16: Condition improved, child more active, pinker, less shortness of breath, no oxygen dependence, skin lesions regressing. Mixed feeding, appetite preserved. Skin pale pink, one vesicle forming on the nose tip; old lesions fading with residual pigmentation, single crusts on the left little toe and hand. Infiltrate on the right shoulder reduced in size, softer. Given clinical improvement and CRP decrease to 29 mg/L, gentamicin was discontinued. After a second telemedicine consultation with the "Dmitry Rogachev National Medical Research Center," viral etiology could not be excluded, so acyclovir was added at 20 mg/kg/day IV in 3 divided doses. Cefoperazone/sulbactam, fluconazole, and local skin treatment continued. Surgery performed to remove the lesion on the right shoulder; specimen sent for histology.

Day 17: Third consultation with the deputy director of neonatology, neonatologists, clinical pharmacologist, pulmonologist, and allergist-immunologist. Decision: continue antibiotics, withhold meropenem + vancomycin given stable clinical picture and declining CRP. Continue fluconazole and acyclovir. Per telemedicine consultation with the "Dmitry Rogachev National Medical Research Center," IV immunoglobulin was added at 1 g/kg over 2 days.

Day 20: Skin pale pink. Lesions resolving with residual pigmentation; crusts shed from the left little toe and hands; crusts persist on the middle finger and scalp, healing. Postoperative wound on the right shoulder, sutures intact. Oral mucosa infiltrate reduced. Day 23: Skin pale pink, residual pigmentation at lesion sites, no new eruptions. Postoperative wound on the right shoulder clean, sutures intact.

At 1 month of age, histology results: Langerhans cell histiocytosis. H&E: 4 IHC: CD1a, Langerin, S100. The report was sent for telemedicine consultation to the "Dmitry Rogachev National Medical Research Center" and the "V.I. Kulakov National Medical Research Center" for further management recommendations.

Conclusion. Based on histology, the diagnosis was confirmed: C96.6 Langerhans cell histiocytosis. The child was transferred from the neonatal pathology department to the oncology unit for specialized treatment. Langerhans cell histiocytosis in newborns presents significant diagnostic challenges due to nonspecific clinical presentation. The gold standard for diagnosis is histological examination with immunohistochemical confirmation. Treatment must be comprehensive, considering the extent of involvement, patient age, and molecular-genetic features. An interdisciplinary approach involving neonatologists, oncologists, immunologists, and other specialists improves prognosis.

Future research should focus on molecular mechanisms of LCH in newborns, developing targeted therapy protocols for this age group, and creating a registry for rare cases.

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References

1. Fayzullina R.M. , Gafurova R.R., Shangareeva Z.A., et al. Gistiocitoz iz kletok Langergansa – trudnyj diagnoz (klinicheskie sluchaj) [Histiocytosis from Langerhans cells – a difficult diagnosis (clinical case)]. Doktor Ru. 2019; 9 (164): 25-29. URL: https://journaldoctor.ru/catalog/pediatriya/gistiotsitoz-iz-kletok-langergansa-trudnyy-diagnoz-klinicheskiy-sluchay/.

2. Klinicheskie rekomendacii po diagnostike i lecheniyu gistiocitoza iz kletok Langergansa u detej. Minzdrav Rossii [Clinical guidelines for the diagnosis and treatment of Langerhans cell histiocytosis in children. Ministry of Health of Rus-