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STEVENS JOHNSON SYNDROME ASSOCIATED WITH COVID-19 IN CHILDREN

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Abstract

COVID-19 in children was previously mild, but in recent years, some "convalescents" have new syndromes 4-12 weeks after acute coronavirus infection, and this is accompanied by a severe course of the disease, accompanied by multiple organ failure and multisystem inflammation. The paper provides a retrospective analysis of the medical history of a newborn child born to a mother who suffered Covid-19 during pregnancy at 29 weeks. The authors discuss possible clinical variants of coronavirus infection and the addition of Stevens-Johnson syndrome, its origin and outcomes

Keywords: COVID-19, post-covid syndrome, children, post-vaccination immunity to measles, multi-system inflammatory syndrome

Introduction. In recent years, among some children who have had a new coronavirus infection, new symptoms and syndromes have begun to appear after 4-12 weeks as a life-threatening immunopathological complication of the underlying disease. This pathological condition, which threatens the patient's life, is called pediatric multisystem inflammatory syndrome (DMVS).[1-4, 8-10]. It is registered in the ICD-10 under the code M35,81 as a multi-system inflammatory syndrome. Previously, the largest number of clinical and laboratory-instrumental manifestations and outcomes of COVID-19 were called pediatric multisystem inflammatory syndrome and [1].

Pediatric multisystem inflammatory syndrome associated with COVID-19 occurs with fever, arterial hypotension/shock, sepsis, systemic vasculitis of small and medium-sized vessels, multiorgan inflammation affecting the skin and mucous membranes, the development of acute respiratory distress syndrome (ARDS), acute respiratory failure (ODN), pulmonary embolism (PE), damage to the heart, gastrointestinal tract, nervous system, lungs, kidneys [1-4].

Earlier, in April-May 2020, for the first time in a number of countries- Italy, France, Switzerland, England, and the United States after coronavirus infection, there were reports of cases of DMVS and Kawasaki-like syndrome followed by the development of multiple organ

failure and shock in children [5-7]. This syndrome occurred not only in children, but also in adults as a complication of COVID-19 [2-5].

At the end of last summer, domestic specialists and doctors from a number of European, North American and Russian countries reported severe diseases in children, manifested by fever and multiple organ changes with characteristic laboratory signs of severe inflammation [9, 11-13]. A link was found between the observed disease and a previously transmitted new coronavirus infection, which in all cases was confirmed by the presence of specific antibodies (IgG) in the blood of patients. Other names of the syndrome found in foreign literature: Kawasaki-like syndrome, Paediatric inflammatory multisystem syndrome (PIMS TS), multisystem inflammatory syndrome in children (MIS-C) [11, 12].

The objective of this paper is to review and analyze the medical history of a newborn with PMIS associated with COVID-19, who received inpatient care in the intensive care and resuscitation unit.

Materials and methods. To obtain information, publications on PMIS associated with COVID-19 were searched in databases such as PubMed, Web of Science, Google Scholar, Clinical Trials, and the CyberLeninka electronic scientific library. Personal observations of the authors were also used.

The diagnosis of PMIS associated with COVID-19 was established by a national-level medical consilium (including experts from scientific centers and universities) based on the detection of class G S-RBD Ig (neutralizing antibodies) to COVID-19. Clinical and laboratory research, diagnostics, and treatment of patients were conducted following the current clinical protocol of the Ministry of Health of the Republic of Uzbekistan.

Clinical case description from personal practice:

Patient A., a full-term male newborn weighing 2500 grams and measuring 52 cm in length at birth, was admitted to the Regional Children's Multidisciplinary Medical Center neonatal intensive care unit immediately after

birth and later transferred to the surgical department with the diagnosis: multisystem inflammatory syndrome associated with COVID-19, Stevens-Johnson syndrome, intra-uterine infection, sepsis (prenatal period, sub-acute fulminant course, septicopyemic form), and severe form. Infection foci included infectious-toxic encephalopathy, infectious carditis, gastroenterocolitis, nephritis, bronchopneumonia in perihilar zones, purulent-necrotic orchitis, epidermal necrolysis of skin and mucous membranes, omphalitis, dry gangrene of bones, and infectious-toxic hepatitis (bilirubinemia). Comorbidities included cytomegalovirus infection (CMV+), herpes simplex virus types 1/2 (HSV1/2+), Epstein-Barr virus (EBV+), infectious-nutritional anemia, and severe protein-energy deficiency (-3SD). Hospitalization lasted 37 days with an extremely severe disease course.

From the patient's history: the child was the second pregnancy, first delivery (the first pregnancy ended in a spontaneous miscarriage), born with umbilical cord entanglement, and scored 6 on the Apgar scale. The mother had COVID-19 during pregnancy at 29 weeks (documented by two positive COVID-19 rapid tests). The mother's S-RBD SARS CoV-2 IgG antibodies were significantly elevated (4330; norm ≥ 4.33). The mother's condition during pregnancy was severe, requiring hospitalization for 17 days with acute COVID-19, high fever (39° – 42° C), lung involvement (30% on MSCT), shortness of breath, diarrhea, systemic vasculitis of small and medium vessels, and multi-organ

erosions on the lips, oral mucosa, tongue, soft palate, pharynx, and larynx, which fused into extensive, severely painful surfaces covered with black fibrinous plaque. The child was fed through a nasogastric tube and had persistent high fever (39° – 40° C) for a week, followed by a rapid temperature drop to 34° C.

Stevens-Johnson syndrome and toxic epidermal necrolysis are typically triggered by drugs or infections. Typical symptoms include skin detachment, fever, body pain, flat red rash, blisters, and ulcers on mucous mem-

branes. In this case, the disease progressed following maternal COVID-19 infection and an allergic reaction to cephalosporins, leading to PMIS and severe septic condition.

Stevens-Johnson syndrome was marked by pain in the skin and mucous membranes, with multiple purplish-red spots, papules, vesicles, and target-like lesions forming on the skin. The child's S-RBD SARS CoV-2 IgG antibodies were significantly elevated (433; norm ≥ 4.33). The eruption phase lasted 2–3 weeks, and ulcer healing did not occur.

The disease was complicated by bladder bleeding, pneumonia, hepatosplenomegaly, colitis, acute renal failure, secondary bacterial infection, and loss of vision and hearing.

The severe course of the disease was accompanied by detachment of large areas of

the epidermis, and extensive erosions formed on the skin and mucous membranes. These lesions were accompanied by water-electrolyte imbalances and massive protein loss. Against the background of these processes and the loss of the skin's barrier function, sepsis developed. Laboratory tests confirmed our diagnosis. The child's indicators were either above or below the normal threshold values. Hyperbilirubinemia was noted, with liver enzyme levels (ALT, AST) elevated by 4 to 5 times, lipid metabolism disorders, and urinary tract damage — the urine was filled with leukocytes and erythrocytes. Blood tests showed pronounced leukocytosis, neutrophilia, and an elevated erythrocyte sedimentation rate (ESR) of 38 mm/h.

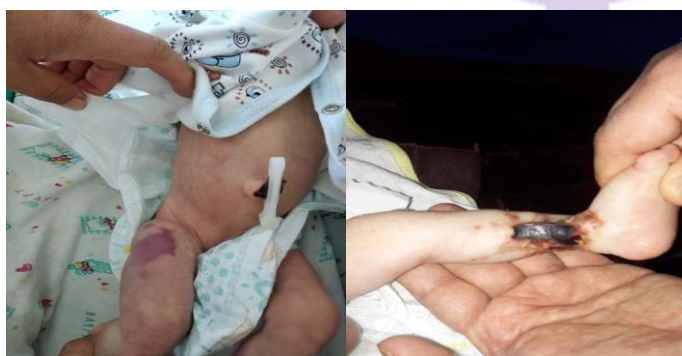


Fig. 1-2: A 2-week-old infant with multisystem inflammatory syndrome associated with COVID-19. Intrauterine infection (IUI), sepsis, Stevens-Johnson syndrome, and dry gangrene of the skin and bones of the left leg.



Fig. 3-4. A 2-week-old infant. Multisystem inflammatory syndrome associated with COVID-19. Intrauterine infection (IUI), sepsis. Stevens-Johnson syndrome. Dry gangrene of the skin and penis.



Fig. 5-6. A 2-week-old infant. Multisystem Inflammatory Syndrome associated with COVID-19. Intrauterine infection (IUI), Sepsis. Stevens-Johnson Syndrome. Dry gangrene of the skin and scrotum.

The immunogram revealed significant leukocytosis of 41,700/ μ L (normal range: 4,500-9,000/ μ L), severe lymphopenia at 7% (normal: 30-42%), elevated T-helper inducers at 56% (normal: up to 48%), and increased T-cytotoxic lymphocytes at 41% (normal: 9-35%). Natural killer cells (NK) and IgE were elevated, phagocytosis was reduced, and circulating immune complexes (CIC) associated with IgM and IgG were increased. Levels of D-dimer, fibrinogen, C-reactive protein, and procalcitonin were also elevated. Procalcitonin plays a crucial role in diagnosing generalized infection as a marker of systemic inflammation induced by bacteria. Its synthesis is primarily induced by endotoxins of gram-negative bacteria; interleukin-6 (IL-6) was also above normal, while tumor necrosis factor-alpha (TNF- α) was low at 0.9 pg/L, indicating an unfavorable disease prognosis.

Bacteriological examination of the blood identified *Staphylococcus epidermidis* and *Staphylococcus aureus*; *Staphylococcus aureus* was also isolated from the urine, *Escherichia coli* from the stool, *Pseudomonas aeruginosa* from the throat, and *Streptococcus haemolyticus*, *Proteus*, and other organisms from the nasal cavity and visible infection sites. This demonstrated widespread colonization of the body with both gram-positive and gram-negative microorganisms.

Symptomatic treatment was aimed at reducing intoxication, desensitization, alleviating inflammation, and accelerating the epithelialization of affected skin areas. The treatment involved antibiotics (ampicillin, meropenem, vancomycin), desensitizing agents, bacteriophages, anticoagulants as indicated, anti-inflammatory drugs (salicylates), calcium preparations, ethacridine lactate, and levamisole to control exacerbations, corticosteroids, and detoxifying therapy.

Local treatment focused on reducing inflammation, swelling, and promoting epithelialization of the affected skin. Pain relievers, antiseptic agents, and proteolytic enzymes were used. Despite intensive anti-shock therapy, the child died on the 37th day of life.

Conclusion. Thus, this infant was diagnosed with Multisystem Inflammatory Syndrome (MIS), a newly recognized condition temporarily associated with the SARS-CoV-2 virus and capable of leading to severe and life-threatening disease progression. MIS associated with COVID-19 is a delayed immunological phenomenon linked to the development of inflammation following symptomatic or asymptomatic COVID-19 infection.

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