Chickenpox in HIV-infected 11-years old child with lethal outcome

Halyna Lytvyn¹, Iryna Dybas², Olga Hladchenko³, Natalia Ivanchenko⁴, Filip Pajak⁵

¹Assoc. Prof., Department of pediatric infectious diseases, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +38(067)7420493, Email: golytvyn2002@gmail.com
²Assoc. Prof., Department of pediatric infectious diseases, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +38(097) 2898285, Email: idybas24@gmail.com
³Assist prof., Department of pediatric infectious diseases, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +38(096) 7775377, Email: hladchenko.olya@gmail.com
⁴Assist prof., Department of infectious diseases, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +38(067) 1674584, Email: timknat@ukr.net
⁵Post-graduate student, Medical faculty, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +48695522032, Email: phillip.pajak@gmail.com

Article History
Received: 17 June 2020
Reviewed: 18/June/2020 to 28/July/2020
Accepted: 29 July 2020
E-publication: 04 August 2020
P-publication: September - October 2020

Citation

Publication License
This work is licensed under a Creative Commons Attribution 4.0 International License.

General Note
Article is recommended to print as color digital version in recycled paper.

ABSTRACT
The case presents a severe form of generalized chickenpox in an 11-year-old HIV-positive child. Simultaneous lack of prior antiretroviral therapy, concealment of the child’s HIV status, late request for medical help and many factors were seen. Delayed adequate specific treatment led to a dramatic lethal course of the disease.
Keywords: children, HIV, varicella, immunosuppression, complications

1. INTRODUCTION

Varicella (chickenpox) takes the first place among highly contagious pediatric infectious diseases with an airborne mechanism of transmission. Annually in Ukraine 120-150 thousand pediatric cases are registered, among around 80-90 mil cases reported globally. It takes the third position after acute respiratory viral infections and acute gastrointestinal tract infections. Varicella Zoster Virus can lead to two clinical forms, distinguished as separate diseases: Varicella (chickenpox) or Shingles (Herpes Zoster). Although immunocompetent children that suffer from varicella have mild or medium severe course of disease, we tend to observe increased prevalence of complications. Among them pneumonia, encephalitis, phlegmon - especially at early age of life or adolescence. Varicella’s lethality remains relatively high – 0.01% - 0.05%, varying between 1.7 per 100 000 of children from 1 year 14 years old, to 26.0 per 100 000 people in age 39-40 years old (Kramaryev, 2017; Bayanova et al., 2019). Of special attention are immunocompromised pediatric patients, which account for higher risk of severe, generalized forms of disease. Severe course is typical for subjects with primary immunodeficiencies, onco-hematologic pathologies, newborns and children after cytostatic treatment or high steroid therapies. Research data on the peculiarities of chickenpox in HIV-infected people are of great importance. Ukraine remains the European leader in terms of HIV spread. According to UNAIDS experts, the amount of HIV infected people makes 240 000 cases in the country. Public Health Institute at Health Ministry of Ukraine in 2019 mentioned 13 000 new cases reported (including 62 of children up to 14 years) (SNID v Ukraini: statystyka, 2019).

The course of varicella at HIV-positive children is characterized by prolonged rash period, more diffuse and accompanied by high fever that may last over 2 weeks (Ruleva et al., 2014). According to reported observations, risk of generalized infection at such subjects makes 36% (The Pink Book: Course text book 12th ed., 2012). At HIV-positive children severe course of disease develops 15 times more often in relation to HIV-negative subjects (Ruleva et al., 2014). There is relatively little research reported on lethality of varicella HIV+ children. According to Son M., Shapiro E. D. 58% HIV+, varicella patients developed pneumonia and lethality among made 43 % (Son et al., 2010).

2. CASE PRESENTATION

An 11-year-old child was admitted to Lviv Regional Infectious Hospital at 16th day of disease with diagnosis of varicella, bilateral bronchopneumonia; severe respiratory failure and severe cardiac insufficiency. Mother stated that in the last half a year prior to admission, the child frequently had episodes of upper respiratory tract infections, obstructive bronchitis and sinusitis, each time receiving a course of antibiotics. Mother denied HIV possibility and did not agree for a test. Prolonged duration and worrying features of the disease led to necessity of the testing, after which mother confessed giving birth ten years ago to a child that was being cured at a local pediatrician with inosine pranobex and antihistamine medications. However, the rash lasted up to 2 days periodicity, malaise increased, cough, nausea, vomiting appeared and temperature reached 39°C. In such circumstances mother consulted infectionist but refused hospitalization. On the 16th day of disease the general state of the child dramatically worsened: signs of respiratory failure appeared, cough increased. The first hospitalization took place at an intensive care unit in CRL, and then the child got transferred to Lviv Regional Clinical Hospital.

At admission general state was critical due to signs of severe respiratory failure, developed on the basis of bilateral focal pneumonia. Skin was pale, visible perioral cyanosis and acrocyanosis. Whole body was covered with small polyformic elements, mostly vesicles (Photo 1).

Temperature of the body 36.6, Respiratory Rate (RR) - 28/min, Heart Rate (HR) - 88, Arterial Pressure (AP) - 110/88, SpO2 - 88%, spontaneous respiration, inefficient. On auscultation - weak respiratory sounds at mid-lower segments, bilaterally, scattered dry rales. Mechanical ventilation started (PC+BIPAP, PEEP 12, Prms 26-28, FiO2 0.6-0.7). The big amount of viscous sputum was sucked off the endotracheal tube.

Blood analysis showed: Hb - 120 g/L, RBC – 4.31*10^12/L, HCT - 50% PLT - 225*10^9, WBC – 8.0*10^9/L, Neu-87.2%, Lym- 4.8%, Mxd-8.0%, ESR – 6 mm/h. Coagulation: prothrombin time 22", prothrombin index 68.1%, fibrinogen – 2.48 mg/L. Cerebrospinal fluid
revealed no pathologic changes. In sputum - C. Albicans, S. Aureus; vesicular fluid - S. Aureus. X-ray of thorax - signs of pneumonia: bilateral infiltrative focal shadows on all parts of lungs, emerging with lung roots and heart shadow (Photo 2).

![Photo 1](image1)

**Photo 1** Skin with small polyformic elements, mostly vesicles

![Photo 2](image2)

**Photo 2** Bilateral pneumonia

ECG - sinus tachycardia, HR - 130/min, posterior-lateral repolarization disturbances. HIV rapid-test - positive. ELISA detected HIV antibodies, Herpes 1, 2 antibodies - negative, VZV antibodies (Herpes 3) – 7.5 DU/ml (negative at 0.0-8.0 DU/ml), VZV IgG – 9.62 DU/ml (doubtful at 9.0-11.0 DU/ml).

The child was consulted by pediatric intensivist, TB specialist, pulmonologist, and laryngologist. Since the moment of hospitalization (16th day of disease), intravenous acyclovir 20 mg/kg/day was started simultaneously with 2 antibiotics - carbapenem and tricyclic glycopeptide (‘tiaktam’ 60 mg/kg/day and vancomycin 40 mg/kg/day. Normal human immunoglobulin was used (‘bioven mono’ – 12.5 g), co-trimoxazol (‘biseptol’ 120 mg/kg/day), fluconazol (100 mg/day), dexamethason 0.2 mg/kg/day) and detoxification therapy. Despite the given therapy, the general condition of the child deteriorated, signs of respiratory failure increased. On the 19th day of the disease the child died.

3. DISCUSSION
The mechanisms of origin, development and course of chickenpox, compared with other diseases, have their own characteristics. They are primarily due to the fact that the VZV genome encodes immunomodulatory proteins that allow the virus to evade the action of immune response factors. Key moment of general process is the activation of cytoplasmic transcription factor NF-κB (Deev, 2015; Leuridan et al., 2011). Its activation leads to expression of aggressive molecules (ICAM, VCAM) and proinflammatory cytokines:
gamma-interferon (IFN-γ), Alfa-tumor necrotic factor (TNF-a), Interleukins - IL6, IL8 (Como et al., 2018; Deev, 2015). NF-kB induces also expression of the major histocompatibility complex (MHC) of the first class (MHC-1) by antigen-presenting cells, stimulating the activation of T cells (Leuridan et al., 2011). VZV interrupts NF-kB factor migration to cell nucleus, by blocking its activation (Nezgoda & Levytska, 2017). Another strategy of virus to paypass immunologic control involves MHC-I, MHC-II protein expression. In infected cells, MHC-1 molecule transport from Golgi apparatus to cell membrane is interrupted, as a result blocking their presentation and cytolysis by CD8+ lymphocytes (Deev, 2015). One more mechanism of immunomodulation is that infected cells lower expression of INF-γ-induced MHC of 24 I class, which subsequently leads to decreasing cells’ ability to present antigen to CD4+ lymphocytes. Blocking of IFN-γ action on MHC-II expression interrupts T-lymphocytes sensitization to VZV peptides, which inhibits clonal proliferation of the virus-specific T-helpers and release of cytokines in skin replication sites. That gives the virus the required time interval for replication and accumulation of a sufficient number of virus-infected cells (Qi et al., 2016; Nezgoda & Levytska, 2017).

The rapid appearance of new elements on the skin may be associated with the recirculation of T lymphocytes through existing elements of the rash, their infection with the development of secondary T-cell-associated viremia and re-introduction of the virus into skin cells (Kleinschmidt-DeMasters & Gilden, 2001). This process of new rashes can be interrupted only by the inclusion of a specific T-cell response (Deev, 2015).

Simultaneously with the development of HIV infection, a deficiency of both humoral and cellular factors of the immune system is formed. The consequence of continuous polyclonal activation of B-lymphocytes is hyperglobulinemia (Ig G), but the quality of antibodies deteriorates and B-cell function becomes defective, which leads to immune response decrease. Depletion of cellular and humoral immune systems is the cause of potentially high risk of infection and severe chickenpox course in HIV patients (De Milito et al., 2004; Laing et al., 2018).

Management of such patients requires the concomitant use of specific antiviral (antiherpetic) therapy with ART therapy in the early stages of chickenpox (must be started within 24 hours of the rash) (Guidelines for the Prevention and Treatment of Opportunistic Infections In HIV-Exposed and HIV-Infected Children, 2020). The only effective method of preventing chickenpox and complications is vaccination. According to WHO recommendations, the administration of chickenpox vaccine is safe for HIV-infected children with CD4+ T-lymphocyte count of more than 200 cells / mm3 (≥15%). The effectiveness of vaccination against chickenpox increases with the prescription of ART within 3 months before its implementation (Mofenson et al., 2009).

4. CONCLUSION

The clinical case presents the description of a severe course of the generalized form of chickenpox in the HIV-infected child with lethal outcome. Late treatment, refusal of hospitalization and prescribed therapy, concealment of life history of the child’s HIV status- lack of appropriate testing and antiretroviral therapy, late administration of acyclovir and immunomodulatory therapy, this all led to a dramatic end of the disease. The only effective method of preventing chickenpox and its complications in HIV-infected children is vaccination.

Acknowledgement

We thank patient’s mother and our colleagues from Lviv Regional Infectious Hospital who participated in and contributed samples to the study.

Author Contributions

Research concept and design of research  Halya Lytvyn, Iryna Dybas
Collecting material  Olga Hladchenko, Natalia Ivanchenko
Material processing  Halya Lytvyn, Iryna Dybas
Writing text  Iryna Dybas, Filip Pajak
Text editing  Halya Lytvyn, Natalia Ivanchenko

Funding

This study has not received any external funding.

Conflict of Interest

The authors declare that there are no conflicts of interests.
Informed consent
Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval for study protocol /study design /Methodology
The study was approved by the Medical Ethics Committee of Danylo Halytskyi Lviv National Medical University (ethical approval code: 171/20).

Data and materials availability
All data associated with this study are present in the paper and/or the Supplementary Materials.

Peer-review
External peer-review was done through double-blind method.

REFERENCES AND NOTES