CASE REPORT

24(105), September - October, 2020

ISSN 2321–7359
EISSN 2321–7367

Medical Science

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

Halyna Lytvyn[1], **Iryna Dybas**[2], **Olga Hladchenko**[3], **Natalia Ivanchenko**[4], **Filip Pajak**[5]

[1]Assoc. Prof., Department of peadiatric infectious diseases, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +38(067)7420493, Email: golytvyn2002@gmail.com

[2]Assoc. Prof., Department of peadiatric infectious diseases, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +38(097) 2898285, Email: idybas24@gmail.com

[3]Assist prof., Department of peadiatric infectious diseases, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +38(096) 7775377, Email: hladchenko.olya@gmail.com

[4]Assist prof., Department of infectious diseases, Danylo Halytskyi Lviv, National Medical University, Ukraine; tel. +38(067) 1674584, Email: timknat@ukr.net

[5]Post-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

Halyna Lytvyn, Iryna Dybas, Olga Hladchenko, Natalia Ivanchenko, Filip Pajak. Chickenpox in HIV-infected 11-years old child with lethal outcome. *Medical Science*, 2020, 24(105), 3101-3105

ABSTRACT

The case presents a severe form of generalized chickenpox in an 11-year-old HIV-positive child. Simultaneous lack of prior anti retro viral 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 being HIV positive, refusing Anti-Retroviral Therapy (ART) during pregnancy stated that after delivery the newborn was under supervision of AIDS Center till 18th month of life, subsequently without mothers allowance to apply ART nor test.

Epidemiological interview revealed the patient was attending a school with known chickenpox cases. The disease itself started typically with maculo-papulo-vesicular rash on the scalp and face that later spread to the torso and extremities, visible mucous membranes, genitals. Exanthema appearance followed subfebrile temperature with signs of general intoxication. In this period the child was being cured at a local pediatrician with inosine pranobex and antihistamine medications. However, the rash lasted till the 12th day of disease with 1-2 days periodicity, malaise increased, cough, nausea, vomiting appeared and temperature reached 39^{o}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, P_{ins} 26-28, FiO_2 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).

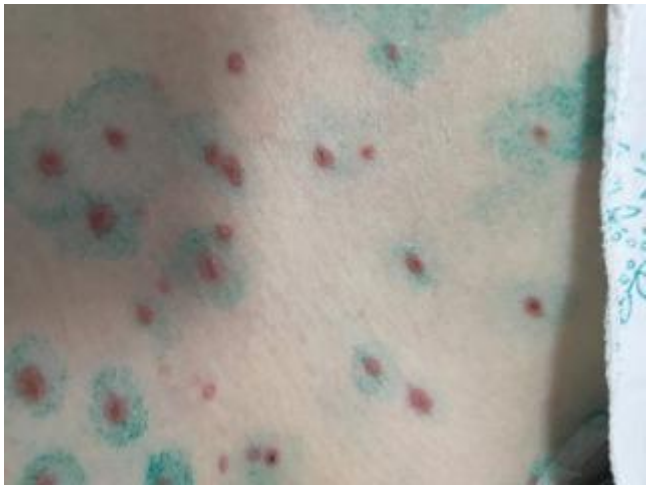

Photo 1 Skin with small polyformic elements, mostly vesicles

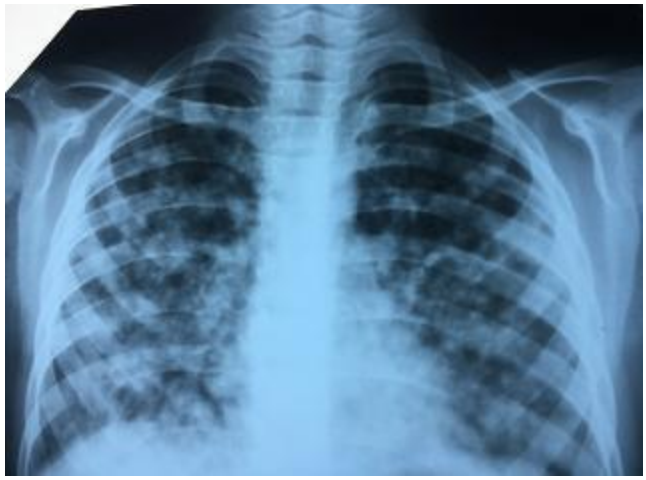

Photo 2 Bilateral pneumonia

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-kB (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	Halyna Lytvyn, Iryna Dybas
Collecting material	Olga Hladchenko, Natalia Ivanchenko
Material processing	Halyna Lytvyn, Iryna Dybas
Writing text	Iryna Dybas, Filip Pajak
Text editing	Halyna 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

1. Bayanova T.A., Kudryavtseva D.P., Plotnikova Y.K., Botvinkin A.D. The change in the incidence of some herpes virus infections in populations with a high prevalence of HIV infection. *HIV Infection and Immunosuppressive Disorders*. 2019;11:75-84. https://doi.org/10.22328/2077-9828-2019-11-3-75-84
2. Como C.N., Pearce C.M., Cohrs R.J., Baird N.L. Interleukin-6 and type 1 interferons inhibit varicella zoster virus replication in human neurons. Virology, 2018; 522:13–8.
3. De Milito A, Nilsson A, Titanji K, et al. Mechanisms of hypergammaglobulinemia and impaired antigen-specific humoral immunity in HIV-1 infection. Blood. 2004;103:2180-6.
4. Deev V. V. Chickenpox in children: peculiarities of pathogenesis, clinics, treatment. The thesis for the degree of Candidate of Medical Sciences, 2015:113.
5. Diversification of the antigen-specific T cell receptor repertoire after varicella zoster vaccination / Qi Q., Cavanagh M.M., Le Saux S., NamKoong H., Kim C. / Sci Transl Med. 2016 Mar 30;8(332):332ra46.
6. Guidelines for the Prevention and Treatment of Opportunistic Infections In HIV-Exposed and HIV-Infected Children, 2020, https://aidsinfo.nih.gov/guidelines
7. http://www.cdc.gov/vaccines/pubs/pinkbook/varicella.html.
8. Kleinschmidt-DeMasters B.K., Gilden D.H. Varicella-Zoster virus infections of the nervous system: clinical and pathologic correlates. Arch. Pathol. Lab. Med 2001;125:770-780.
9. Kramaryev S. O. Osoblyvosti suchasnogo perebigu vitryanoyi vispy u ditej. Dytyachyj likar. 2017:12-5
10. Laing K. J., Ouwendijk W. J. D., Koelle D. M., Verjans M. G. M.,Immunobiology of Varicella-Zoster Virus Infection. JID 2018; 218: S68-74
11. Leuridan E., Hens N., Hutse V. Kinetics of maternal antibodies against rubella and varicella in infants. Vaccine, 2011;29: 2222-26.
12. Mofenson L.M., Brady M.T., Danner S.P., et al. Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children: Recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. MMWR Recomm Rep. 2009;58:1
13. Nezgoda I.I., Levytska L.I. Chickenpox in children. Infectious deseise. Infekcijni hvoroby, 2017;1:60-70.
14. Qi Q., Cavanagh M.M., Le Saux S., NamKoong H., Kim C.Diversification of the antigen-specific T cell receptor repertoire after varicella zoster vaccination. Sci Transl Med 2016; 8:332ra46.
15. Ruleva A.A., Kharit S.M., Snegova N.F. Varicella vaccination in children infected with HIV (literature review). Epidemiologiya i Vaktsinoprofilaktika. 2014;3:50-5
16. SNID v Ukraini: statystyka. http://www.antiaids.org/news/aids_stat/snd-v-ukran-statistika-na-01112019-11352.html
17. Son M., Shapiro E.D., La Russa P., Neu N. Effectiveness of varicella vaccine in children infected with HIV. J. Infect. Dis. 2010; 201:1806-10