Med Pregl 2024; LXXVII (7-8): 257-261. Novi Sad: juli-avgust.

CASE REPORTS
PRIKAZI SLUČAJEVA

MULTI-ORGAN COMPLICATIONS ASSOCIATED WITH ADULT VARICELLA ZOSTER VIRUS INFECTION – CASE REPORT

MULTIORGANSKE KOMPLIKACIJE INFEKCIJE VIRUSOM VARICELLA ZOSTER U ODRASLOM DOBU – PRIKAZ SLUČAJA

Karla MUTIBARIĆ[1,2], Aleksandar ĐURIĆ[2,3] and Mirna ĐURIĆ[1,2]

ORCID NUMBER
Karla Mutibarić – 0009-0002-1537-397X
Aleksandar Đurić – 0000-0003-0897-4128
Mirna Đurić – 0000-0002-1639-7159

Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica[1]
University of Novi Sad, Faculty of Medicine Novi Sad[2]
Institute for Oncology of Vojvodina, Sremska Kamenica[3]

Case report
UDK 616.614-06:616.24
https://doi.org/10.2298/MPNS2408257M

Abstract

Introduction. The varicella-zoster virus is the causative agent of chickenpox, a disease that predominantly affects the pediatric population. Although the condition typically follows a benign course, it can lead to prolonged and multisystem involvement in both immunocompromised and immunocompetent, adults. This paper aims to present a case of an adult patient with pneumonia, pulmonary embolism, antiphospholipid syndrome, liver lesions, and thrombocytopenia following exposure to the virus, highlighting the increased risk of complications in adulthood. **Case Report.** A 25-year-old female was admitted to the Institute for Pulmonary Diseases of Vojvodina with fever, fatigue, malaise, and the onset of exanthema accompanied by dyspnea. The patient had no history of chronic diseases but was previously hospitalized during pregnancy due to eclampsia. Clinical findings and serological analyses confirmed a primary varicella-zoster virus infection. Chest radiography revealed pathognomonic bilateral nodular pneumonia, warranting further radiological evaluation due to the severity of the findings. Elevated D-dimer levels raised suspicion of pulmonary embolism, which was subsequently confirmed through computed tomography pulmonary angiography. While adult age and history of smoking were identified as risk factors, the extent of the clinical findings prompted immunological testing, leading to a diagnosis of antiphospholipid syndrome. **Conclusion.** This case underscores the importance of early recognition and comprehensive management of varicella-zoster pneumonia. A multidisciplinary approach is essential to ensure favorable outcomes in patients with severe complications.

Key words: Varicella Zoster Virus Infection; Multiple Organ Failure; Chickenpox; Antiphospholipid Syndrome; Pneumonia; Pulmonary Embolism

Sažetak

Uvod. Varičela zoster virus izaziva ovčije boginje, bolest koja pogađa dečiju populaciju. Mada bolest najčešće ima benigni tok, može biti i protrahovana i zahvatati više tkiva i organa kod imunokompromitovanih, ali i imunokompetentnih, zaraženih odraslih osoba. Cilj rada je prikaz slučaja bolesnice obolele od pneumonije i plućne embolije, sa antifosfolipidnim sindromom, lezijom jetre i trombocitopenijom, izazvanom ekspozicijom virusu u odraslom dobu, kada je incidencija nastanka komplikacija najveća. **Prikaz slučaja.** Pacijentkinja starosti 25 godina hospitalizovana je na Institutu za plućne bolesti Vojvodine povodom tegoba u vidu temperature, slabosti i malaksalosti, praćenih razvojem egzantema i dispnoičnih tegoba. Bolesnica je bez istorije hroničnih bolesti, tokom trudnoće bila hospitalizovana zbog eklampsije. Na osnovu kliničke slike i seroloških analiza potvrđena je primoinfekcija varičela zoster virusom. Radiogramom grudnog koša verifikovana je patognomonična obostrana nodularna pneumonija. S obzirom na masivnost nalaza, dijagnostički tok zahtevao je detaljniju radiološku obradu. Budući da je registrovana višestruko povišena vrednost D-dimera sumnjalo se na plućnu emboliju, koja je potvrđena kompjuterizovanom tomografijom sa pulmoangiografijom. Faktori rizika za nastanak komplikacija bili su adultni uzrast i pušački staž, međutim s obzirom na opsežnost nalaza postavljena je sumnja na imunokompromitovanost, te su urađena i imunološka ispitivanja, kojima je utvrđen antifosfolipidni sindrom. **Zaključak.** Kroz prikaz slučaja naglašavamo značaj pravovremenog prepoznavanja i sveobuhvatnog lečenja varičela zoster pneumonije, uz multidisciplinarni pristup koji je ključan u postizanju povoljnog ishoda.

Ključne reči: infekcije varičela zoster virusom; multiorganska disfunkcija; varičela infekcija; antifosfolipidni sindrom; pneumonija; plućna embolija

Introduction

Disseminated varicella infection, although rare, has been documented in both immunocompromised and immunocompetent adults [1, 2]. The report aims to present a rare case of disseminated varicella-zoster virus infection in an adult patient complicated by pneumonia, pulmonary embolism, antiphospholipid syndrome, liver lesions, and thrombocytopenia.

Case Report

We report the case of a 25-year-old female admitted to the Institute for Pulmonary Disease of Vojvodina.

✉ Corresponding author: Karla Mutibarić, E-mail: karla.mutibaric@mf.uns.ac.rs

Abbreviations

AST – aspartate transaminase
ALT – alanine transaminase
LDH – lactate dehydrogenase
GGT – gamma-glutamyltransferase

Her symptoms began five days prior to hospitalization with high fever, weakness, and malaise, followed by the development of exanthema. Over the next few days, her condition worsened, and two days before admission, she developed dyspnea. The patient's medical history was notable only for a previous pregnancy complicated by eclampsia. She had no known chronic illnesses, allergies, alcohol abuse, or family history of disease. A smoker with a 5 pack-year history, she was unvaccinated against varicella. Epidemiologically, her son was diagnosed with varicella two weeks prior. On admission, she was afebrile, dyspneic, normocardic, and normotensive, with a diffuse polymorphous rash. Auscultation revealed normal breath sounds with bilateral crackles.

Clinical evaluation and serological analyses confirmed a primary varicella-zoster virus infection.

Chest X-ray revealed bilateral multiple confluent nodules, predominantly in the lower lobes. Blood gas analysis indicated hypoxemic respiratory insufficiency. Electrocardiography showed sinus rhythm at 80 bpm, with a Q wave and inverted T wave in lead DIII. Laboratory tests revealed leukocytes within reference range, mild erythrocytosis, thrombocytopenia, eosinopenia, elevated C-reactive protein, and significantly raised D-dimer levels. Elevated aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), and gamma-glutamyltransferase (GGT) enzyme levels was also noted **(Figure 1).**

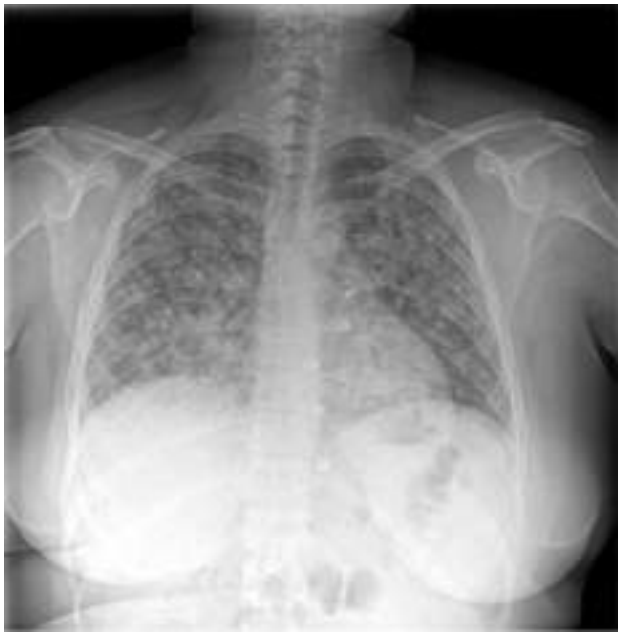
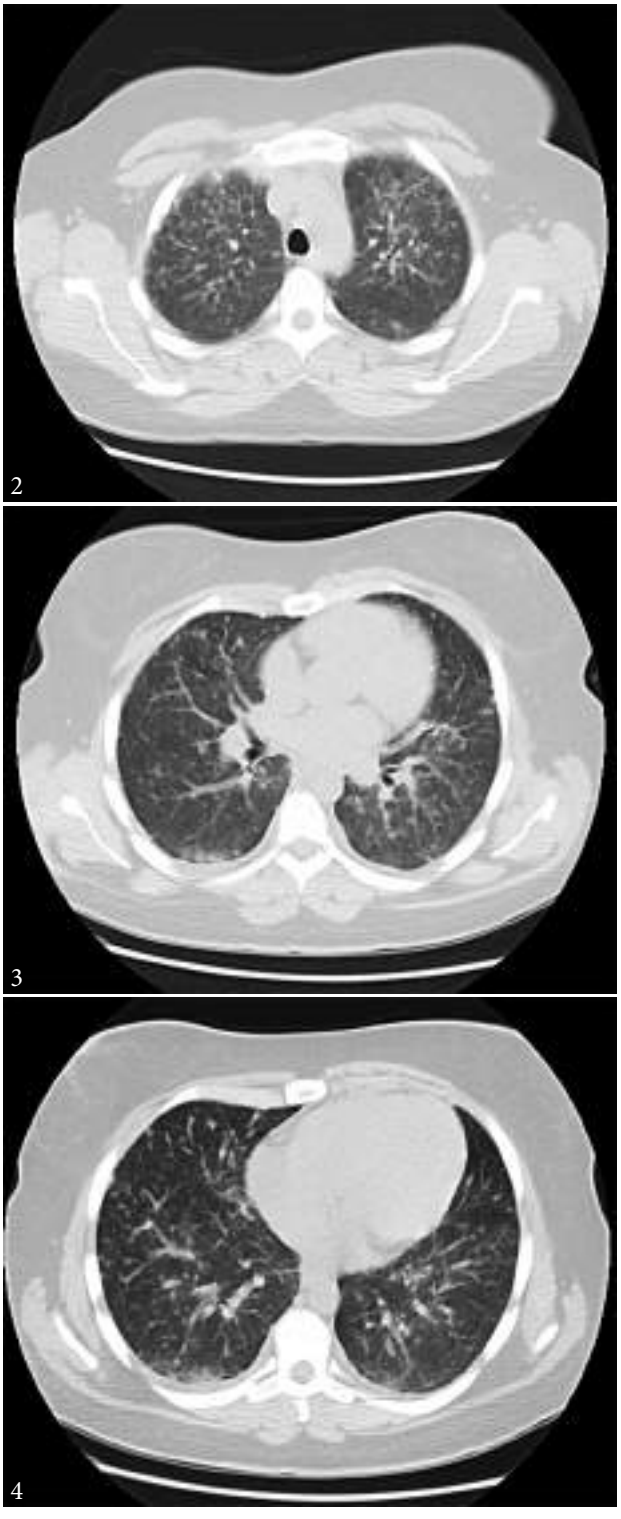


Figure 1. Chest X-ray on admission

Computed tomography pulmonary angiography (CTPA) demonstrated increased lung parenchyma density across all segments with bilateral polygonal ground-glass opacities and numerous semi-solid to solid nodules (up to 8 mm in diameter); enlarged mediastinal lymph nodes at positions 7-12 mm, 10R-14 mm; bilateral pleu-



Figures 2, 3 and 4. Chest CT scan

ral effusions (7 mm on the right, 8 mm on the left); filling defects in bilateral basal segmental and S1 pulmonary arteries on the right. Cranial computed tomography findings were normal **(Figures 2, 3 and 4)**.

Abdominal ultrasonography showed hyperechoic structure suggestive of diffuse fatty infiltration of the liver, with otherwise normal findings.

The patient initially received outpatient treatment with oral first-generation cephalosporins. Upon hospital admission, intravenous acyclovir, third-generation cephalosporins, glucocorticoid, oxygen therapy, and supportive care were initiated. Consultation with infectious disease specialists led to a 10-day course of antiviral and antibiotic therapy, alongside corticosteroid therapy with gradual dose tapering.

Parenteral anticoagulants were administered during hospitalization and transitioned to direct oral anticoagulants prior to discharge.

On the seventh hospital day, inflammation markers, blood counts, and D-dimer levels showed significant improvement. Liver enzyme levels AST, ALT, GGT, while still elevated, demonstrated a partial decrease.

Immunological testing came negative for HBs antigen, anti-HCV, anti-HIV, and multiple seromarkers. However, it identified a borderline positive beta-2 glycoprotein 1 IgM antibody and a positive anticardiolipin IgM antibody.

A follow-up chest X-ray at discharge showed complete regression of parenchymal shadows.

The treatment resulted in the disappearance of symptoms, complete radiological regression, normalization of inflammation markers, and partial decrease in hepatic enzyme values, and the patient was discharged in good general condition, cardiorespiratory compensated, and advised on further home care **(Figure 5)**.

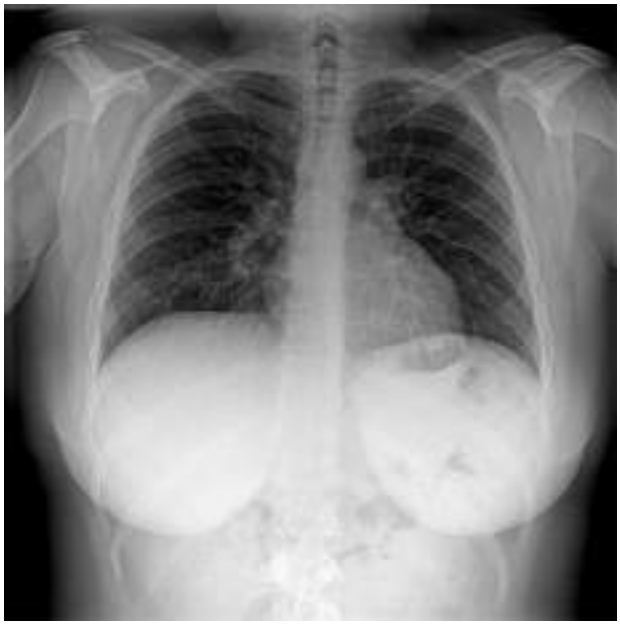


Figure 5. Chest X-ray at discharge

Discussion

Varicella-zoster virus primarily causes varicella (chickenpox) during its primary activation and herpes zoster (shingles) upon reactivation [3, 4]. Varicella predominantly affects pediatric populations, often occurring in collective settings during winter and spring. The disease's severity increases when transmission occurs within households, as seen in our patient [5].

Vaccination significantly reduces household transmission. Adults who are vaccinated contribute to herd immunity, protecting vulnerable populations such as young children or individuals with certain medical conditions. The varicella-zoster vaccine not only prevents chickenpox but also reduces the risk of shingles later in life. For immunocompromised individuals, varicella-zoster immunoglobulin is used as post-exposure prophylaxis [1, 6, 7]. Considering our patient's environment, which included a child in a collective setting, vaccination is highly advisable.

Adults face a higher risk of severe varicella complications, including respiratory complications affecting 5-15% of cases, with pneumonia occurring in approximately 1 in 400 individuals. Risk factors include pregnancy, lung disease, smoking, and immunosuppression. A higher number of skin lesions (>100) also correlates with increased viremia and pneumonia risk. Respiratory symptoms such as dyspnea, fever, cough (sometimes with hemoptysis), and chest pain typically appear within a week of symptom onset, as observed in our patient who was also a smoker. In rare cases, respiratory disease may progress to acute respiratory distress syndrome, often requiring invasive ventilation and hemodynamic monitoring in intensive care units [8–10].

Our patient also developed pulmonary embolism, a rare but documented complication of varicella-zoster infection [11–16]. Notable thrombotic complications such as purpura fulminans, necrotizing vasculitis, cerebral venous thrombosis, deep vein thrombosis, and pulmonary embolism have been reported. The mechanisms underlying these thrombotic complications are multifactorial, primarily involving endothelial injury, protein S deficiency, and the formation of antiphospholipid antibodies, as seen in our case [11, 17]. The presence of beta-2 glycoprotein 1 IgM and anticardiolipin IgM antibodies, along with the patient's history of pulmonary embolism, preeclampsia and eclampsia, fulfilled the diagnostic criteria for antiphospholipid syndrome [18]. The link between varicella-zoster virus and antiphospholipid syndrome is rarely discussed in

the literature, but immune responses triggered by the virus may enhance antiphospholipid antibody production, increasing thrombotic risk in susceptible individuals [19–21].

Hepatotoxicity in varicella infection usually presents as elevated liver enzymes and liver lesions, but fulminant hepatic failure due to extensive viral replication and hepatocellular destruction due to virus-induced cell lysis, a complication of progressive varicella, has also been reported [22, 23]. Another possible cause of liver damage may be clotting issues related to antiphospholipid syndrome. In our case, the patient exhibited a 16-fold elevation of liver enzymes and fatty liver infiltration.

Thrombocytopenia, often asymptomatic, can manifest as petechiae or bruises. Severe hemorrhagic complications, although rare, include intracranial hemorrhage [24]. In this case, thrombocytopenia was mild and asymptomatic.

Diagnosis is based on clinical presentation, isolation of viral antigens or serological tests for viral antibodies. Disease severity and risk factors guide further diagnostic strategies. Other authors followed a similar approach, conducting radiological imaging such as X-ray, computed tomography with pulmonary angiography, serological tests for vasculitis, connective tissue disorders (antinuclear antibodies, anticardiolipin antibodies), and antiphospholipid antibodies, protein S deficiency, human immunodeficiency virus, hepatitis antigens and antibodies [12].

First-line antiviral treatment involves acyclovir, administered orally or intravenously, with the latter preferred for severe and disseminated cases, including pneumonia, encephalitis, thrombocytopenia, and hepatitis, and immunocompromised patients. The use of acyclovir is recommended within the first 24 hours of rash onset. The use of acyclovir in pregnant women is permitted in indicated cases. Antiviral treatment is recommended for 7-10 days, depending on the clinical presentation, extending to 14 days for severe cases. Other antivirals include valacyclovir, famciclovir, brivudine, and foscarnet [3, 5, 8, 25].

The use of corticosteroids remains controversial. While they may reduce inflammation, their immunosuppressive effect can lead to adverse outcomes [25].

Despite a reported mortality rate of 10–30% for varicella pneumonia, rising to 50% for cases requiring mechanical ventilation [5], our patient achieved full recovery and was discharged in good general condition for further home care.

Conclusion

While varicella typically follows a benign course in childhood, complications and severe outcomes are more common in adults. Early identification of at-risk individuals, timely diagnosis, and appropriate treatment are critical. Exclusion of potential multi-organ complications through thorough evaluation ensures better outcomes in complex cases.

References

1. Andrei G, Snoeck R. Advances and perspectives in the management of varicella-zoster virus infections. Molecules. 2021;26(4):1132.

2. Miyokawa R, Aronowitz P. Varicella pneumonia in an immunocompetent adult. J Gen Intern Med. 2019;34(11):2682-3.

3. CDC. Chickenpox (varicella) [Internet]. [cited 2024 Oct 7]. Available from: https://www.cdc.gov/chickenpox/hcp/clinical-overview/?CDC_AAref_Val=https://www.cdc.gov/chickenpox/hcp/index.html

4. Cvjetković D, Jovanović J, Hrnjaković-Cvjetković I, Brkić S, Bogdanović M. Reaktivacija herpes zoster infekcije varicela-zoster virusom. Med Pregl. 1999;52(3-5):125-8.

5. Ayoade F, Kumar S. Varicella-zoster virus (chickenpox). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; [updated 2022 Oct 15; cited 2024 Oct 7]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448191/

6. Centers for Disease Control and Prevention (CDC). Varicella vaccination information for healthcare professionals [Internet]. [updated 2021 Apr 28; cited 2024 Oct 7]. Available from: https://www.cdc.gov/vaccines/vpd/varicella/hcp/index.html

7. Centers for Disease Control and Prevention. ACIP Recommendations: Varicella (chickenpox) vaccine [Internet]. 2024 [cited 2024 Oct 7]. Available from: https://www.cdc.gov/acip-recs/hcp/vaccine-specific/varicella.html

8. Mohsen AH, McKendrick M. Varicella pneumonia in adults. Eur Respir J. 2003;21(5):886-91.

9. Đurić M, Považan Đ, Jovanović J, Medenica M. Varicelozna pneumonija - prikaz slučaja. Pneumon. 2004;41:91-7.

10. Denny JT, Rocke ZM, McRae VA, Denny JE, Fratzola CH, Ibrar S, et al. Varicella pneumonia: case report and review of a potentially lethal complication of a common disease. J Investig Med High Impact Case Rep. 2018;6:2324709618770230.

11. Gillispie A, Dessie S, Aguilar R, Nwanwene K, Bandak G, Khalil E, et al. Bilateral pulmonary embolism associate with varicella zoster meningoencephalitis in an immunocompetent adult: a case report and literature review. Marshall J Med. 2020; 6(4):33.

12. Paul G, Paul BS, Singh G. Unseen face of varicella-zoster infection in adults. Indian J Crit Care Med. 2016;20(12):731-4.

13. Gogos CA, Apostolidou E, Bassaris HP, Vagenakis AG. Three cases of varicella thrombophlebitis as a complication of varicella zoster virus infection. Eur J Clin Microbiol Infect Dis. 1993;12(1):43-5.

14. Viseux V, Darnige L, Carmi E, Chaby G, Poulain JF, Cevallos R, et al. Pulmonary embolism and transitory anti-beta2-GPI antibodies in an adult with chicken pox. Lupus. 2000; 9(7):558-60.

15. Dahan E, Simsolo C, Merei M, Vigder F, Tatoor I, Blum A. Varicella zoster infection and pulmonary complications. Eur J Intern Med. 2005;16(6):449-50.

16. Khan R, Yasmeen A, Pandey AK, Al Saffar K, Narayanan SR. Cerebral venous thrombosis and acute pulmonary embolism

following varicella infection. Eur J Case Rep Intern Med. 2019; 6(10):001171.

17. Sandhya AS, Prajapat B. Pulmonary embolism following varicella infection. J Clin Diagn Res. 2018;12(3):14-5.

18. Barbhaiya M, Zuily S, Naden R, Hendry A, Manneville F, Amigo MC, et al. The 2023 ACR/EULAR antiphospholipid syndrome classification criteria. Arthritis Rheumatol. 2023;75(10): 1687-702.

19. Avcin T, Toplak N. Antiphospholipid antibodies in response to infection. Curr Rheumatol Rep. 2007;9(3):212-8.

20. Josephson C, Nuss R, Jacobson L, Hacker MR, Murphy J, Weinberg A, et al. The varicella-autoantibody syndrome. Pediatr Res. 2001;50(3):345-52.

21. Uthman IW, Gharavi AE. Viral infections and antiphospholipid antibodies. Semin Arthritis Rheum. 2002;31(4):256-63.

Rad je primljen 1. VII 2024.
Recenziran 29. VII 2024.
Prihvaćen za štampu 23. XI 2024.
BIBLID.0025-8105:(2024):LXXVII:7-8:257-261.

22. Abro AH, Abdou AMS, Ustadi AM, Hussaini HS, Javeed NY, Saleh AA, et al. Hepatic dysfunction is frequent in varicella infection. Rawal Medical Journal. 2008;33(2):201-4.

23. Arvin AM. Varicella-zoster virus. Clin Microbiol Rev. 1996;9(3):361-81.

24. Teng SL, Wu CC, Tan TK, Tsai CK, Lau WH. Chicken pox associated thrombocytopenia complicated with intracranial hemorrhage in adult - report of a case. Resuscitation & Intensive Care Med. 2017;4:194-8.

25. Mirouse A, Vignon P, Piron P, Robert R, Papazian L, Géri G, et al. Severe varicella-zoster virus pneumonia: a multicenter cohort study. Crit Care. 2017;21(1):137.