



Case Report

Varicella pneumonia in an immunocompetent adult patient: Case report and review of the literature

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ABSTRACT

Varicella is a childhood disease characterized by its self-limiting and benign nature. However, it can also affect the adult population due to risk factors, leading to infection with numerous complications involving the central nervous system, kidneys, respiratory system, and skin. Varicella pneumonia, one of the most feared complications in adults, occurs in approximately 1 out of 400 patients with the disease. This complication primarily affects male patients with a history of heavy smoking and immunosuppression, either due to an underlying disease such as HIV and cancer, drug use, pregnancy or pulmonary disease. It is recommended that this complication should be treated with intravenous acyclovir at a dose of 10 mg/kg/8 hours. The prognosis depends on the development of respiratory failure; up to 50 % of patients with this complication require invasive mechanical ventilation. Here, we report the clinical case of an immunocompetent patient with a typical presentation of varicella that rapidly progressed to a respiratory infection requiring antiviral treatment and invasive mechanical ventilation.

1. Introduction

Varicella is a highly contagious infection caused by the varicella zoster virus (VZV), which is transmitted by direct contact with the lesions of an infected person or by inhalation of aerosols produced by an infected person. In most cases, VZV infection is mild and self-limiting, characterized by symptoms such as rash, generalized pruritus, headache, fever, asthenia, and adynamia [1]. It is a typical childhood disease, with 57 % of cases occurring in those under 9 years of age, 6.3 % in the 20–24 age group, 10 % in the 25–44 age group, and less than 1 % in individuals over 45 years old [2]. VZV is characterized by a neurotrophic nature and the ability to remain latent in the sensitive ganglionic nerves until it becomes active and causes herpes zoster [3].

Varicella is highly contagious because it can be transmitted up to 2 days before skin lesions appear, leading to outbreaks [3]. Therefore, it is considered a public health concern, with morbidity and mortality in adults 10–20 times higher than in healthy children [4]. Universal vaccination against varicella is an extremely important public health policy to reduce both the number of cases of varicella infection and the incidence of varicella pneumonia [5]. However, due to its course and mode of transmission, the disease

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spreads rapidly in the unvaccinated or immunosuppressed population, including those receiving corticosteroid treatment and those with underlying conditions such as HIV, diabetes mellitus, and cancer [6].

Colombia reported 1,202,576 cases of chickenpox to the National Surveillance System (Sivigila) between 2007 and 2023 (2023 to week 52), with an average annual incidence of 154 cases per 100,000 inhabitants, with 2020 and 2021 being the years with the lowest notification, corresponding to 36 and 28 cases per 100,000 inhabitants respectively. Reduction that could have been influenced by multiple factors related to the occurrence of the new coronavirus (COVID-19) pandemic. As of December 30, 2023, 31,361 cases of chickenpox were reported, an increase of 38 % (8694 cases) compared to 2022; with an incidence in the general population of 60 cases per 100,000 inhabitants; in children under five years of age, 282 cases per 100,000 inhabitants and in children under one year of age, 261 cases per 100,000 inhabitants. Men accounted for 52.5 % (16,466 cases) of notification. The distribution by age shows a higher proportion of cases in the group of 1–4 years with 8586 cases, corresponding to 27 % of the national notification. This phenomenon coincides with what has been documented by other Latin American countries, where the disease is mainly concentrated in the school population [7]. Varicella can cause serious complications such as bacterial superinfection, pneumonia, encephalitis, myelitis, retinitis, hepatitis, and disseminated intravascular coagulation (DIC) [8]. Varicella pneumonia is the main complication of this viral infection, occurring in 1 out of 400 patients with this disease. Important risk factors for this complication include smoking, male gender, immunosuppression (due to pathology or treatment), pregnancy, and underlying pulmonary disease. Globally, about 7000 deaths occur annually due to varicella pneumonia, with approximately half of the cases will requiring mechanical ventilation [9].

We report the case of a 45-year-old female immunocompetent patient with an epidemiologic link to varicella with a history of chronic obstructive pulmonary disease (COPD) and heavy smoking. The patient presented with maculopapular skin lesions that progressed to generalized vesicular involvement along with dyspnea and evidence of cotton-like infiltrates on chest X-ray. These findings, along with the varicella episode, led to the diagnosis of varicella pneumonia as a major complication of this viral infection, as confirmed by varicella-zoster virus-polymerase chain reaction (VZV PCR).

2. Case presentation

This is a 45-year-old patient with a history of COPD, moderate smoking (15 pack-years) and previous use of psychoactive substances up to 7 years ago; there is no information on varicella vaccination. The patient was referred from a second-level facility to the intensive care unit (ICU) with a 5-day history of unquantified fever and a maculopapular rash that evolved into generalized vesicles and crusts (Fig. 1). The patient was living with individuals experiencing varicella outbreak. On admission to the ICU, she presented with a cough with hemoptysis, rapid respiratory deterioration, and an oxygen saturation (SaO_2) of 62 %. The patient required orotracheal intubation and support with invasive mechanical ventilation (IMV).



Fig. 1. Varicella lesions on the face. Crusted lesions with central depression are shown.

Physical examination revealed a patient supported with IMV, blood pressure 95/65 mmHg, heart rate 62 beats/minute and respiratory rate 15 breaths/minute, temperature 36.4 °C, SaO₂ 95 %, dry mucous membranes without jaundice, symmetrical chest with decreased expansibility, with low intensity heart sounds, pulmonary hypoventilation without presence of over-aggregate sounds. Initial hemogram with 7850 leukocytes/mm³, hemoglobin 15.2 g/dL, 108,000 platelets/mm³, arterial blood gases with pH 7.35, PCO₂ 45.4 mmHg, HCO₃ 24.7 mEq/L, PAFI 103, normal sodium, potassium and serum creatinine, glutamic pyruvic transaminase (GPT) 60 U/L and glutamic oxaloacetic transaminase (GOT) 118 U/L, lactate dehydrogenase (LDH) 1904 U/L. Prolonged thrombocytopenia was noted during the first few days. Chest x-ray showed diffuse cottony infiltrates without pleural effusion (Fig. 2).

Varicella pneumonia (VP) was suspected due to skin lesions, epidemiological link, and severe respiratory compromise. Intravenous acyclovir at a dose of 10 mg/Kg/dose every 8 hours was initiated and continued for 10 days. Negative results were reported for IgM for VZV, bacterial culture of endotracheal secretion, and influenza A H1N1, as well as negative serial smear microscopy.

Due to the high suspicion of VP, VZV PCR was requested by endotracheal secretion, which was positive. Right basal infiltrates appeared on the chest X-ray, and the leukocyte count increased to 18,200/mm³. Chest CT showed perihilar interstitial infiltrates and bibasal pneumonic consolidating infiltrates predominantly on the right, so treatment was started with cefepime 2 g intravenously every 8 hours and vancomycin 1 g intravenously every 12 hours, resulting in clinical improvement. Extubation was achieved on the 14th day after initiating ventilatory support.

On day 3 after withdrawal of ventilatory support, orotracheal intubation was performed again due to hyperactive delirium and persistently decreased SaO₂. Tracheostomy was planned due to prolonged mechanical ventilation, but the patient suffered a cardiorespiratory arrest and died during the surgical procedure on the 19th day of hospitalization.

3. Discussion

Varicella is a globally distributed disease that primarily affects children and usually follows a benign course [10]. However, if it affects the adult population, it may lead to multiple complications. It is characterized by its rate of contagion through saliva droplets or contact with skin lesions [11]. VZV is a double-stranded DNA virus belonging to the Herpesviridae family [10,11].

This etiological agent affects only humans and not animals. After primary infection, the virus may remain latent in the dorsal and/or cranial sensory root ganglia. Subsequently, herpes zoster (HZ), characterized by a vesicular rash along the course of a dermatome [3,12], may occur upon the occurrence of an event that causes a decrease in the specific immune response to VZV.

Varicella is a disease with a worldwide distribution; in temperate countries, it is almost exclusively a childhood disease with a 90 % attack rate in children aged 0–5 years [13]. Vaccination, introduced in the 1990s, is a protective factor against varicella, which has shown a rapid reduction of varicella cases [5,14] as well as a decrease of more than 80 % in the number of hospitalizations, with an efficacy of more than 90 % for up to 10 years [15], thus reducing the risk of presenting infections and complications at advanced age.

The varicella vaccine has a live attenuated strain; therefore, it is contraindicated during pregnancy [16]. Therefore, it is necessary to identify if a patient is susceptible to VZV infection during pregnancy and to take preventive measures, such as post-exposure pro-

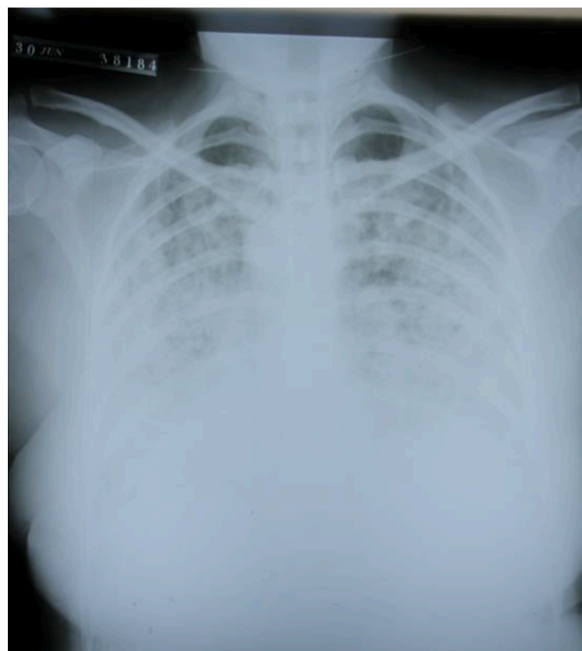


Fig. 2. Chest X-ray on admission to the ICU. Bilateral symmetrical cottony infiltrates are evidenced.

phylaxis. This prophylaxis may include the administration of oral acyclovir, which has shown comparable efficacy to varicella immune globulin (VZIG) within the first 4 days after exposure [16].

Varicella is much more common in countries with a temperate-cold climate, where 90 % of cases are reported before the age of 12 years [17]. There are usually large periodic outbreaks with an interepidemic cycle of 2–5 years. In the United States, United Kingdom and Japan, 80 % of people were infected by the age of 10 years; while in countries such as India and Southeast Asia, age-specific incidences are highest in the 20–30 age group [18]. High population density and early schooling are factors associated with a higher number of varicella cases [17]. In Latin America, in the course from 2011 to 2020, there was an incidence rate of varicella of 270 per 100,000 inhabitants, with a hospitalization rate of 3.5 per 100,000 people [19]. In Colombia, a total of 896,199 cases of varicella (annual average of 89,620 cases) were reported to the Public Health Surveillance System between 2011 and 2020, and 48 % (8796) of the cases occurred in women [7,17]. However, the highest mortality and complication rates occurred in older patients.

A study conducted by the General Health Reporting System of Mexico reported 17,398 cases, of which 27.1 % of people with VZV infection had complications including neuralgia (11 %), meningoencephalitis (5.4 %), disseminated disease (2.8 %), and varicella pneumonia (2.5 %), and others such as varicella-induced ileus, cerebellar ataxia, and soft tissue involvement (5.4 %) [2,5,20]. Infection may be more severe in immunocompromised patients, transplant recipients, patients with human immunodeficiency virus (HIV) infection, underlying pulmonary disease, chronic use of immunosuppressive drugs such as steroids, and altered or deficient cellular immunity [9,11]. VP is one of the complications that can occur in healthy patients without pathologic antecedents and is more common in men, pregnant women, the elderly, or those with severe cutaneous vesicular involvement [9].

The clinical symptoms of varicella are usually mild and occur between 7 and 21 days after exposure to the virus. Initial stages include rhinorrhea,odynophagia, fever, and general malaise [3,11], followed by a pruritic rash characterized by small red papules that rapidly evolve into vesicles and crusts. These lesions manifest at different stages at a generalized level, as shown in the present clinical case. Reinfection caused by this disease can lead to high mortality rates and is common in immunocompromised individuals [11].

Respiratory symptoms in VP appear from day 1–7 after eruption, manifested by dry cough, hemoptysis, chest pain,odynophagia, dyspnea, and fever [11,14], concomitant with skin lesions in different stages of evolution [14]. In the clinical case, the patient presented with a rapidly progressive condition, coughing for only one day and subsequent episodes of dyspnea and hypoxemia, which required immediate orotracheal intubation.

Diagnosis is based on clinical findings, but laboratory tests are still necessary for identifying disseminated infections or atypical disease course [11]. In this case, clinical diagnosis was promptly suspected due to the characteristic skin lesions and the epidemiological link provided by the family. Molecular tests such as VZV polymerase chain reaction (PCR), known for their high sensitivity (97.7 %) and specificity (96.8 %), are used for laboratory diagnosis. Samples from skin lesions, blood or respiratory sources are required for testing [11]. Serological tests are essential for ruling out reactivation infection. In the patient of the clinical case, Ig M for VZV was reported negative, however, as mentioned above, this test has a lower sensitivity than VZV PCR tests, in addition, it depends on the day of the course of the disease in which the test is performed, because a peak of IgM is presented between day 2–5 after the appearance of lesions on the skin, and its value remains positive during the first 9 days of the disease, to then remain positive only the IgG of VZV [6]. Therefore, a VZV PCR test was requested and was positive.

Several case reports have shown no changes in white blood cell count, but evidence of thrombocytopenia [10,11], similar to the present report. Other case reports coincided with transient thrombocytopenia and alterations of the hepatic enzymatic profile (specifically GOT, GPT, and LDH), as observed in our report [21]. Chest radiographs may show diffuse bilateral infiltrates and nodules similar to those seen in tuberculosis, whereas chest tomography may show nodular opacities, patchy ground-glass opacities, or even miliary patterns with rapid resolution similar to skin eruptions [14]. As shown in Fig. 2, a pattern of cottony infiltrates was observed in both lung fields and perihilar infiltrates was observed on chest CT, correlating with the previously described pattern characteristic of varicella pneumonia.

Treatment for VP involves the use of acyclovir at a dose of 10 mg/kg every 8 h [11], depending on the response of the patient, for 7–10 days. In the reported case, treatment was prolonged to 10 days. Various studies have suggested alternative medications for VP management, such as valacyclovir at a dose of 1 g every 8 hours [22], a prodrug taken orally and activated by the patient's metabolic components, achieving a high availability. Another option is famciclovir, an inactive form of penciclovir and used in immunocompromised or immunocompetent patients over 25 years [23].

Purified immunoglobulins containing anti-VZV antibodies, which can be administered intramuscularly within 96 hours to 10 days after the onset of skin lesions [11] are a beneficial approach for VP patients. Corticosteroids have also been used to reduce the progression of the disease, the most common being methylprednisolone at a dose of 40 mg per day [24], with dexamethasone as an alternative. Antihistamines have not demonstrated a significant benefit, whereas calamine-based lotions may be applied to skin lesions [25]. Oxygen therapy was employed in cases of VP with SaO₂ less than 92 %, as shown in the case under discussion.

The main complications of varicella pneumonia are related to varicella-induced acute respiratory distress syndrome [11,25], which is a potentially fatal complication, because about 50 % of VP cases require management with IMV in ICU [9]. Other associated complications include DIC [Disseminated intravascular coagulation] because of viremia, acute renal injury and acute heart failure in patients with a history of heart disease [26].

Although Takahashi developed the first chickenpox vaccine in 1972, it was not adopted in the United States until 1995. A significant decrease in the incidence of chickenpox has been achieved in children in the United States, unfortunately after the adoption of this vaccination program. Vaccination doubts have arisen about the vaccine, which has caused mild to severe outbreaks in some communities. Lifelong immunity against chickenpox has been achieved, but immunity may wane over time. Overall, following the introduction of treatment with two doses of live attenuated varicella vaccine (VarV), the incidence of varicella has decreased and, to this day, VarV has been adopted in routine vaccination programs for children in 36 countries and regions, including the United States,

Australia and Germany [27]. Pneumonia is the most common serious complication of chickenpox in adults, in whom pneumonia has been reported to occur in < 5 %–50 % of all cases of chickenpox infection [28]. On the other hand, it should be considered that most studies on chickenpox pneumonia in adults have tended to focus on immunocompromised patients and pregnant women, but this complication can also occur in immunocompetent adults [29].

The prognosis for VP remains uncertain. In 2014, the World Health Organization reported that approximately 4 million patients worldwide were hospitalized due to varicella-associated complications, which resulted in high mortality rates [30]. VZV-infected individuals are at risk of secondary bacterial or viral infection, as observed in the current case [31].

4. Conclusion

Varicella is a typically benign childhood disease; however, its presentation in adults can be aggressive, leading to complications such as varicella pneumonia, which is associated with high mortality rates, particularly in elderly, immunocompromised patients, and smokers. Although immunocompromised individuals are at the highest risk, immunocompetent patients may also be affected, highlighting the importance of childhood vaccination and timely monitoring of preventable risk factors in childhood.

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CRedit authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- [1] L. Falleiros, M.C. Pirez, M.L. Avila, M. Cashat, C.I. Parellada, W. Lara, Burden of varicella in Latin America and the Caribbean: findings from a systematic literature review, *BMC Publ. Health* 19 (2019) 1–18.
- [2] M. Vázquez, P. Cravioto, F. Galván, D. Guarneros, V.H. Pastor, Varicela y herpes zóster: retos para la salud pública, *Salud Publica Mex.* 59 (6) (2017) 650 [Internet].
- [3] A.C. Agüero Sánchez, J. Salazar Mayorga, A. Valverde Jiménez, Varicela en el embarazo, infección potencialmente peligrosa para la madre y el feto, *Rev. Medica Sinerg.* [Internet] 5 (2) (2020) e331.
- [4] M.C. Rojas, G. Rodríguez, Varicela en un hombre de 33 años, *Infectio* 26 (2022) 87–90.
- [5] H. Salo, J. Perälä, T. Hannila-Handelberg, E. Sarvikivi, O. Luomala, J. Ollgren, et al., Decline in varicella cases contacting primary health care after introduction of varicella vaccination in Finland – a population-based register study, *Vaccine* [Internet] 41 (43) (2023) 6535–6541.
- [6] N. Okumura, M. Ishikane, S. Fukushi, S. Yamada, W. Ochi, N. Iwamoto, et al., Varicella pneumonia in an immunocompetent, unvaccinated man: a case report, *IJID Reg* [Internet] 2 (2022) 60–62.
- [7] Protocolo de vigilancia en Salud Pública, Varicela [Internet]. Versión 6, 16 junio de 2024. Aviable in: https://www.ins.gov.co/buscador-eventos/Lineamientos/Pro_Varicela.pdf.
- [8] Pramodman Singh Yadav, et al., Varicella pneumonia in an immunocompetent child: a case report, *IDCases* 33 (2023) e01870.
- [9] J.P. Camargo, Infección por varicela con compromiso multisistémico en adulto previamente sano, *Acta Méd. Colomb.* 41 (2) (2016) 144–147 [Internet].
- [10] F.M. Kaaniche, A. Chaari, R. Ammar, M. Bahloul, M. Bouaziz, Varicella pneumonia in an immunocompetent adult: a case report, *Trends Anaesthesia Critical Care* 5 (5) (2015) 146–148.
- [11] M. Aabdi, M. Hamza, L. Moussa, B. Houssam, H. Brahim, Acute respiratory distress syndrome caused by varicella pneumonia in immunocompetent adult: clinical case, *Ann. Med. Surg.* 2012 (62) (2021) 383–385.
- [12] L. Lancheros, Oscar Bernal, Manifestaciones neurológicas del herpes virus simple y varicela zóster, *Acta Neurol. Colomb.* 37 (2021) 1–12.
- [13] Vaibhav Misra, et al., Acute rise in the incidence of chickenpox due to temperature variation in a specific locality of gwalior city, *Indian J. Community Med.: Off. Public. Indian Assoc. Prevent. Soc. Med.* 46 (2) (2021) 323.
- [14] T.-A. Ho, J. Burnell, R. Gupta, Varicella pneumonia: adult complications of a childhood disease, *Chest* 160 (4) (2021) A385.
- [15] Fernanda Hammes Varela, Leonardo Aratijo Pinto, Marcelo Comerlato Scotta, Global impact of varicella vaccination programs, *Hum. Vaccines Immunother.* 15 (3) (2019) 645–657.
- [16] B. Sile, K.E. Brown, C. Gower, J. Bosowski, A. Dennis, M. Falconer, J. Stowe, N. Andrews, G. Amirthalingam, Effectiveness of oral aciclovir in preventing maternal chickenpox: a comparison with VZIG, *J. Infect.* 85 (2) (2022) 147–151.
- [17] L.H.F. Arlant, M.C.P. Garcia, M.L. Avila Agüero, M. Cashat, C.I. Parellada, L.J. Wolfson, Burden of varicella in Latin America and the Caribbean: findings from a systematic literature review, *BMC Publ. Health* 19 (1) (2019).
- [18] Organización Mundial de la Salud. Parte Epidemiológico Semanal Vacunas contra la varicela y el herpes zóster: Documento de posición, junio de 2014 [Internet] 2014. Aviable in: https://www.who.int/immunization/policy/position_papers/Varicella_Herpes_zoster_Vaccine_PP_ES_2014.pdf.
- [19] Resumen anual de la actividad de la enfermedad, Boletín de Control de Enfermedades (DCN). Varicela y Zoster, 2019_ DCN - Departamento de Salud de Minnesota [Internet], 2019 Fecha de consulta: 9 de mayo de 2022. Aviable in: <file:///C:/Users/LENOVO/Documents/INS/VARICELA/Varicela%20y%20Zoster,%202019.%20DCN%20-%20Departamento%20de%20Salud%20de%20Minnesota.html>.
- [20] Z. Elfessi, M. Murtagh, L. Hammad, S. Aadil Anvery, Chickenpox-induced ileus: a case report, *Visual J. Emerg. Med.* 33 (2023) 101872.

- [21] Gilberto Serrano Ocaña, Juan Carlos Ortiz Sablon, Ilen Ochoa Tamayo, Neumonía Varicelosa, Presentación de un caso. Hospital Dora Ngiza Port Elizabeth Sudáfrica, *MediSur* 7 (1) (2019) 45–50.
- [22] F.K. Al-Ani, J. Sirajudeen, P.T.S. Kandalam, A. Al Aani, Un neumotórax por varicela: informe de un caso de neumotórax secundario a una infección por VZV, *Revista abierta de medicina interna* (9) (2019) 78–82.
- [23] J.T. Denny, Z.M. Roche, V.A. McRae, et al., Varicella pneumonia: case report and review of a potentially lethal complication of a common disease, *J. Investigat. Med. High Impact Case Rep.* (6) (2018) 2324709618770230.
- [24] A. Elena-González, R. Dolz-Aspas, Neumonía por virus de la varicela-zóster en adulto inmunocompetente., *Atención Primaria Práctica* 1 (4) (2019) 66–67.
- [25] Henry Díaz Londres, Ernesto Vilches Izquierdo, Lianne Ramos Marrero, Neumonía por varicela, *Revista Cubana de Medicina Intensiva y Emergencias* 18 (1) (2019) 1–10.
- [26] Davide Mangioni, et al., Adjuvant treatment of severe varicella pneumonia with intravenous varicella zoster virus-specific immunoglobulins, *Int. J. Infect. Dis.* 85 (2019) 70–73.
- [27] Mona Marin, et al., Global varicella vaccine effectiveness: a meta-analysis, *Pediatrics* 137 (2016) 3.
- [28] Abdul H. Mohsen, M.W. McKendrick, Risk factors for pneumonia in adults with chickenpox, *J. Infect. Dis.* 186 (7) (2002) 1053-1053.
- [29] Ran Cheng, et al., Prevalence and progression of pneumonia in immunocompetent adults with varicella, *Virology* 21 (1) (2024) 39.
- [30] World Health Organization, Varicella and herpes zoster vaccines: WHO position paper, June 2014, *Weekly Epidemiological Record = Relevé épidémiologique hebdomadaire* 89 (25) (2014) 265–287.
- [31] Ulrich Heininger, F. Jane, Seward. Varicella, *Lancet* 368 (9544) (2006) 1365–1376.