

NOTES

Characteristics of radiological changes in lungs during varicella zoster viral infection

Željko Mijailović¹, Predrag Čanović¹, Zoran Todorović¹, Olgica Gajović¹, Ljiljana Nešić¹, Zorana Đorđević¹, Jelena Mijailović², Dejan Petrović³

¹Infectious Disease Clinic, ²Department of Transfusion Medicine, ³Urology and Nephrology Clinic; Clinical Centre Kragujevac, Kragujevac, Serbia

Corresponding author: Željko Mijailović; Infectious Disease Clinic, Clinical Centre Kragujevac, Zmaj Jovina St. 30, 34000 Kragujevac, Serbia; Phone: +381 34 370 078, fax: +381 343 70 078; E-mail address: mijailovic@sbb.rs

Original submission: 23 May 2010; **Revised submission:** 28 December 2010; **Accepted:** 12 February 2010.

Med Glas Ljek komore Zenicko-doboj kantona 2011; 8(2):280-283

ABSTRACT

The objective of this research was to analyse the varicella patients' data in order to determine the following: general frequency of pneumopathies and types of lung changes according to X-ray presentation and the changes on the computed tomography. It examined 101 patients with the clinical presentation of varicella and some of the X-ray entities of varicella pneumopathies. Radiological techniques included chest X-ray and CT scans. Familiarity with clinical, laboratory and radiological characteristics of the disease may be of utmost importance for early recognition.

Key words: varicella, radiological characteristics

INTRODUCTION

Varicella pneumopathies take a significant place among complications that arise in the course of varicella-zoster viral infection (1-4). After all, pulmonary complications in the course of varicella represent one of the most common causes of lethal outcome (5). However, of all varicella pneumopathies, the primary varicella pneumonia takes the most prominent place due to its significance and severity. It is a pneumonia caused by direct influence of the Varicella-Zoster virus (VZV) itself (6). It seems that lung affection by VZV occurs much more frequently than previously thought (haematogenically nonetheless), usually during the secondary viraemia

(7). Not unlike other viruses, direct influence of VZV instigates inflammatory process primarily in the lung interstitium (interstitial type of pneumonia) (8). On average, Varicella-Zoster virus pneumonia (VZVP) occurs once in 400 cases of varicella, with a mortality rate of 2.15 - 50%. The published incidence rates range from 5 - 50% (9). Primary varicella pneumonia radiologically presents in a manner similar to other atypical pneumonia where inflammatory process occurs primarily in the lung interstitium (inhomogeneous opacities with poor demarcation, accompanied with the presence of pulmonary markings - the so called "ground glass"). The changes can present as nodular or reticular opacities in both lungs, inhomogeneous opacities or diffuse alveolar infiltration (10). Sometimes, however, they can present in the form of disseminated bronchopneumonic foci (nodules). With the progression of the disease, nodules grow and merge together, producing extensive infiltrates, esp. in the vicinity of hilus and base of a lung (11). The chest CAT scan in varicella patients shows uneven ground-glass attenuations and confluent lesions (12).

The objective of our research was to determine the overall incidence of pneumopathy in varicella patients and their distribution by age and gender, as well as types of lung changes according to radiographic appearance and CAT scan findings. The paper will mainly appeal to the practicing physicians, and its results may lead physicians to consider even the gravest forms of the disease.

PATIENTS AND METHODS

In the retrospective-prospective research, the analysis included patients with clinical diagnosis of varicella and some of the radiographic entities found in varicella pneumopathies (increased pulmonary markings, localised bronchopneumonic infiltrate, diffuse bronchopneumonic infiltrates and atypical pneumonia), treated at the Infectious Diseases Clinic, Clinical Centre of Kragujevac, during the 2002-2006 period. Approval of the Ethics Committee of the Clinical Center of Kragujevac as well as a written consent from the patients were obtained for the research. All analysed patients were admitted during the rash stage of the disease. Varicella was diagnosed using the epidemiological

data and typical clinical presentation, whilst the pneumopathy diagnosis was made using radiological presentation. Radiological examination, radiography and computed tomography (CT) of lungs were performed in all patients immediately upon admission, whilst those who had changes observed on their first X-ray scan, underwent a follow-up X-ray scan 14 days later. The lung changes observed on x-ray scans were classified to the corresponding radiological categories (increased pulmonary markings, localised bronchopneumonic infiltrate, diffuse bronchopneumonic infiltrates and atypical pneumonia) and CT forms (individual nodular changes, diffuse nodular changes, confluent nodular changes and mediastinal lymphadenopathy). Based on severity of clinical symptoms (intensity of difficulties - duration of fever symptoms, the presence of coughing, breathing difficulty, chest pain), the extension of the physical findings (altered breath sound, related lung sounds, duration of altered physical findings), the intensity of changes in laboratory parameters (platelet count, lactate dehydrogenase and alanine aminotransferase activity), and type and extension of radiological findings, the patients were divided into three groups, those with mild, moderate and severe clinical picture. We also examined the incidence of pneumopathy by gender and age (0-7, 8-15, 16-22, 23-29 and over 30 years of age), as well as the impact that certain risk factors had on its frequency and severity (smoking, malignant diseases, chronic diseases and other immunodeficiency conditions).

Statistical data analysis was performed using methods of descriptive and analytical statistics, with the $p < 0.001$ level of statistical significance.

RESULTS

During the 2002-2006 period 390 patients who exhibited the clinical picture of varicella were observed and treated, of whom 101 (25.9%) had clinical and/or radiological picture of a varicella pneumopathy. Median age of subjects with mild, moderate and severe clinical picture was 25.26 ± 10.76 , 23.93 ± 13.93 and 30.40 ± 6.24 years, respectively. The incidence of varicella pneumopathy was lowest in the age groups of 0-7 and 8-14 years (10.9%), and highest in age group of over 30 (41.6%). The age groups of 15-22 and

23-30 had the incidence of 16% and 22%, respectively. The research group comprised 70 males (69.3%) and 31 females (30.7%). Among the subjects, two patients (2%) had malignant disease (Hodgkin's lymphoma and adenocarcinoma of the colon), three (3%) had other chronic diseases (ulcerative colitis, hyperthyroidism), 14 (13.9%) had chronic obstructive pulmonary disease, and 62 (61.4%) were active smokers.

Between the subject groups with varicella pneumopathies who had different degrees of clinical picture severity, a statistically significant difference in the prevalence of patients with certain radiographic types of pneumopathies was found ($p = 0.000$) (Table 1). Majority of subjects with mild clinical picture had more increased pulmonary markings, 58 (95.1%) than the subjects with moderate clinical picture, which most frequently presented localised bronchopneumonic infiltrate, 12 (40%); diffuse bronchopneumonic infiltrate was presented in majority of subjects, nine (90%) with severe clinical picture. The patients who suffered from malignant diseases had the most severe clinical presentation of pneumopathy along with two patients with chronic diseases (ulcerative colitis, hyperthyroidism), whilst eight (26.7%) with chronic obstructive pulmonary disease had the moderate form. In

Table 1. Radiographic findings and severity of clinical symptoms

Parameters	No (%) of patients with			
	Mild clinical symptoms	Moderate clinical symptoms	Severe clinical symptoms	
Radiographic types of pneumopathies	Increased pulmonary markings	58 (95.1%)	10 (33.3%)	1 (10%)
	Localised bronchopneumonic infiltrate	0	12 (40%)	0
	Diffuse bronchopneumonic infiltrate	0	2 (6.7%)	9 (90%)
	Interstitial (atypical) pneumonia	3 (4.9%)	6 (20%)	0
CT scan	Individual nodular changes	0	12 (40%)	0
	Diffuse nodular changes	0	2 (6.7%)	8 (80%)
	Confluent nodular changes	0	0 (0%)	2 (20%)
	Mediastinal lymphadenopathy	61 (100%)	16 (53.3%)	0

the group with severe clinical picture, nine patients (90%) were active smokers. CT findings had a statistically significant difference relative to the clinical course of varicella pneumopathy ($p=0.000$). All subjects with mild form of the disease were presented with mediastinal lymphadenopathy on their CT scans. In patients with the moderate form, the most common diagnosis was mediastinal lymphadenopathy, too, in 16 (53.3%) subjects, whilst 12 (40%) had individual nodular changes. In the severe form group, most subjects, eight of them (80%), had diffuse nodular changes.

DISCUSSION

Prevalence of varicella at 25% in our sample is consistent with already-published values, i.e. 5 - 50% (12, 13). The relatively low incidence of pneumopathy in our research could be attributed to the absence of previously determined immunodeficiency conditions in our patients. In some studies, higher frequency of VZV-related pneumonia was determined among younger males (77%, median age 36.4 years) (14), a result consistent with this research, whilst in others, elderly males were those who contracted the disease more frequently (9). In the children's population, infants and children of up to one year of age are at increased risk for serious complications, the mortality in this group being higher than in other children (1, 2). In our research, the youngest did not have the most severe forms of the disease in most cases and this age group did not have a case of lethal outcome.

Our research results have shown that increased pulmonary markings were found in 68.3% subjects, by all means the most common form of pneumopathy in patients with mild form of the disease (95.1%). This is consistent with the results of other authors (10).

Radiographic picture of atypical (interstitial) pneumopathy was usually found in patients with moderate form of the disease. Nodular, and sometimes reticular opacities, spread to both lungs (11). De La Pena et al. demonstrated increased interstitial pattern in 63% of patients and micronodules in 37% of them (15). According to the obtained results, all patients with localized bronchopneumonic infiltrates belonged to the group with moderate form of

the disease, radiological type of diffuse bronchopneumonic infiltrates was usually found in the group with severe disease form. In this type of lung changes we have encountered numerous, often confluent small patchy shadows of various, micro- and macronodular sizes. They were heterogeneous, medium in intensity, and poorly demarcated. Smokers were significantly represented in all patient groups. This evidence suggests that smoking is an important predisposing factor for the development of the most serious forms of the Varicella-Zoster virus pneumonia (VZVP) (15).

CT scans of pulmonary parenchyma have shown that all of our patients with mild clinical picture had mediastinal lymphadenopathy and, more or less pronounced, pretracheal, paratracheal and interaortocaval lymphadenopathy, and diffuse nodular and confluent changes as the most severe forms of CT manifestations were usually presented in patients with severe clinical picture. These were characterized by numerous unequally limited attenuations, as described above, with a tendency to merge together in two patients with the most severe forms of the disease. Immunodeficiency is certainly one of the most important predisposing factors for the onset of the most severe form of primary varicella pneumonia. It is especially common in people with impaired cellular immune response (HIV/AIDS, patients having malignant diseases or undergoing chemotherapy, organ and bone marrow recipients, etc.). In those cases pneumonia is usually progressive with frequent lethal outcomes (16). This argument is supported by our observations - two patients with the most severe form of pneumonia had a pre-existing malignant disease and were receiving immunosuppressive therapy. In the most severe cases, respiratory distress syndrome may develop (alveolar-capillary block) with lethal outcome (17). In people with impaired immune system (malignant disease, chemotherapy, systemic diseases, AIDS, organ and bone marrow transplants during immunosuppressive therapy, malnutrition, etc.), varicella could be presented as a very severe, even fatal disease. Mortality rate in this population is 15-18% (18-20).

Patients with clinically most severe forms of the disease had the most extensive radiological

changes (disseminated bronchopneumonic foci and/or confluent nodular changes). Their detection might prove vital for the further course of the disease.

ACKNOWLEDGMENTS/ DISCLOSURES

Competing interests: none declared.

REFERENCES

- Kernbach-Wighton G, Oechmichen M, Saterms KS. Fatal outcome of varicella in children. *Legal Medicine* 2003; 5:233-236.
- Park SM. 50 Years Ago in The Journal of Pediatrics: Serious complications of varicella, including fatalities. *The J Pediatr* 2007; 150:473.
- Alexandar G, Basheer HM, Ebrahim MK, Ghoneim I. Idiopathic purpura fulminans and varicella gangrenosa of both hands, toes and integument in a child. *Br J Plast Surg* 2003; 56:194-5.
- Levy MH, Quiltz S, Lorraine CZ, Hunt W, Matthews R, Robertson PW. Pox in the docks: varicella outbreak in an Australian prison system. *J Public Health* 2003; 117:446-51.
- Avnon LS, Smolikov A, Almog Y. Varicella pneumonia in southern Israel: clinical characteristics, diagnosis and therapeutic considerations. *Isr Med Assoc J* 2009; 11:261-5.
- Whitley RJ. Varicella-zoster virus. In: Mandell GL, Bennett JE, Dolin R, ur. *Principles and practice of Infectious Diseases*. 6th ed. Philadelphia: Churchill Livingstone, 2005: 1780-6.
- Heininger U, Seward JF. Varicella. *Lancet* 2006; 368:1365-76.
- Pfeiffer H, Varchmin-Schulteß K, Brinkmann B. Sudden death in childhood due to varicella pneumonia: a forensic case report with clinical implications. *Int J Leg Med* 2006; 120:33-5.
- Chiner E, Ballester I, Betlloch I, Blanquer J, Aguar MC, Blanquer R, Fernández-Fabrellas E, Andreu AL, Briones M, Sanz F. Varicella-zoster virus pneumonia in an adult population: has mortality decreased? *Scand J Infect Dis* 2010; 42:215-21.
- Čanović P. Pneumopathies during morbilli, varicella and influenza. University of Kragujevac, Kragujevac 1998; Ph. D. Thesis.
- Mijailović Ž. Clinical-radiological characteristics of varicella pneumopathy and the influence of certain factors on their incidence, development and outcome. University of Kragujevac, Kragujevac 2008; Ph. D. Thesis.
- Almuneef M, Memish ZA, Balkhy HH, Alotaibi B, Helmy M. Chickenpox complications in Saudi Arabia: is it time for routine varicella vaccination? *Int J Infect Dis* 2006; 10:156-61.
- Seward JF, Galil K, Damon I. Development and experience with an algorithm to evaluate smallpox cases in the United States, 2002-2004. *Clin Infect Dis* 2004; 39:1477-83.
- Frangides CY, Pneumatics I. Varicella-zoster virus pneumonia in adults: report of 14 cases and review of the literature. *E J Int Med* 2004; 15:364-70.
- De la Pena L, Izaguirre D, Aguirrebengoa K, Grande C, Montejo M. Varicella pneumonia in the adult: study of 22 cases. *Enferm Infect Microbiol Clin* 2000; 18:493-5.
- Caberon-Ruiz S, Cisneros JM, Galle EL, Ordonez A, Hinojosa RF, Risco MJE, Hernandez A. Characteristics and repercussions of varicella-zoster virus infection in cardiac transplant. *Transplant Proc* 2003; 35:2004-5.
- Von Mach MA, Kaes J, Omogbehin B, Sagoschen I, Wiechelt J, Kaiser K. An update on interventional lung assist devices and their role in acute respiratory distress syndrome. *Lung* 2006; 184:169-75.
- Beby-Defaux A, Brabant S, Chatellier D, Bourgoin A, Robert R, Ruckes T, Agius G. Disseminated varicella with multiorgan failure in an immunocompetent adult. *J Med Virol* 2009; 81:747-9.
- Banz K, Wagenpfeil S, Neiss A, Hammerschmid ET, Wutzler P. The burden of varicella in Germany. Potential risk and economic impact. *Eur J Health Econ* 2004; 5:46-53.
- Etzioni A, Eidenschenk C, Katz R, Beck R, Casanova JL, Pollack S. Fatal varicella associated with selective natural killer cell deficiency. *J Pediatr* 2005; 146:423-5.

Radiološke karakteristike plućnih promena u toku varicelozne infekcije

Željko Mijailović¹, Predrag Čanović¹, Zoran Todo-
rović¹, Olgica Gajović¹, Ljiljana Nešić¹, Zorana Đ
orđević¹, Jelena Mijailović², Dejan Petrović³

¹Klinika za infektivne bolesti, ²Odeljenje za transfuziologiju,

³Klinika za nefrologiju i urologiju; Klinički centar Kragujevac, Kragujevac, Srbija

SAŽETAK

Cilj istraživanja bio je da kod bolesnika s varicelom utvrdimo opštu učestalost pneumopatija i tipove plućnih promena prema radiografskom izgledu i nalazu na kompjuterizovanoj tomografiji. U radu smo obradili 101 bolesnika s kliničkom slikom varicele i nekim od radiografskih entiteta variceloznih pneumopatija. Poznavanje kliničkih, laboratorijskih i radioloških karakteristika variceloznih pneumopatija, može da predstavlja veoma značajan faktor u njihovom ranom prepoznavanju.

Cljučne reči: varicela, radiološke karakteristike