Original Article

# Clinical and radiological features of a cluster of immunocompetent adolescents with varicella pneumonia: a descriptive study

**Hanting Li[1,2#], Lu Chen[3#], Leqing Chen[1,2#], Yanqing Fan[3], Yuting Zheng[1,2], Qingyue Luo[1,2], Xiaoyu Han[1,2], Heshui Shi[1,2]**

[1]Department of Radiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [2]Hubei Province Key Laboratory of Molecular Imaging, Wuhan, China; [3]Department of Radiology, Wuhan Jinyintan Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

*Contributions:* (I) Conception and design: H Shi, X Han; (II) Administrative support: H Shi; (III) Provision of study materials or patients: Lu Chen, Y Fan; (IV) Collection and assembly of data: H Li, Lu Chen, Leqing Chen, Y Zheng, QY Luo; (V) Data analysis and interpretation: H Li, Lu Chen, Leqing Chen, X Han; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

*Correspondence to:* Xiaoyu Han, MD, PhD; Heshui Shi, MD, PhD. Department of Radiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Road, Wuhan 430022, China; Hubei Province Key Laboratory of Molecular Imaging, Wuhan, China. Email: xiaoyuhan1123@163.com; heshuishi@hust.edu.cn.

**Background:** Varicella pneumonia is one of the most common and severe complications of chickenpox infection. This study aimed to describe the clinical and radiological features of varicella pneumonia in a cluster of immunocompetent adolescents.

**Methods:** A retrospective analysis was conducted on a cohort of adolescent patients diagnosed with varicella pneumonia at Wuhan Jinyintan Hospital between February 2023 and May 2023. The clinical and imaging data were collected and analyzed. A total of 116 patients were divided into two groups by the absence (group 1, n=57) or presence (group 2, n=59) of lower respiratory symptoms for data comparison.

**Results:** Among 116 patients (median age, 16 years; 60 males), rash (100%) was the most prevalent clinical symptom. The most common respiratory symptom and sign were fever (42.2%) and coarse breath sounds (41.4%). Chest computed tomography (CT) performed within five days of symptoms onset revealed multiple (89.7%), peripheral (51.7%), and ill-defined (73.3%) lung nodules in most patients, which gradually improved 6–10 days after symptom onset. Group 2 had higher levels of interleukin-6 (P<0.001), C-reactive protein (P=0.02), serum amyloid-A protein (P=0.002), longer hospital stays (P=0.04), more involved lung lobes (P=0.02), and a higher incidence of multiple nodules (P=0.043) than those of group 1.

**Conclusions:** In immunocompetent adolescents, clustered varicella pneumonia often presents as mild and more uniform in clinical and radiological presentations than sporadic cases. The most common CT findings were multiple pulmonary nodules. Patients with lower respiratory symptoms exhibited more severe clinical and radiological manifestations. Generally, it is not recommended that patients undergo frequent CT scans in a short period.

**Keywords:** Varicella; pneumonia; adolescent; immunocompetent; computed tomography (CT)

Submitted Jan 26, 2024. Accepted for publication Jun 05, 2024. Published online Jul 23, 2024.
doi: 10.21037/jtd-24-149
**View this article at:** https://dx.doi.org/10.21037/jtd-24-149

## Introduction

Varicella (chickenpox) is an infectious disease caused by varicella-zoster virus (VZV) (1,2). The incidence of varicella varies between 13 and 16 cases per 1,000 persons annually, exhibiting significant yearly fluctuations (3). Varicella is highly contagious, with a remarkably high attack rate that is estimated to be approximately 90% among close contacts (4,5). It is especially likely to spread in areas with high population densities (1,6), leading to outbreaks that significantly affect public health, society, and the economy (7). Varicella infections can cause serious complications, and even death. One of the most common and severe complications of chickenpox infection is pneumonia, which carries a mortality rate of 6–30% (8-10). It is more common in older adolescents and adults than in children. Schools are susceptible to outbreaks of VZV-related community-acquired pneumonia (VZV-CAP).

Chest computed tomography (CT) radiography is an important tool for detecting pulmonary infections. The diagnosis of varicella pneumonia relies on imaging identifying new pulmonary infiltrates in the context of an active chickenpox infection, while seeking and excluding alternative causes for pulmonary infiltrates. Effective treatment and prognosis depend on an accurate radiological diagnosis, and a good knowledge of these radiological findings has diagnostic value. In addition, a thorough understanding of the clinical and radiological features of eruptive varicella pneumonia not only contributes to providing early warning signals, but also decision-making support and countermeasures. It facilitates the development of effective prevention and control strategies, which reduce the impact of disease on public health, the economy, and society. Previous studies have mostly focused on children, pregnant women, and adults and were mostly limited to case reports and investigations into sporadic cases. There is a lack of research on clustered and eruptive varicella pneumonia in immunocompetent adolescents. Our current understanding of varicella pneumonia remains limited.

Therefore, this study aimed to describe the clinical and radiological features of eruptive VZV-CAP in a cluster of immunocompetent adolescents. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-149/rc).

### Highlight box

**Key findings**

- A more comprehensive understanding of the clinical and radiological features of varicella pneumonia in adolescents with eruptive varicella has been achieved.

**What is known and what is new?**

- For cases of clustered outbreaks of varicella pneumonia, the improvement of computed tomography (CT) findings lags behind clinical improvement.
- In immunocompetent adolescents with varicella pneumonia, the predominant presentation is mild, characterized by multiple subpleural small nodules in both lungs. These nodules persist for an extended duration, with subtle changes in a short period.

**What is the implication, and what should change now?**

- A comprehensive understanding of varicella pneumonia in adolescents prone to eruptive varicella infections is crucial for timely management, minimizing adverse effects.

## Methods

### *Patients*

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective study was approved by the Ethics Committee of Wuhan Jinyintan Hospital (Approval No. KY-2024-12). Informed consent was not required for this retrospective study.

We conducted a retrospective study involving 116 patients diagnosed with chickenpox pneumonia at Wuhan Jinyintan Hospital between February 2023 and May 2023 (*Figure 1*). The inclusion criteria were as follows: (I) patients with a positive result for varicella virus DNA; and (II) patients were assessed through thin-section CT scans. The exclusion criteria were as follows: (I) patients with suboptimal CT image quality or incomplete clinical data; (II) patients with known pre-existing immunodeficiency; and (III) patients with sporadic occurrences.

A physician with extensive experience in chest radiology retrieved patients' electronic medical records and extracted the following information: demographic information, exposure history, clinical signs and symptoms, laboratory examination results, chest CT images, dates of admission and discharge, treatment, and disease outcome. In our study, the symptoms and signs of respiratory infections include fever, coarse breath sounds, sore throat, cough, expectoration, runny nose, nausea, and dry throat. Patients were categorized into two groups based on the manifestation of lower respiratory symptoms (fever, cough, and expectoration). Group 1 consisted of 57 patients

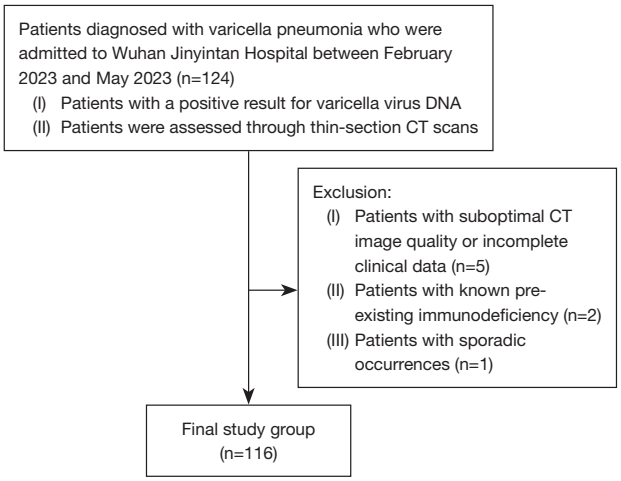


**Figure 1** Flow diagram of patient inclusion and exclusion. CT, computed tomography.

without lower respiratory symptoms, whereas group 2 comprised 59 patients with lower respiratory symptoms.

### *CT image acquisition*

All patients underwent supine position scanning using either a SOMATOM Perspective scanner (Siemens Healthineers, Forchheim, Germany) or NeuViz Prime scanner (Neusoft Corporation, Liaoning Province, China). Scans were performed from the level of the upper thoracic inlet to the inferior level of the costophrenic angle, with the following parameters: detector collimation widths of 128 mm × 0.6 mm and 128 mm × 0.625 mm; tube voltage of 130 or 120 kV; and tube current ranging from 130 to 316 mA. Images were reconstructed with a slice thickness of 1 mm and an interval of 1 mm, respectively. Chest exams were carried out without the use of intravenous contrast, being sent to the digital system.

### *Image interpretation*

Images were independently analyzed by two chest radiologists with five and two years of experience who did not have access to the clinical or laboratory findings. In case of any disagreements, they were resolved through discussion and consensus.

For each patient, the CT images were evaluated for (I) the predominant CT pattern, including nodular and patchy types; (II) the location of lesions, the number of lung lobes involved, along with the size and number of nodules (unifocal, multifocal corresponding to ≥3 in number); and (III) other manifestations, such as axillary lymphadenopathy, halo sign, reticular opacities, and pleural thickening. For follow-up CT scans, a comparative analysis was conducted to categorize the evolution of lesions as no change, resolution, or progression compared to the previous chest CT of the same patient.

### *Statistical analysis*

Analyses were conducted using the IBM SPSS software (version 26.0). $P<0.05$ was considered statistically significant. Distribution normality was assessed using the Kolmogorov-Smirnov test. Normally distributed data were presented as the mean [standard deviation (SD)], non-normally distributed data as the median [interquartile range (IQR)], and categorical variables as the frequency (%). The comparison of unordered categorical variables was conducted using either the Pearson chi-squared test or Fisher's exact test. Non-normally distributed continuous variables and ordered categorical variables were compared between the groups using the Wilcoxon rank-sum test.

## Results

### *Clinical findings*

The clinical characteristics of all patients on admission were summarized in *Tables 1*,*2*. A total of 116 adolescents were included in this study, including 60 men and 56 women, with a median age of 16 (range, 12 to 19) years. All patients were students, without any significant medical history or underlying diseases. Fifty-five patients (47.4%) contracted the disease without any apparent cause, while 61 (52.6%) had a history of exposure to patients with varicella. Among them, 50 (43.1%) were exposed to classmates with chickenpox in school. The median time between the onset of symptoms and admission was 1.5 (range, 0 to 4) days, while the median length of hospital stay was 7 (range, 6 to 13) days. Group 1 had a substantially shorter hospital stay than group 2 [7.00 (IQR: 7.00–8.00) *vs.* 8.00 (IQR: 7.00–8.00) days, P=0.04]. However, there were no significant differences in age, sex, or time from symptom onset to hospitalization between the two groups (*Table 1*).

The most prevalent clinical symptom was the classic chickenpox rash (116 cases, 100.0%), followed by dizziness (57 patients, 49.1%). Swollen tonsils were the most common sign (84 patients, 72.4%), followed by coarse

**Table 1** Baseline characteristics of patients with varicella pneumonia

| Parameter | All patients (n=116) | Group 1 (n=57) | Group 2 (n=59) | P |
|---|---|---|---|---|
| Sex | | | | |
| Male | 60 (51.7) | 27 (47.4) | 33 (55.9) | 0.36 |
| Female | 56 (48.3) | 30 (52.6) | 26 (44.1) | |
| Age, years | 16.00 (14.00–17.00) | 16.00 (13.00–17.00) | 16.00 (14.00–17.00) | 0.81 |
| HR, bpm | 88.00 (84.00–108.00) | 88.00 (82.00–95.50) | 90.00 (85.00–108.00) | 0.08 |
| Rate, bpm | 19.00 (19.00–20.00) | 20.00 (19.00–20.00) | 19.00 (19.00–21.00) | 0.84 |
| Systolic blood pressure, mmHg | 118.50 (110.00–119.00) | 118.00 (110.00–119.00) | 119.00 (109.00–119.00) | 0.91 |
| Diastolic blood pressure, mmHg | 71.00 (69.00–72.00) | 71.00 (68.00–71.50) | 71.00 (71.00–73.00) | 0.39 |
| The time interval from the onset of symptoms to admission, days | 1.50 (1.00–2.00) | 1.00 (1.00–2.00) | 2.00 (1.00–2.00) | 0.70 |
| The length of hospital stay, days | 7.00 (7.00–8.00) | 7.00 (7.00–8.00) | 8.00 (7.00–8.00) | 0.04* |

Group 1 consisted of patients without lower respiratory symptoms, whereas group 2 comprised patients with lower respiratory symptoms. Data are presented as median (IQR) or n (%). *, P<0.05 between groups 1 and 2. HR, heart rate; IQR, interquartile range.

breath sounds (48 patients, 41.4%). Only 59 patients had symptoms of the lower respiratory tract, including fever in 49 (42.2%), cough in 12 (10.3%), and sputum production in three (2.6%). Most patients presented with rash as the initial symptom (83 patients, 71.6%) (*Table 2*). Among the 49 patients who had rash with fever, 29 patients (59.2%) experienced fever on the same day as the rash, 16 patients (32.7%) developed fever 1–4 days after the rash appeared, and four patients (8.2%) had fever symptoms one day before the rash.

### *Laboratory examinations*

The laboratory examination results of all patients on admission were summarized in *Table 3*. The lymphocyte count was decreased in 36 patients (31.0%), leukocytes count was decreased in 27 (23.3%), and neutrophils count was decreased in 11 (9.5%). Hepatic dysfunction was present in 12 patients (10.3%), including six patients (5.2%) with increased gamma-glutamyl transpeptidase, 11 patients (9.5%) with increased aspartate aminotransferase, and 11 patients (9.5%) with increased alanine aminotransferase. In many patients, the levels of lactate dehydrogenase, creatine kinase isoenzyme, creatine kinase, and cardiac troponin were increased (58.6%, 13.8%, 2.6% and 0.9%, respectively). Sixty-nine individuals (59.5%) exhibited abnormal electrocardiograms, with sinus arrhythmia (54 patients, 78.3%) being the most prevalent abnormality. Additionally, 15 patients (12.9%) had anemia. The concentrations of interleukin-6 [IL-6, 8.36 (IQR: 4.15–11.28) *vs.* 4.29 (IQR: 2.54–6.83) pg/mL, P<0.001], C-reactive protein [CRP, 10.30 (IQR: 3.20–17.80) *vs.* 5.80 (IQR: 2.40–11.65) mg/L, P=0.02] and serum amyloid-A protein [SAA, 48.20 (IQR: 22.80–110.10) *vs.* 22.60 (IQR: 6.45–58.35) mg/L, P=0.002] in group 2 were significantly higher than those in group 1. Other laboratory test findings showed no significant differences between the two groups (*Table 3*).

### *CT findings*

The CT findings of the patients were summarized in *Table 4*. The median time interval between symptom onset and the initial CT scan was 2 (IQR: 1–3) days. The CT scans of 115 (99.1%) patients were conducted within five days after the onset of the initial symptoms. At this point, all patients were in a stage characterized by papulo-vesicular-pustular and had abnormal CT imaging features.

Among the 116 patients, pulmonary nodules were the predominant CT finding in 112 patients (96.6%), while the predominant CT pattern in four patients (3.4%) was characterized by patchy shadows (*Figure 2*). Bilateral lung involvement was observed in 102 patients (87.9%). Five of the lung lobes were involved in 76 patients (65.5%). Each lung lobe is at risk of being affected, with the right lower lobe being the most often affected (103 patients, 88.8%). Group 2 was more prone to involving a greater number of lung lobes than group 1 (P=0.02). The lesions in

**Table 2** Clinical symptoms of patients with varicella pneumonia

| Parameter | Result (n=116) |
|---|---|
| Symptoms | |
| Skin rash | 116 (100.0) |
| Enlarged tonsils | 84 (72.4) |
| Grade I | 82 (97.6) |
| Grade II | 2 (2.4) |
| Fever, ℃ | 49 (42.2) |
| 37.3–38.0 | 14 (28.6) |
| 38.1–39.0 | 25 (51.0) |
| >39.0 | 1 (2.0) |
| Unknown | 9 (18.4) |
| Dizziness | 57 (49.1) |
| Coarse breath sounds | 48 (41.4) |
| Headache | 16 (13.8) |
| Sore throat | 16 (13.8) |
| Cough | 12 (10.3) |
| Expectoration | 3 (2.6) |
| Runny nose | 3 (2.6) |
| Nausea | 3 (2.6) |
| Dry throat | 1 (0.9) |
| Vomiting | 1 (0.9) |
| The initial symptom | |
| Rash | 83 (71.6) |
| Rash with fever | 28 (24.1) |
| Fever | 4 (3.4) |
| Cough | 1 (0.9) |

Data are presented as n (%).

60 patients (51.7%) were primarily distributed in peripheral or subpleural areas of bilateral lung tissue (*Table 4*).

All 116 patients (100%) had pulmonary nodules, with the largest lesions measuring 8 mm (IQR: 6–10 mm) and the smallest nodules measuring 2 mm (IQR: 2–2 mm). A total of 104 patients (89.7%) presented with multiple nodules. Patients with multiple nodules in group 2 significantly outnumbered those in group 1 (96.6% *vs.* 82.5%, P=0.04, *Figure 3*). Among them, 85 patients (73.3%) had nodules with ill-defined borders. Other pulmonary CT findings included halo signs (13 patients, 11.2%) and linear opacities (six patients, 5.2%). Thoracic CT findings included pleural thickening (13 patients, 11.2%), and enlarged axillary lymph nodes (54 patients, 46.6%) (*Table 4*).

Follow-up CT imaging was performed in 111 patients (95.7%). The median time interval between symptom onset and the second CT scan was 7 (IQR: 6–8) days, coinciding with the crust-dominated phase in all patients.

Three patterns of evolution were observed among these 111 patients throughout the series of CT scans: radiographic improvement [type 1, median stay 7 (IQR: 7–8) days] (*Figure 4*), observed in 84 patients (75.7%); unchanged radiographic appearance [type 2, median stay 8 (IQR: 7–8) days], observed in twelve patients (10.8%); and radiographic deterioration [type 3, median stay 8 (IQR: 7–8) days] (*Figure 5*), observed in 15 patients (13.5%). There were no significant differences in the patterns of CT image evolution between the two groups (*Table 4*, *Figure 6*). The proportion of patients with well-defined boundaries of the pulmonary nodules in the second CT scan images of 111 patients was substantially greater than that in the first CT scan images (66.7% *vs.* 26.7%, P<0.001).

### *Treatment and outcome*

After admission, all 116 patients (100%) received antiviral medication with acyclovir or ganciclovir, while patients with involvement of other organs received symptomatic treatment. For instance, 35 patients (30.2%) received anti-infective therapy, 17 (14.7%) received leukocyte-boosting therapy, 15 (12.9%) received nutritional myocardial treatment with cyclophosphamide, 5 (4.3%) received blood-boosting therapy, and four (3.4%) received hepatoprotective and liver enzyme-reducing therapy. Eventually, 115 patients (99.1%) were discharged with a clinical cure as the outcome, and one patient (0.9%) was transferred to another hospital for additional treatment for personal reasons. During treatment, 1 patient (0.9%) developed an Aspergillus infection, 1 (0.9%) had COVID-19, and 2 (1.7%) had influenza.

## Discussion

VZV, a human alpha herpesvirus of the genomes, is responsible for varicella (chickenpox) and zoster (shingles). Pneumonia is a frequent and serious complication of chickenpox infection. The characteristic features of varicella pneumonia include lymphoplasmacytic inflammation,

**Table 3** Laboratory findings of patients with varicella pneumonia

| Parameter | All participants (n=116) | Group 1 (n=57) | Group 2 (n=59) | P value |
|---|---|---|---|---|
| Leucocyte count, $\times10^9$/L | 4.31 (3.54–5.38) | 4.34 (3.63–4.97) | 4.28 (3.48–5.51) | 0.64 |
| <3.5 | 27 (23.3) | 11 (19.3) | 16 (27.1) | 0.32 |
| ≥3.5 | 89 (76.7) | 46 (80.7) | 43 (72.9) | |
| Lymphocyte count, $\times10^9$/L | | | | |
| <1.0 | 36 (31.0) | 17 (29.8) | 19 (32.2) | 0.78 |
| ≥1.0 | 80 (69.0) | 40 (70.2) | 40 (67.8) | |
| Neutrophil count, $\times10^9$/L | | | | |
| <1.5 | 11 (9.5) | 7 (12.3) | 4 (6.8) | 0.31 |
| ≥1.5 | 105 (90.5) | 50 (87.7) | 55 (93.2) | |
| Interleukin-6, pg/mL | 5.81 (4.15–9.19) | 4.29 (2.54–6.83) | 8.36 (4.15–11.28) | <0.001* |
| C-reactive protein, mg/L | 6.65 (2.40–14.35) | 5.80 (2.40–11.65) | 10.30 (3.20–17.80) | 0.02* |
| Procalcitonin, ng/mL | 0.08 (0.03–0.14) | 0.07 (0.03–0.13) | 0.08 (0.04–0.14) | 0.16 |
| Serum amyloid A protein, mg/L | 34.35 (13.68–69.10) | 22.60 (6.45–58.35) | 48.20 (22.80–110.10) | 0.002* |
| Ferritin, ng/mL | 76.96 (40.48–117.68) | 76.95 (36.20–97.95) | 76.95 (48.75–130.60) | 0.051 |
| Aspartate aminotransferase, U/L | | | | |
| ≤40 | 105 (90.5) | 52 (91.2) | 53 (89.8) | 0.80 |
| >40 | 11 (9.5) | 5 (8.8) | 6 (10.2) | |
| Alanine aminotransferase, U/L | | | | |
| ≤40 | 105 (90.5) | 51 (89.5) | 54 (91.5) | 0.71 |
| >40 | 11 (9.5) | 6 (10.5) | 5 (8.5) | |
| Prealbumin, mg/L | | | | |
| <200 | 18 (15.5) | 6 (10.5) | 12 (20.3) | 0.14 |
| ≥200 | 98 (84.5) | 51 (89.5) | 47 (79.7) | |
| Lactate dehydrogenase, U/L | | | | |
| <245 | 48 (41.4) | 20 (35.1) | 28 (47.5) | 0.18 |
| ≥245 | 68 (58.6) | 37 (64.9) | 31 (52.5) | |
| Creatine kinase, U/L | | | | |
| ≤174 | 113 (97.4) | 56 (98.2) | 57 (96.6) | >0.99 |
| >174 | 3 (2.6) | 1 (1.8) | 2 (3.4) | |
| Creatine kinase isoenzyme, U/L | | | | |
| ≤25 | 100 (86.2) | 49 (86.0) | 51 (86.4) | 0.94 |
| >25 | 16 (13.8) | 8 (14.0) | 8 (13.6) | |
| Abnormal electrocardiogram | 69 (59.5) | 35 (61.4) | 34 (57.6) | 0.68 |
| Sinus arrhythmia | 54 (78.3) | 28 (80.0) | 26 (76.5) | 0.59 |
| Sinus bradycardia | 12 (17.4) | 7 (20.0) | 5 (14.7) | 0.50 |
| Right axis deviation | 11 (15.9) | 6 (17.1) | 5 (14.7) | 0.71 |
| Early repolarization | 8 (11.6) | 1 (2.9) | 7 (20.6) | 0.06 |
| Right bundle branch block | 5 (7.2) | 4 (11.4) | 1 (2.9) | 0.20 |
| Other abnormalities | 12 (17.4) | 3 (8.6) | 9 (26.5) | 0.08 |

Group 1 consisted of patients without lower respiratory symptoms, whereas group 2 comprised patients with lower respiratory symptoms. Data are presented as median (IQR) or n (%). *, P<0.05 between groups 1 and 2. IQR, interquartile range.

**Table 4** The initial CT features of patients with varicella pneumonia

| Parameter | Result (n=116) | Group 1 (n=57) | Group 2 (n=59) | P |
|---|---|---|---|---|
| Predominant CT pattern | | | | |
| Nodular predominant type | 112 (96.6) | 54 (94.7) | 58 (98.3) | 0.36 |
| Patchy predominant type | 4 (3.4) | 3 (5.3) | 1 (1.7) | |
| Lung involvement | | | | |
| Unilateral | 14 (12.1) | 9 (15.8) | 5 (8.5) | 0.23 |
| Bilateral | 102 (87.9) | 48 (84.2) | 54 (91.5) | |
| Number of involved lung lobes | 5.00 (3.00–5.00) | 5.00 (2.00–5.00) | 5.00 (4.00–5.00) | 0.02* |
| 1 | 9 (7.8) | 7 (12.3) | 2 (3.4) | |
| 2 | 13 (11.2) | 9 (15.8) | 4 (6.8) | |
| 3 | 11 (9.5) | 7 (12.3) | 4 (6.8) | |
| 4 | 7 (6.0) | 2 (3.5) | 5 (8.5) | |
| 5 | 76 (65.5) | 32 (56.1) | 44 (74.6) | |
| Predominant distribution of lesions | | | | |
| Peripheral | 60 (51.7) | 33 (57.9) | 27 (45.8) | 0.19 |
| Non-peripheral | 56 (48.3) | 24 (42.1) | 32 (54.2) | |
| Nodule | | | | |
| Maximum diameter, mm | 8.00 (7.00–10.00) | 8.00 (7.00–10.00) | 8.00 (7.00–11.00) | 0.75 |
| Minimum diameter, mm | 2.00 (2.00–2.00) | 2.00 (2.00–3.00) | 2.00 (2.00–2.00) | 0.27 |
| Number | | | | |
| 1 | 7 (6.0) | 6 (10.5) | 1 (1.7) | 0.04* |
| 2 | 5 (4.3) | 4 (7.0) | 1 (1.7) | |
| ≥3 | 104 (89.7) | 47 (82.5) | 57 (96.6) | |
| Margin definition | | | | |
| Well-defined | 31 (26.7) | 14 (24.6) | 17 (28.8) | 0.60 |
| Ill-defined | 85 (73.3) | 43 (75.4) | 42 (71.2) | |
| Enlarged axillary lymph nodes | 54 (46.6) | 26 (45.6) | 28 (47.5) | 0.84 |
| Halo sign | 13 (11.2) | 9 (15.8) | 4 (6.8) | 0.12 |
| Pleural thickening | 13 (11.2) | 9 (15.8) | 4 (6.8) | 0.12 |
| Linear opacities | 6 (5.2) | 3 (5.3) | 3 (5.1) | >0.99 |
| Evolution patterns of CT images | 111 (95.7) | 54 (96.4) | 57 (96.6) | |
| Type 1 | 84 (75.7) | 42 (77.8) | 42 (73.7) | 0.52 |
| Type 2 | 12 (10.8) | 4 (7.4) | 8 (14.0) | |
| Type 3 | 15 (13.5) | 8 (14.8) | 7 (12.3) | |

Group 1 consisted of patients without lower respiratory symptoms, whereas group 2 comprised patients with lower respiratory symptoms. Type 1: radiographic improvement; Type 2: unchanged radiographic appearance; Type 3: radiographic deterioration. *, P<0.05 between groups 1 and 2. Data are presented as median (IQR) or n (%). CT, computed tomography; IQR, interquartile range.

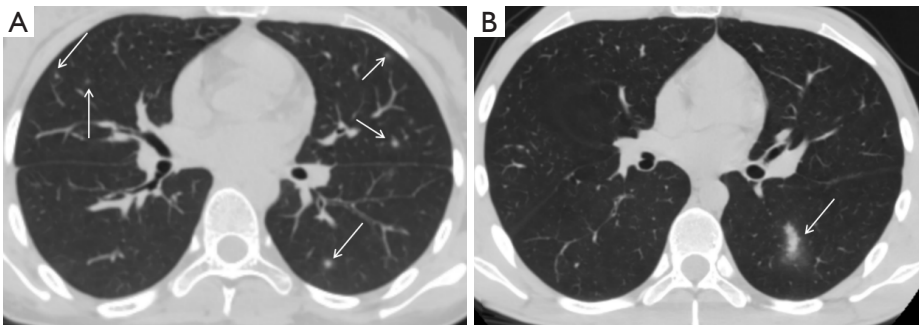


**Figure 2** Chest CT in patients with varicella pneumonia. (A) A 17-year-old female, day 2 after symptom onset, showing multiple pulmonary nodules in both lungs (arrows). (B) A 17-year-old male, day 2 after symptom onset, the main CT findings were is small consolidations (arrow) in the lower left lobe. CT, computed tomography.

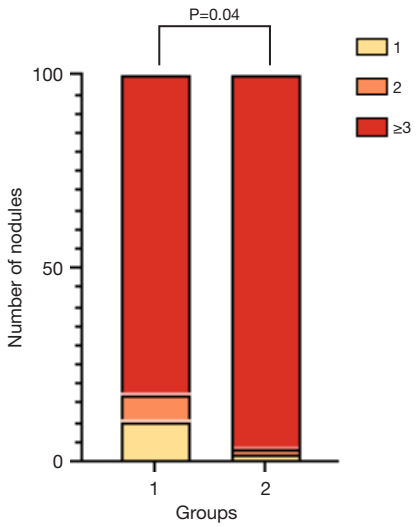


**Figure 3** Number of nodules in group 1 and group 2. The stacked bars show the proportion of patients with the various number of nodules. The patients were divided into two groups based on the absence (group 1) or presence (group 2) of lower respiratory symptoms.

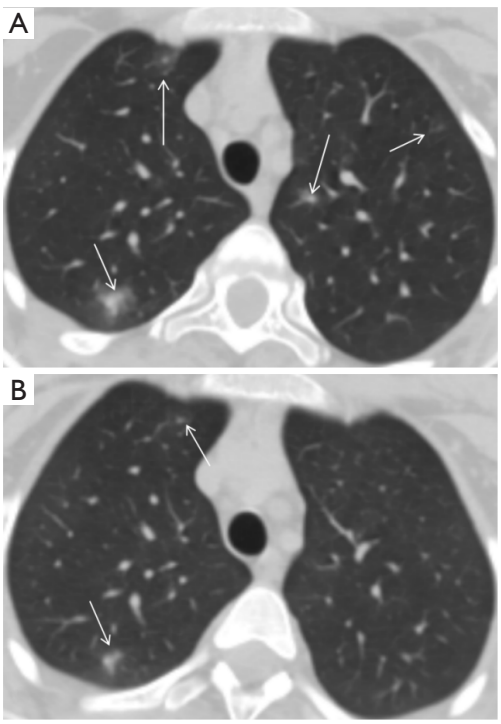


**Figure 4** Chest CT scans from a 13-year-old female. (A) Day 2 after symptom onset, the main CT findings predominantly consist of multiple pulmonary nodules (arrows) in both lungs. The largest lesion is observed in the upper lobe of the right lung, presenting as an ill-defined solid nodule. (B) Day 6, compared to the previous images, the nodules (arrows) have significantly decreased in size. CT, computed tomography.

edema, fibrin deposition, necrosis, hemorrhaging, and loss of normal lung architecture (11). In our study, all patients were students attending school, and the outbreaks occurred in high-density areas. Compared to sporadic cases, all patients exhibited a certain degree of resemblance in their clinical symptoms and radiological findings.

Varicella has a distinct seasonal cycle, with the first patient in our study presenting in February, toward early spring, aligning with the typical appearance of chickenpox each year (12). The most common signs and symptoms were characteristic rashes and swollen tonsils. This is because primary VZV infection begins with viral replication in the epithelial cells of the upper respiratory mucosa, as the virus prefers to infect skin and T cells (13). Compared to

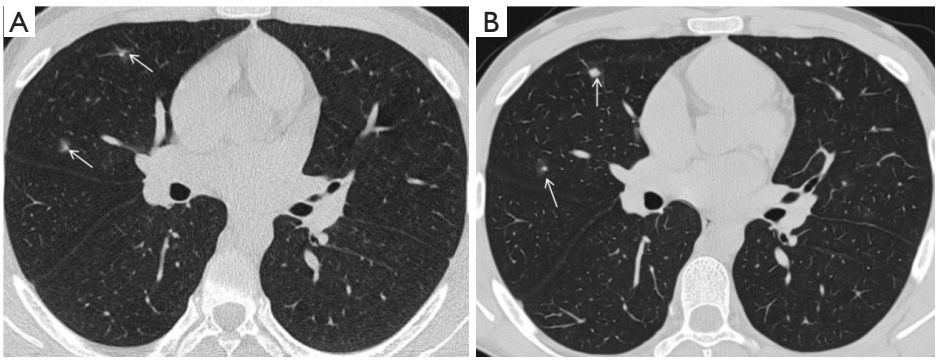


**Figure 5** Chest CT scans from a 14-year-old male. (A) Day 2 after symptom onset, the main CT findings predominantly consist of multiple pulmonary nodules (arrows) in both lungs. The largest lesion is observed in the middle lobe, presenting as an ill-defined solid nodule. (B) Day 7, compared to the previous images, the nodules (arrows) in the middle lobe have enlarged, and an increased in the number of nodules. CT, computed tomography.

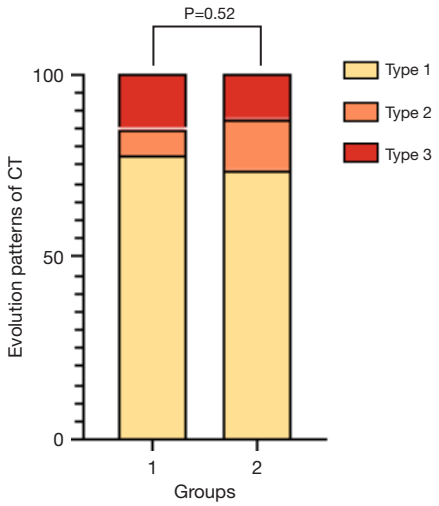


**Figure 6** Evolution patterns of CT images in group 1 and group 2. Stacked bars show the proportion of patients in whom the evolution pattern of the CT images was type 1 (radiographic improvement), type 2 (unchanged radiographic appearance) or type 3 (radiographic deterioration). The patients were divided into two groups based on the absence (group 1) or presence (group 2) of lower respiratory symptoms. CT, computed tomography.

previously reported sporadic cases (10,14,15), all patients in our study had mild clinical symptoms and lacked diverse presentations, such as chest pain, hemoptysis, dyspnea, and hypoxemia. Only some patients exhibited lower respiratory symptoms and signs, with the most common signs being coarse breath sounds. About 42.2% of patients experienced fever. Fever may occur before or within four days after the onset of the rash. Most notably, most patients had elevated levels of inflammatory markers. Patients with lower respiratory symptoms had significantly higher levels of inflammatory markers (IL-6, CRP, and SAA) than those without lower respiratory symptoms. This indicates that pneumonia should be considered even in the absence of lower respiratory symptoms, particularly with mild elevations in inflammatory markers. Additionally, patients without lower respiratory symptoms had shorter hospital stay.

Chickenpox infection can involve multiple organs. In our study, we observed that in addition to pneumonia, most patients presented with myocardial injury. Some patients exhibited liver dysfunction, anemia, decreased white blood cells and lymphocytes, and concurrent bacterial or viral infections. In contrast to previous studies and case reports (8,16-18), we found no cases of neurological, renal, or ophthalmic involvement.

We searched for patients diagnosed with chickenpox infection who met our inclusion and exclusion criteria and underwent CT scans during this period, and found that all patients, regardless of the presence of lower respiratory symptoms, exhibited pulmonary abnormalities. This suggests that the actual incidence of varicella pneumonia in immunocompetent adolescents may be higher than that previously reported. This could be related to the fact that many previous studies were based on X-ray and CT images (*Figure* 7), which may not have been as prevalent.

Our study indicates that pulmonary lesions may appear within five days following the initial symptoms, sometimes even earlier. The majority of patients exhibited CT findings consistent with previous reports (19,20), showing multiple, bilateral, peripheral pulmonary nodules, along

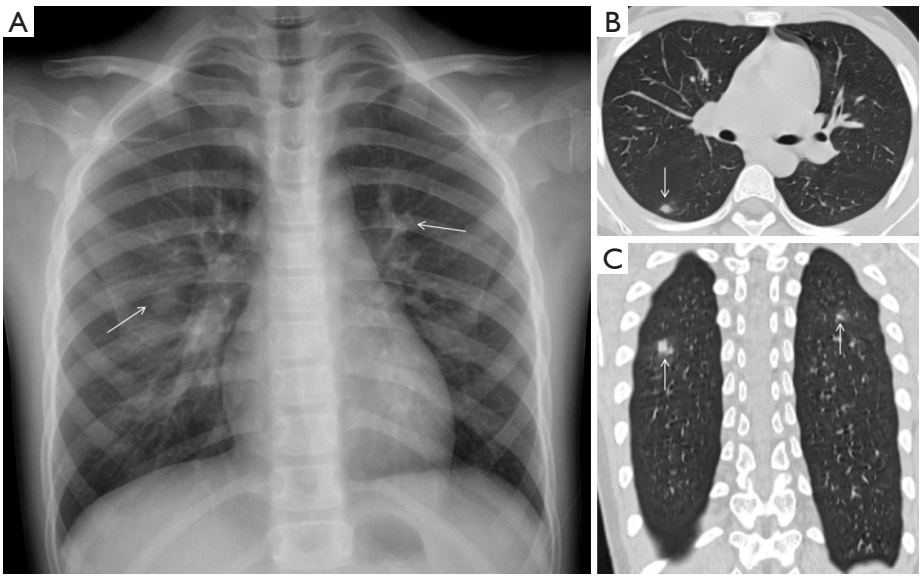


**Figure 7** Chest radiography (A) and CT (B,C) scans from a 12-year-old female. Day 2 after symptom onset, the main CT findings predominantly consist of multiple pulmonary nodules (arrows) in both lungs. The largest lesion is observed in the lower lobe of the right lung, presenting as an ill-defined solid nodule. CT, computed tomography.

with enlarged axillary lymph nodes. Additionally, some patients exhibited non-specific features, such as pleural thickening, halo signs, and linear opacities. However, we did not observe any signs of pleural effusion or calcification. Compared to previous reports and studies on sporadic cases (10,21,22), our patients exhibited fewer CT findings of ground-glass opacities or consolidative infiltrates, and there was a lack of cases predominantly presenting as miliary nodules. We conclude that individuals infected by the same source may exhibit similar radiographic manifestations. Patients with lower respiratory symptoms tended to exhibit more severe pulmonary abnormalities, with involvement of a greater number of lung lobes and multiple nodules.

Comparative analysis of the initial and follow-up CT images for each patient showed that pulmonary nodules with ill-defined boundaries within five days of the initial symptoms were common. From six to ten days after symptom onset, most patients showed improvement and resolution of lesions, with CT scans demonstrating well-defined pulmonary nodules. Notably, in some cases, the lesions either remained constant or worsened. Nonetheless, 115 patients finally recovered clinically and were discharged as varicella rashes crusted. This suggests that the severity of the rash may not necessarily correlate with the severity of pneumonia. Pulmonary involvement in varicella pneumonia can persist for a long duration, and in rare cases, it may indefinitely manifest as pulmonary nodules and calcified nodules (23). In our study, regardless of the type of evolution pattern observed in CT images, the changes in pulmonary lesions were relatively minor. Therefore, physicians should consider a comprehensive evaluation of the patient's symptoms, medical history, and other clinical information to determine the need for follow-up CT.

Our study had several limitations. First, this study has a retrospective nature, introducing the possibility of selection bias in the choice of study subjects. second, it is a single-center study, and further multi-center studies are needed to validate our findings.

## Conclusions

In conclusion, clustered VZV-CAP outbreaks in immunocompetent adolescents exhibit mild clinical symptoms and CT imaging features. Compared to sporadic cases, patients in clustered outbreaks tend to present with more consistent clinical and imaging features. The most common symptoms were varicella rashes and swollen tonsils. Multiple organs or systems, particularly the heart, can be affected. On CT scans taken within five days from the onset of symptoms, pulmonary lesions are frequently characterized by multiple, bilateral, peripheral, and ill-defined nodules. The lesions in most patients gradually improve and are absorbed within

6–10 days after the onset of symptoms. Patients with lower respiratory symptoms exhibited significantly higher levels of inflammatory markers, more severe pulmonary manifestations, and longer hospital stays than those without lower respiratory symptoms. In the absence of necessity, it is recommended that patients undergo a follow-up chest X-ray in the short term.

## Acknowledgments

We would like to thank all colleagues for helping us during the current study and all the selfless volunteers who participated in the study.
*Funding:* This work was supported by the National Natural Science Foundation of China (grant No. U22A20352, 82071921), the Key Research and Development Projects of Hubei Province (grant No. 2020BAB022), and the Nature Science Foundation of Hubei Province (grant No. 2022CFB230).

## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-149/rc

*Data Sharing Statement:* Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-149/dss

*Peer Review File:* Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-149/prf

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-149/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was reviewed and approved by the Ethics Committee of Wuhan Jinyintan Hospital (Approval No. KY-2024-12). Informed consent was not required for this retrospective study.



## References

1. Paradis EM, Tikhonov O, Cao X, et al. Phase 3, open-label, Russian, multicenter, single-arm trial to evaluate the immunogenicity of varicella vaccine (VARIVAX™) in healthy infants, children, and adolescents. Hum Vaccin Immunother 2021;17:4183-9.
2. Arvin AM. Creating the "Dew Drop on a Rose Petal": the Molecular Pathogenesis of Varicella-Zoster Virus Skin Lesions. Microbiol Mol Biol Rev 2023;87:e0011622.
3. Gershon AA, Breuer J, Cohen JI, et al. Varicella zoster virus infection. Nat Rev Dis Primers 2015;1:15016.
4. Lu JY, Zhang ZB, He Q, et al. Association between climatic factors and varicella incidence in Guangzhou, Southern China, 2006-2018. Sci Total Environ 2020;728:138777.
5. Jung J, Ko YJ, Kim YE, et al. Epidemiological Impact of the Korean National Immunization Program on Varicella Incidence. J Korean Med Sci 2019;34:e53.
6. Sun X, Zhu Y, Sun H, et al. Comparison of varicella outbreaks in schools in China during different vaccination periods. Hum Vaccin Immunother 2022;18:2114255.
7. Goh AEN, Choi EH, Chokephaibulkit K, et al. Burden of varicella in the Asia-Pacific region: a systematic literature review. Expert Rev Vaccines 2019;18:475-93.
8. Dooling K, Marin M, Gershon AA. Clinical Manifestations of Varicella: Disease Is Largely Forgotten, but It's Not Gone. J Infect Dis 2022;226:S380-4.
9. John KG, John TJ, Taljaard JJ, et al. The outcome of severe varicella pneumonia with respiratory failure admitted to the intensive care unit for mechanical ventilation. Eur Respir J 2018;52:1800407.
10. Mirouse A, Vignon P, Piron P, et al. Severe varicella-zoster virus pneumonia: a multicenter cohort study. Crit Care 2017;21:137.
11. Ouwendijk WJ, van den Ham HJ, Delany MW, et al. Alveolar barrier disruption in varicella pneumonia is associated with neutrophil extracellular trap formation. JCI Insight 2020;5:e138900.

 

12. Chen B, Sumi A, Wang L, et al. Role of meteorological conditions in reported chickenpox cases in Wuhan and Hong Kong, China. BMC Infect Dis 2017;17:538.
13. Zerboni L, Sen N, Oliver SL, et al. Molecular mechanisms of varicella zoster virus pathogenesis. Nat Rev Microbiol 2014;12:197-210.
14. Mangioni D, Grasselli G, Abbruzzese C, et al. Adjuvant treatment of severe varicella pneumonia with intravenous varicella zoster virus-specific immunoglobulins. Int J Infect Dis 2019;85:70-3.
15. Shrestha N, Bhatta K, Rai A, et al. Varicella Pneumonia in an Immunocompetent Middle-aged Adult Male: A Case Report. JNMA J Nepal Med Assoc 2022;60:651-3.
16. Olivieri B, Betterle C, Zanoni G. Vaccinations and Autoimmune Diseases. Vaccines (Basel) 2021;9:815.
17. Leung J, Broder KR, Marin M. Severe varicella in persons vaccinated with varicella vaccine (breakthrough varicella): a systematic literature review. Expert Rev Vaccines 2017;16:391-400.
18. Nash PS, Humphries F, Benjamin L, et al. Varicella zoster vasculopathy associated with deep intracerebral haemorrhage. J Neurol 2023;270:2320-4.
19. Hammer MM, Gosangi B, Hatabu H. Human Herpesvirus Alpha Subfamily (Herpes Simplex and Varicella Zoster) Viral Pneumonias: CT Findings. J Thorac Imaging 2018;33:384-9.
20. Koo HJ, Lim S, Choe J, et al. Radiographic and CT Features of Viral Pneumonia. Radiographics 2018;38:719-39.
21. dos Santos MC, Alecrim MG. Images in clinical medicine. Varicella pneumonia in an adult. N Engl J Med 2010;362:1227.
22. Franquet T. Imaging of pulmonary viral pneumonia. Radiology 2011;260:18-39.
23. Isobe T, Umemoto J, Kobayashi M, et al. Varicella-zoster Virus Related Pulmonary Granulomas in Which Varicella-zoster Virus DNA Was Demonstrated in a Thoracoscopic Lung Biopsy Specimen. Intern Med 2019;58:2101-5.

**Cite this article as:** Li H, Chen L, Chen L, Fan Y, Zheng Y, Luo Q, Han X, Shi H. Clinical and radiological features of a cluster of immunocompetent adolescents with varicella pneumonia: a descriptive study. J Thorac Dis 2024;16(7):4379-4390. doi: 10.21037/jtd-24-149