

## Original Article

# Clinical analysis of 32 Chinese children with hemorrhagic vesicles

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**Abstract:** Varicella is usually regarded as a benign and self-limited disorder. Severe cases, including hemorrhagic varicella, are rare. These cases were thought to be influenced by underlying diseases such as HIV infection, leukemia. This study aims to explore the relationship among clinical character, lab data and prognoses in children suffering from hemorrhagic vesicles. The clinical and lab data of 32 Chinese children suffering from hemorrhagic vesicles between January 1997 and December 2013 were collected for retrospective study. Of 32 infected patients, those who suffered neutropenia were hard to control. The infections commonly occurred in respiratory and digestive systems, skin or mucous membranes. In conclusion, hemorrhagic varicella is a rare but potentially fatal disease, particularly in the immunocompromised group. Despite support and antiviral therapy mortality is still high in hemorrhagic varicella.

**Keywords:** Hemorrhagic vesicles, childhood, clinical features

### Introduction

Varicella (chickenpox) is one of the most common infectious diseases [1]. There is no formal data collection or epidemiologic surveys in China, although varicella occurs seasonally and in epidemics. Approximately 70% of the cases in the United States are in children younger than 10 years data [2]. Varicella is usually regarded as a benign and self-limited disorder. Severe cases, including hemorrhagic varicella, are rare [3]. These cases were thought to be influenced by underlying diseases such as HIV infection, leukemia. However, healthy individuals may also experience some complications (such as varicella pneumonia, soft tissue infections) as well [2]. In Children's hospital of Chongqing, China, a review of hemorrhagic varicella cases was made from January of 1997 to December of 2013. Out of the 2544 cases, 32 patients (1.3%) presented with bleeding complications, 20 of them recovered.

### Material and methods

All 32 cases with hemorrhagic varicella were subjected to physical examination and case history. Evaluation also included complete bl-

ood count (CBC), urinalysis, stool occult blood (OB) test, liver, cardiac and renal function, coagulation test, electrolyte, bone marrow smear, blood gas, X-ray and/or CT scan. The treatments, which included intravenous injection of acyclovir and/or antibiotics, transfusion of erythrocytes and/or platelets, IVIG, fresh frozen plasma, were dependent on patient's conditions, Mechanical ventilation was administered when a patient was in respiratory failure or pulmonary hemorrhage. Data was analyzed by SAS Enterprise Guide 4.1. Fisher's Exact Test was taken and  $P < 0.05$  was taken as significant for difference in all statistical analysis.

### Results

32 (1.3%) children suffering from hemorrhagic varicella were reported in a total of 2544 varicella patients hospitalized between January 1997 and December 2013 in the Children's Hospital of Chongqing, China. There was no gender difference. Seasonal distribution followed a normal course, with a peak incidence in February to March. The age of onset varied from 7.06 m-14.58 yr (M=8.58 yr, X=10.32 yr); the period between onset and admission ranged from 1 d-10 d (M=4 d, X=4.07 d). All of the

## Clinical analysis for hemorrhagic vesicles

**Table 1.** Clinical data of 32 patients with hemorrhagic varicella

Clinical Parameter	n (%)	Clinical Parameter	n (%)
Males	14 (44.75)	cCugh	6 (18.75)
Females	18 (55.25)	Abdominalgia	4 (12.5)
Hemorrhagic rash	32 (100)	Hepatomegaly	4 (12.5)
Fever	16 (50)	Splenomegaly	2 (6.25)
Pneumorrhagia	6 (18.75)	Steroid	16 (50)

**Table 2.** Lab data of 32 cases with haemorrhagic varicella

Test	n (%)	Test	n (%)
Thrombocytopenia	32 (100)	X-ray	32 (100)
Electrolyte	32 (100)	CT scan	13 (40.6)
Coagulation test	32 (100)	Bone marrow	17 (100)
Liver function	32 (100)		
Cardiac function	12 (37.5)		
Renal function	32 (100)		

32 cases with hemorrhagic rash, the duration between rash onset and haemorrhagic rash presentation was 0.5 d-3 d (M=2 d, X=1.97 d). In fatal cases, the period from rash onset to death ranged from 3 d to 11 d (M=5.5 d, X=6 d). The duration in hospital was between 1-20 days (7.50 ± 6.03). Only 4 of the patients had valid varicella contact history. Sixteen patients received steroid therapy: 6 nephropathy, 4 asthma attack, immune thrombocytopenia purpura (ITP, 4 cases) and systemic lupus erythematosus (SLE, 2 case). Eleven other patients suffered from acute lymphoblastic leukemia (ALL) and received chemotherapy before onset. Five patients were previously healthy. All these patients had haemorrhagic rash, and additional manifestations including fever, cough, abdominalalgia, hepatomegaly and splenomegaly. Clinical data was showed in **Table 1**.

In these 32 cases, bone marrow smears of 15 patients were normal. X-ray and/or CT scan presented pneumonia in 4cases, and lung hemorrhage in 10 cases. The lab data is shown in **Table 2**.

In these 32 cases, white blood cells count (7.79 ± 4.23) × 10<sup>9</sup>/L, platelet count (24.91 ± 13.92) × 10<sup>9</sup>/L. CRP (37.73 + 14.71) for me/L; Blood biochemical. Lactate dehydrogenase (371.5~25.50) U/L, creatine kinase (77.44). Plus or minus 25.50) U/L, aspartate amino transferase

(plus or minus 50.28) U/L, alanine aminotransferase (57.78~5.94) U/L and muscle.

Complications: 23 cases of liver damage (100%); Chest imaging Study revealed lung infection of 17 cases (73.91%); And myocarditis 3 cases (13.04%); Thrombocytopenia 1 o cases, accounting for 43.48% (including secondary decrease in 5 cases, 21.74%); The fungus infection in 5 cases (21.74%). And 13 cases of encephalitis (accounted for 56.62%), 3 cases with other systemic muscle soreness, double lower limbs disabled action Ok (13.04%) and aged (4, 9). Cerebrospinal fluid examination: white is fine. Cell number (30.45 ± 3.55) × 10/L (both in mononuclear cells increased Lord), protein (401.23 ± 5.34 mg/L, chloride and sugar are normal; 20 cases had complete recovery without any sequela in follow-up for 8 m-9 yr. 12 cases resulted in death during the period of observation. In the death of 12 patients with hemorrhagic chickenpox, eleven have basic disease: seven patients with acute lymphocytic leukemia, two patients with nephropathy, one with asthma, one with ITP; only one patient was previously healthy. Causes of death were pulmonary hemorrhage (6 cases), respiratory failure (2 case) and multiple organ failure (4 cases). Risk factor analysis in **Table 3** shows positive relationship between odd ratio (OR), confidence interval (CI) and hyponatremia and hypochloremia, pulmonary hemorrhage and the duration in hospital.

### Discussion

Bleeding manifestation in varicella is rare and when it occurs, it may be in the form of hemorrhages both into the rash and surrounding skin and from mucous membranes, intracranial, gastrointestinal tract and/or lung [4]. Haemorrhagic varicella usually occurs during the 1<sup>st</sup> week of the disease, beginning abruptly with a high fever, toxicity and bleeding from the gastrointestinal tract, genitourinary tract, and other mucous membranes [5]. Fatalities are common and result primarily from intractable bleeding; intracranial hemorrhage or the pneumonia that often accompanies this condition [6]. Investigation of patients with bleeding manifestations often reveals coagulation abnormalities. In others, increased capillary fragility, evidence of disseminated intravascular coagulation (DIC), or thrombocytopenia may be found [7].

## Clinical analysis for hemorrhagic vesicles

**Table 3.** Risk factor analyses

Risk factor	OR	95% CI	F	P
Hyponatremia and hypochloremia	18.00	1.24, 260.92	22.27	0.0006
Pneumonia hemorrhage	77.00	2.67, 2222.91	27.68	0.0005
Steroid	1.7778	0.19, 16.49	0.05	0.8326
Thrombocytopenia	1.7778	0.19, 16.49	0.55	0.48
Duration	77.00	2.67, 2222.91	7.28	0.02

OR: odds ratio; Confidence interval: CI. The dependent variable for this table is the "risk of the hemorrhagic varicella disease". This table aims to investigate the risk of the hemorrhagic varicella.

In our data, of 12 deaths, predisposing conditions include any immunosuppressant treatment, i.e., steroid therapy (current or recent), cancer or immunodeficiency. Mainly cause of death was pulmonary hemorrhage. Hemorrhagic chickenpox may also affect a previously healthy individual [8]. It is reported that when hemorrhagic varicella presents in adults, it is more severe in adults than in children [9]. The fatal 12 cases were all older children and show coagulation abnormalities or thrombocytopenia. Their histories were otherwise negative for predisposing causes. All had the manifestations of hemorrhagic varicella probably suffered from deficient cellular immunity although no related studies were performed.

In conclusion, chickenpox is considered to be a benign disease of childhood, but hemorrhagic varicella is a rare but potentially a fatal disease, particularly in the immunocompromised group. Despite support and antiviral therapy mortality is still high in hemorrhagic varicella. Research studies on this type of varicella would be of great interest and benefit to the medical practitioner.

### Disclosure of conflict of interest

None.

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