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# Varicella-Zoster Virus Encephalitis with Hyponatremia in an Immunocompetent Elderly Patient: A Case Report

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**Abstract:** As a common cause of viral encephalitis, varicella-zoster virus (VZV) may invade the central nervous system of immunosuppressed patients during reactivation. Herein, we report a rare case of an immunocompetent patient with VZV encephalitis who developed severe hyponatremia and was considered to have a suspected primary infection. The patient was diagnosed with the support of second-generation sequencing and had persistent hyponatremia after being cured. Although rare, this case suggests that VZV encephalitis may occur in unexpected patients and present with unusual clinical manifestations, requiring advanced detection methods and clinical expertise for resolution.

**Keywords:** Varicella-zoster virus encephalitis; Immunocompetent; Hyponatremia

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## 1. Introduction

The central nervous system (CNS) involvement of varicella-zoster virus (VZV) is more commonly seen during reactivation, and the most common manifestation is vasculopathy that presents as headache, cognitive decline, and/or focal neurological deficits [1,2]. However, due to the lower VZV antibody levels compared to other countries [3], VZV encephalitis shows different epidemiological characteristics and clinical manifestations in China.

CNS diseases caused by primary VZV infection are rare, seen in around 1 per 4,000 cases, predominantly in children [3]. Herein, we report the rare case of an immunocompetent elderly patient with encephalitis and hyponatremia during suspected primary VZV infection and briefly summarize and discuss related reports.

## 2. Case presentation

A nearly 70-year-old man was admitted to the Affiliated Infectious Diseases Hospital of Soochow University

on 27 September 2023 due to rash, nausea, and gait disturbance. The patients had developed nausea and gait disturbance 10 days before this admission with a diagnosis of cerebrovascular diseases in the community hospital. He had moderate hyponatremia (Na: 126 mmol/L) owing to the anorexia, and received the treatment accordingly until rash and fever (the thermal spike was 38.3℃) appeared. By the consultation of a dermatologist, the patient was believed to have chickenpox and was delivered to our hospital the next day.

After admission, the patient was in a state of somnolence and his clinical signs included headache, neck stiffness, and several small blisters on the trunk. An urgent blood test showed severe hyponatremia (Na: 119 mmol/L). Therefore, we decreased intracranial pressure, increased serum sodium, and performed a lumbar puncture in this patient. Cerebrospinal fluid (CSF) showed a white blood cell count of 328/μL with elevated protein (++) and normal pressure (80 mm$H_2O$). Meanwhile, we sent blood and CSF samples to detect possible pathogens and assess immune function. Eventually, we found VZV both in the blood (by polymerase chain reaction) and CSF (by next-generation sequencing, 257 sequences), weakly positive VZV IgM antibody and negative VZV IgG antibody. No evidence of human immunodeficiency virus, tumors, or autoimmune diseases was found. As a result, we administered an antiviral therapy with acyclovir (10 mg/kg three times/day for 10 days). Subsequently, the patient regained consciousness and the symptoms were relieved.

Despite the treatment, the hyponatremia continued (**Figure 1**). During the antiviral treatment (the first 10 days of hospitalization), the blood sodium remained at 120–127 mmol/L with an intravenous supplement of 18.48 g sodium chloride per day, while the patient followed a strict high sodium diet. We invited an endocrinologist to determine the cause. After a series of examinations, he was diagnosed with suspected cerebral salt-wasting syndrome and we adjusted the treatment accordingly. With the patient gradually recovering, the blood sodium sustained at 125 mmol/L and no longer raised. On the 21st day of hospitalization, the patient was urged to be discharged with a 130 mmol/L blood sodium. The follow-up indicated persistent hyponatremia (124 mmol/L on the third day, 127 mmol/L on the tenth day, and 126 mmol/L on the 20th day after discharge), and the patient refused further treatment due to the absence of discomfort.

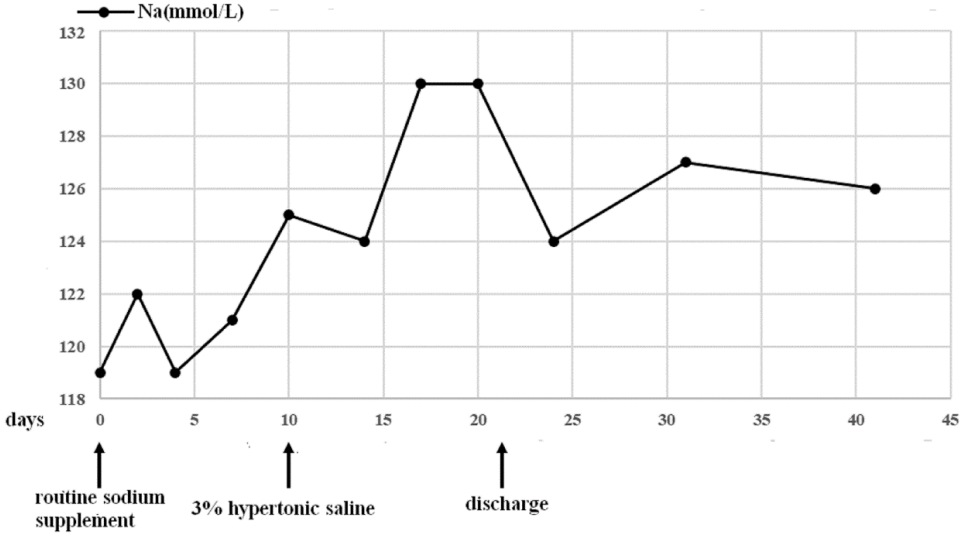


**Figure 1.** The sodium levels and therapeutic modalities in the patient after admission

## 3. Discussion

Although the patient was nearly 70 years old, he had several small blisters on the trunk, gait disturbance, and a negative VZV IgG antibody, which partly matched primary VZV infection [3]. We inquired about the epidemiology history in detail and the patient denied a medical history of chickenpox and admitted a close contact history of herpes zoster. We suspected that he may had a primary VZV infection.

VZV infection involving the CNS was traditionally thought to be seen primarily in immunocompromised patients [1-3]. However, no significant abnormalities were observed in cellular and humoral immunity, and no evidence of human immunodeficiency virus, tumors, or autoimmune diseases was found in this patient. Therefore we searched the cases of immunocompetent elderly patients (**Table 1**) [4-8], which revealed that there had been increasing numbers of this disease entity involving immunocompetent patients even without rash and typical symptoms. It is necessary for clinicians to pay more attention to VZV infection in CNS diseases.

**Table 1.** Summary of the characteristics of immunocompetent elderly patients

| Case | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Sex | Male | Male | Male | Female | Male | Male |
| Age (years) | 77 | 86 | 63 | 79 | 73 | 78 |
| Initial symptoms | Urinary retention, weakness, and paresthesia | Altered mental status, confusion, and right-sided facial swelling | Headache, dysphagia, hearing loss, and left-sided facial asymmetry | Progressive gait disturbance | Gait disturbance and urinary retention | Progressive paraparesis and sensory loss, malaise, and fevers |
| Rash appearance | 10 days prior to the onset | 3 days prior to the onset | No rash | 11 days prior to the onset | 5 days prior to the onset | No rash |
| Fever | No fever | No fever | No fever | Mild fever | No fever | No fever |
| Complication | Longitudinal transverse myelitis | Acute encephalitis | Cranial polyneuropathy | Myelitis | Myelitis | Extensive encephalomyelitis |
| Outcome | Sphincter dysfunction | Death | Left peripheral facial neuropathy and hearing loss | Numbness in the distal part of both lower limbs | Severe anorexia | Global areflexia, impaired proprioceptive and vibratory sensation |

Hyponatremia was rare with an unknown mechanism in VZV infection. In the reported cases (**Table 2**) [9-15], hyponatremia mostly occurred in immunodeficient individuals and was believed to be caused by inappropriate antidiuretic hormone secretion (SIADH). The mechanism of SIADH is not clear but could be postulated as stimulation of cranial nerve by VZV involvement leading to excess antidiuretic hormone secretion by posterior pituitary gland stimulation, or it may be related to antiviral drug (acyclovir) [9,10]. Besides, there were other patients who had SIADH due to their underlying diseases and corresponding medications [11-13]. However, our patient's condition was not consistent with SIADH by the consultation of an endocrinologist and was healthy before this illness. Moreover, the hyponatremia demonstrated persistent non-recovery and asymptomatic. This suggests that there are further complex mechanisms in CNS infection of VZV.

**Table 2.** Summary of the characteristics of hyponatremia in VZV infection

| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| Sex | Male | Male | Male | Female | Female | Male | Female | Male |
| Age (years) | 58 | 38 | 88 | 82 | 50 | 57 | 64 | 84 |
| Possible causes of immunodeficiency | Type 2 diabetes mellitus | Hypercholesterolemia and diabetes | Alzheimer's disease, ischemic heart disease, and hypertension | Type 2 diabetes mellitus, paroxysmal atrial fibrillation, hypertension, Hashimoto's thyroiditis, and anxious syndrome | Autologous stem cell transplantation for acute myeloid leukemia | Allogeneic peripheral blood stem cell transplantation for chronic myeloid leukemia | Waldenström macroglobulinemia with a treatment of fludarabine, cyclophosphamide, and rituximab | Unmentioned |
| Initial symptoms | Painful skin eruptions | Fever, headache, pain around skin eruptions, and discomfort of eyes | Acute abdominal pain | Mental confusion | Severe epigastric pain and repeated vomiting | Severe abdominal pain accompanied by nausea, vomiting, and constipation | Abdominal pain and absolute constipation | Acute onset unsteadiness, confusion, and bizarre behavior |
| Rash appearance | With the onset | With the onset | 3 days prior to the onset | 2 days prior to the onset | 7 days after onset | 9 days after onset | 16 days after onset | No rash |
| Serum sodium level at admission | 114 mmol/L | 116 mmol/L | 105 mmol/L | 105 mmol/L | 123 mmol/L | 120 mmol/L | 119 mmol/L | 127 mmol/L |
| Severity of VZV infection | Complicated with corneal erosions, ophthalmoplegia, and post-herpetic neuralgia | Complicated with corneal erosions and post-herpetic neuralgia | Unmentioned | Localized herpes zoster infection | Complicated with visceral disseminated VZV infection | Unmentioned | Complicated with visceral disseminated VZV infection | Unmentioned |

## 4. Conclusion

CNS diseases caused by VZV could be atypical and occur in immunocompromised populations, which requires increasing attention of clinical physicians. The association between VZV and hyponatremia needs further investigation to improve prognosis and reduce complications.

## Disclosure statement

The authors declare no conflict of interest.

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