



# First case report of pulmonary embolism with Zoster Sine Herpete

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## ABSTRACT

**Background:** Varicella-Zoster Virus (VZV) infection is known to cause coagulation abnormalities leading to pulmonary embolism and ischemic strokes. The incidence of vascular and thrombotic complications with Zoster Sine Herpete has been reported very infrequently in the medical literature.

**Case presentation:** A 32-year-old man with no significant past medical history presented to Emergency Room with right-sided facial weakness and headache. We saw no rash on physical examination. A sub-segmental pulmonary embolus was found on C.T. angiography of the chest. VZV was detected on Lumbar Puncture studies. The patient responded well to anti-viral treatment and was discharged home without any complications.

**Conclusion:** The suspicion of thrombo-embolic complications should be high with Zoster Sine Herpete. Screening for coagulopathies and timely initiation of anticoagulation should be carried out in appropriate clinical settings.

## 1. Introduction

Varicella-zoster virus (VZV) is a DNA virus from the Herpesvirus family responsible for the primary varicella infection, informally known as “chickenpox.” The virus persists latently in the spinal and cranial nerve ganglia, and it may reactivate to cause a herpes zoster infection, also known as shingles [1]. When the VZV affects the geniculate ganglion (CN VII), a neurological disorder known as Ramsay Hunt Syndrome may occur [2]. The clinical presentations seen in patients with this syndrome are unilateral facial palsy and vesicular rash in either external auditory canal, tympanic membrane, ipsilateral anterior two-thirds of the tongue, or hard palate. However, when the VZV reactivates, producing radicular pain without a rash, the neurological disorder is known as Zoster Sine Herpete.

In clinical studies, vasculopathy, secondary bacterial infections, pyogenic arthritis, osteomyelitis, orbital cellulitis, and central nervous system infections including meningitis, meningoencephalitis, meningoradiculitis, and cerebellitis have been associated with VZV reactivation [3]. Thrombosis is an atypical complication of VZV seen in adults, and this occurs due to the extensive endothelial damage in various organs caused by the virus [4]. A few thrombosis cases of the cortical venous sinus or deep veins of the lower extremities in adults

have been reported following a VZV infection [5,6]. However, there have been only five reported cases of symptomatic acute pulmonary embolism following a VZV infection or reactivation accompanied by a rash [7–9]. We report the first case of a patient with an asymptomatic acute pulmonary embolism associated with Zoster Sine Herpete.

A 32-year-old caucasian male with no significant past medical history presented to the emergency room with a four-day history of right-sided facial weakness. The weakness was associated with headaches. One week before this event, the patient experienced right-sided earache, sore throat, and neck pain. In the emergency department (E.D.), we received the patient vitally stable (temperature of 36.5 C, heart rate of 82 beats per minute, blood pressure of 134/80 mmHg, respiratory rate of 18 breaths per minute, SpO<sub>2</sub> of 97%). Physical examination revealed tenderness to palpation on the right preauricular region and angle of the mandible, absent furrows on the right side of the forehead, incomplete right eye closure at the effort, and asymmetric mouth at maximum effort (House-Brackman scale IV). Notably, the external auditory meatus did not exhibit a rash, and otoscopic examination by ENT exhibited an erythematous and non-bulging tympanic membrane with no vesicles.

C.T. scan of the temporal bone revealed right mastoid air cells showing changes consistent with possible infection or inflammation (Fig. 1).

A lumbar puncture was performed for concern of varicella infection

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**Abbreviations**

VZV	Varicella Zoster Virus
MRV	Magnetic resonance venography
CT	computerized tomography
DRVVT	Dilute Russell viper venom time (DRVVT) screen ratio

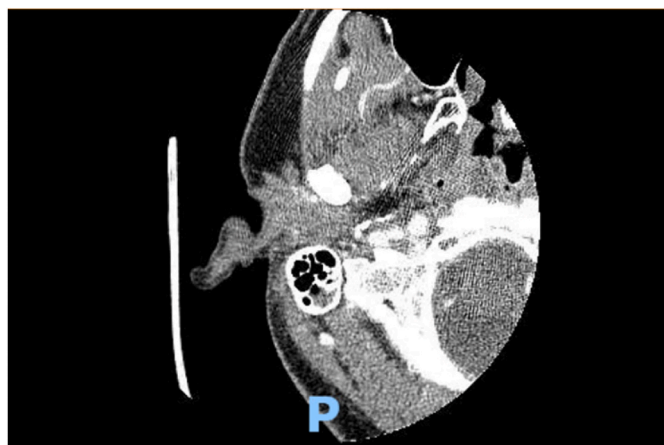


Fig. 1. Opacification of mastoid air cells on C.T. head.

and to rule out CNS infection. Dexamethasone and valacyclovir were started. MRI of the head was performed to characterize further the inflammatory changes found on the C.T. scan. It revealed enhancement involving the labyrinthine and the anterior genu of the right facial nerve, right glossopharyngeal nerve, and mild thickening/enhancement of the pituitary infundibulum. (Fig. 2). These findings were nonspecific for granulomatous diseases such as neurosarcoid, tuberculosis, lymphoproliferative disease, or atypical infections. Relevant workup was sent. The headache improved, but the patient complained of chest pain on hospital day 3. C.T. chest with IV contrast was obtained, and a sub-



Fig. 2. Enhancement of right-sided seventh and ninth nerve and pituitary infundibulum.

segmental pulmonary embolus (P.E.) in the anterior segment of the right lower lobe was reported (Fig. 3). Echocardiography and duplex scan of the lower extremities were unremarkable. MRV of the brain with and without contrast was negative for venous sinus thrombosis. Cerebrospinal fluid (CSF) PCR analysis was positive for Varicella zoster virus (Table 1 and 2). Varicella-Zoster Antibodies (IgG and IgM) were also elevated. Diagnosis of Zoster Sine Herpete was confirmed.

Anticoagulation therapy with low molecular weight heparin 50mg twice a day was initiated. Antiviral was switch to IV Acyclovir, and steroids were given. Coagulation analysis for Anti-cardiolipin antibody, Silica Clotting Time Interpretation and Dilute Russell viper venom time (DRVVT) screen ratio were negative. The patient successfully responded to therapy with the residual moderate facial dysfunction (House-Brackman scale III) and was discharged home on the 7th day of hospitalization with apixaban and valacyclovir for 14 more days. The patient was reported doing well on telehealth follow-up 4 weeks later.

**2. Discussion and conclusion**

The clinical presentation and complications from VZV reactivation can be atypical and have been documented well in clinical literature [10, 11]. The radicular pain arising from VZV's reactivation in the absence of the characteristic rash, otherwise known as Zoster Sine Herpete, is well known [10]. The absence of rash in ZSH is attributed to modifying the body's immune response culminating in the containment of reactivated VZV in neuronal ganglia and prevention of its spread to the skin. The severity of postherpetic pain is stated to be greater in Zoster Sine Herpete as compared to VZV with shingles [12]. The retrospective diagnosis of VZV reactivation from a myriad of clinical presentations becomes daunting in the absence of rash. A strong clinical suspicion and VZV DNA detection in CSF studies and serum/CSF IgG and IgM are diagnostic [13–15].

There is considerable evidence of vasculopathy and hypercoagulable states with concurrent VZV infection leading to focal motor and sensory deficits. Thrombi are formed, which embolize and end up in ischemic strokes and pulmonary embolism [5,16–19]. The vasculitis and clotting abnormalities secondary to zoster-induced protein S deficiency and generation of anti-protein S-autoantibodies are attributed to viral cytotoxicity, long-standing inflammation, and underlying Factor V mutation [7,20,21].

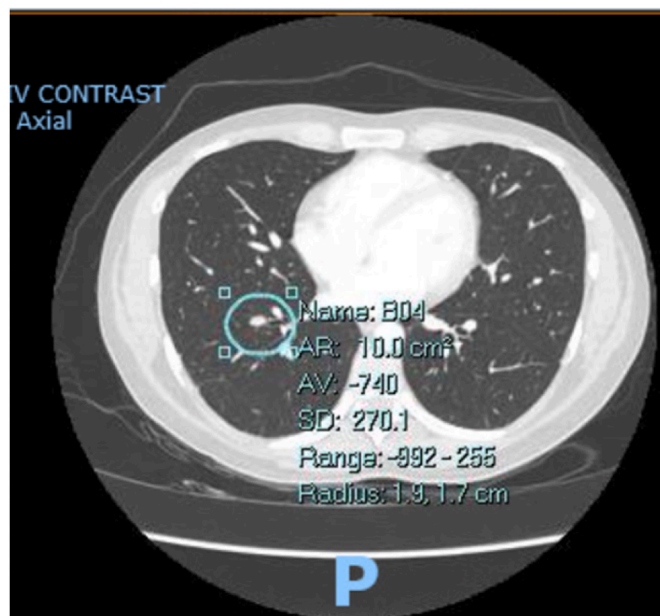


Fig. 3. CTA chest showing right lower lobe pulmonary embolus.

**Table 1**  
CSF studies.

CSF Findings	Tube 1
CSF Color	No color
CSF monocytes/macrophages (15–45%)	10%
CSF segmented neutrophils (0–6%)	0%
Total nucleated cells, CSF (0–5 u/L)	60 u/L
CSF appearance	Clear
CSF lymphocytes (40–80%)	90%
RBC count spinal fluid (0–0 u/L)	100
LDH, CSF	28 U/L
Protein, CSF (15–45mg/dL)	66
Glucose, CSF (45–75 mg/dL)	75
IgG CSF	12
CF Albumin	38
IgG/Albumin Ratio CSF	0.27
IgG Index	1.2
IgG Synthesis	33.5
Quantitative IgA	568
Quantitative IgM	49

**Table 2**  
CSF PCR studies.

CSF PCR Result	Positive for VZV
COVID-19 IgG Antibody Index	Negative
Varicella IgG antibody (Index)	>4000
Varicella IgG interpretation	Positive
Varicella-Zoster IgM (0.00–0.90)	1.48
West Nile IgM	Negative
West Nile IgG	Negative
West Nile Virus by PCR	Not detected
CSF cultures	No growth
HSV ½ PCR	Negative
E. coli K1	Negative
<i>Streptococcus agalactiae</i>	Negative
<i>Streptococcus pneumoniae</i>	Negative
<i>Cytomegalovirus</i>	Negative
<i>Human Herpes Virus 6</i>	Negative
<i>Human parechovirus</i>	Negative
<i>Cryptococcus neoformans/gattii</i>	Negative
Lyme PCR, Result	Negative
<i>Haemophilus influenzae</i>	Negative
<i>Listeria Monocytogenes</i>	Negative
<i>Neisseria Meningitidis</i>	Negative
<i>Human parechovirus</i>	Negative

The majority of the thrombotic complications after VZV reactivation were reported in the pediatric population [22]. Pulmonary embolism has been reported after Varicella infection in an adult with a transient elevation of anticardiolipin antibody [8]. A case of lateral sinus thrombosis has been reported in literature associated with Zoster Sine Herpete, but MRV brain was negative in our patient [23]. This case is unusual as the pulmonary embolism was seen in the absence of a zoster and is one of the first cases of pulmonary embolism in Zoster Sine Herpete. The hypercoagulable workup done was negative. The pulmonary embolism was not accompanied by evidence of right heart strain. Short and long-term thrombotic complications of VZV should be kept in mind, especially in the absence of rash. Vague and nonspecific complaints like chest pain, headache, or altered mental status can be due to underlying emboli. Prompt anticoagulation can prevent a potentially fatal outcome from thrombus formation in the cardiopulmonary and cerebral circulation.

## Declarations

### 2.1. Ethics approval and consent to participate

The case report and manuscript were reviewed with Research Department and Ethics Committee. No experimental intervention was

performed, and any specification of guidelines, legislations, or permissions were not required.

### 2.2. Consent for publication

Patient was contacted during the hospital stay and after discharge. Consent was obtained for the use of patient data, images, CSF studies blood work for the publication of the case for purely educational and research purposes to which the patient and family agreed.

### 2.3. Availability of data and materials

Patient-specific data was obtained from hospital electronic medical records of Northwell Health, and patient identifying information was cropped. Individual images are being sent.

## Competing interests

No competing financial or personal interests are involved for all the authors.

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## Author's contributions

- Manuscript written and data obtained by S.S. M.G. and A.J. (1).
- Proofreading and literature review done by N.M. and A.J. (2).

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