Case Report

Varicella zoster virus associated-polyradiculoneuritis in an elderly woman: A new subtype of varicella zoster virus neuropathy

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Abstract: An 82-year-old Japanese woman without underlying disease was admitted to our hospital 3 days after she noticed lower-limb weakness. At presentation, she had lower-leg motor paralysis with mild upper-limb paresis and left Ramsay Hunt syndrome. Cerebrospinal fluid (CSF) findings revealed moderate pleocytosis. A polymerase chain reaction for varicella zoster virus (VZV) DNA in CSF was positive. MRI using 3D Nerve-VIEW (Philips) and contrast T1 images showed high-intensity lesions on the L2–5 and S1–2 spinal roots. A new subtype of VZV-associated polyradiculoneuritis was diagnosed in this patient. We provide the case details and compare three similar reported cases.

Key words: herpes zoster, varicella zoster virus, polyradiculoneuritis, Ramsay Hunt syndrome, meningitis

Introduction

Varicella zoster virus (VZV) causes chickenpox at the primary infection, then becomes latent in the spinal dorsal root ganglia and can reactivate with aging, immunosuppression, stress, and other factors, occurring as herpes zoster (HZ) at one or two skin segments. Peripheral neuropathy associated with HZ includes post-herpetic neuralgia, Ramsay Hunt syndrome, Guillain–Barré syndrome (GBS), and segmental motor paralysis. We describe the case of an elderly woman without underlying disease who developed GBS-like acute lower-limb paralysis, followed 3 days later by Ramsay Hunt syndrome.

There have been only 2–3 reported cases of VZV-associated polyradiculoneuritis unrelated to the HZ dermatome, and the pathophysiology of VZV radiculopathy has not been clarified. We compare our new case with three similar reported cases with main lesions in spinal nerve roots unrelated to the HZ dermatome, and discuss the differential diagnosis from GBS.

Case Report

The patient was an 82-year-old woman who had had chickenpox infection in childhood, and dyslipidemia. She lived alone but was independent in daily life. She had no history of vaccination with chickenpox live vaccine. She noticed weakness in her lower limbs in February 2021. The following day, she was found crouching in her house, and was transferred to a nearby hospital. She experienced a 38°C fever for 2–3 days. The day after her admission, a HZ rash appeared in the left auricle, together with left peripheral facial palsy, and the patient was transferred to our hospital with suspected GBS (Fig. 1).

On admission, her blood pressure was 124/66 mmHg, pulse 100/min., and body temperature 36.9°C. HZ rash on the left auricle and ear canal was found with neuralgia and left headache. Neurologically, Japan Coma Scale 1–2, left peripheral facial nerve palsy, and left sensory hearing loss were observed without vestibular symptoms, and mild nuchal stiffness was positive. The patient was unable to walk, and both deep upper-limb tendon reflexes were decreased, while lower-limb reflexes disappeared on both sides without pathological reflexes. A

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manual muscle test showed upper limbs 4+ on both sides; lower trunk 3; iliopsoas muscle right 3, left 4; quadriceps right 3, left 4; biceps femoris, tibialis anterior muscle and triceps surae 4 on both sides. Although sensory impairment including radicular pain was not apparent in the four limbs, paresthesia was observed in the distal regions of both lower limbs. There were no urinary disorder or cerebellar symptoms.

Laboratory findings were as follows. White blood cell count 10,330/μl, C-reactive protein (CRP) 0.28 mg/dl; interleukin-2, C3, C4 and lymphocyte proliferation ability test results were normal. Anti-nuclear antibody , anti-SS-A and anti-SS-B antibodies, anti-GQ1b and anti-GM1 antibodies were all negative. Serum VZV enzyme antibody (by an enzyme immunoassay [EIA]) IgG was >128 (reference value <2.0), EIA IgM was 1.84 (ref. value <0.80). Cerebrospinal fluid (CSF) findings showed normal pressure but revealed increased lymphocytes (143 cells/μl, all mononuclear cells, normal value <5), protein content (199 mg/dl, normal value 10–40 mg) and myelin basic protein (MBP, 497 pg/ml, normal value <102). The polymerase chain reaction (PCR) result for VZV DNA in CSF was 7.3×10⁴ copies, and VZV EIA IgG was >12.8(+) >12.8(+) 8.95(+) and VZV IgM was 0.63(+) 1.14(+) 0.22(+) (Fig. 1). Cerebrospinal fluid (CSF) VZV DNA PCR (copy)

<table>
<thead>
<tr>
<th>CSF VZV DNA PCR (copy)</th>
<th>EIA IgG</th>
<th>EIA IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>&gt;12.8(+)</td>
<td>8.95(+)</td>
</tr>
<tr>
<td>VZV</td>
<td>&lt;1.0×10⁴</td>
<td>&lt;1.0×10⁴</td>
</tr>
<tr>
<td>EIA IgG</td>
<td>&gt;12.8(+)</td>
<td>&gt;12.8(+)</td>
</tr>
<tr>
<td>EIA IgM</td>
<td>0.63(+)</td>
<td>1.14(+)</td>
</tr>
<tr>
<td>CSF</td>
<td>0.63(+)</td>
<td>1.14(+)</td>
</tr>
<tr>
<td>CSF</td>
<td>0.22(+)</td>
<td>0.22(+)</td>
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</table>

An 82-year-old Japanese female developed lower trunk weakness and right-dominant motor paralysis in her lower legs, followed by left Ramsay Hunt syndrome and meningitis. CSF findings revealed moderate pleocytosis and increased MBP, and a PCR for VZV DNA in CSF was positive. ACV: acyclovir, CSF: cerebrospinal fluid, CRP: C-reactive protein, EIA: enzyme immunoassay, HZ: herpes zoster, IVD: intravenous drip, MBP: myelin basic protein, ND: not done, PCR: polymerase chain reaction, PSL: prednisolone, VZV: varicella zoster virus.

MRI using 3D Nerve-VIEW imaging (Philips, Amsterdam, the Netherlands) showed high-intensity lesions on the L2–4 spinal roots, and contrast axial T₁WI exhibited enhancement at L3–5 and S1–2 roots (Fig. 2). There were no abnormalities in brain MRI/MRA or spinal cord MRI. Nerve conduction and F-wave findings are listed in Table 1. On day 8 of illness, the nerve conduction velocity and F waves of the patient’s upper limbs was normal. The motor conduction velocity of the left tibial nerve decreased slightly to 39 m/s, and the M-wave of the distal and proximal parts of the right peroneal nerve decreased to 630 and 690 μV, respectively. The amplitude of the sensory nerve action potential and conduction velocity of both sural nerves were normal values. The right peroneal nerve F-wave was not detected on days 8 and 32, whereas the left peroneal nerve F-wave was 38%; after 6 months the frequency of the right peroneal nerve F-wave improved to 43%. The clinical course and lumbar MRI studies primarily suggested several (5–6) lumbar ganglia and nerve root impairments.

We treated the patient for 3 weeks with intravenous acyclovir 750 mg/day and oral prednisolone administration, which was gradually reduced from 60 mg/day. After 2 weeks, the patient’s lower-limb muscle strength improved, and she was able to walk a few meters with assistance; 2 months later, she was transferred to a rehabilitation hospital.
Fig. 2 MRI findings in lumbar nerve roots.
A: On day 13 of illness, lumbar root coronary MRI using 3D Nerve-VIEW imaging (Philips) showed high-intensity lesions on both sides at L2–4 spinal roots (arrows); B, C: Gd-enhanced T₁WI with fat suppression axial images exhibited enhancement on both sides at the L3–4 nerve roots (arrows). MRI images (3 T, 3D Nerve-VIEW; TR 2,400.0 ms, TE 81.4 ms, T₁WI; mDIXON TR18, 12.6).

Table 1 Peroneal and tibial motor nerve conduction and F-wave studies.

<table>
<thead>
<tr>
<th></th>
<th>M-wave distal/prox AMP (mV)</th>
<th>DL (ms)</th>
<th>MCV (m/s)</th>
<th>Minimum Latency of F-wave (ms)</th>
<th>F-wave Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rt-peroneal nerve</td>
<td>630/690 uV (N &gt; 2)</td>
<td>4.1</td>
<td>41.3</td>
<td>NR</td>
<td>0</td>
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<tr>
<td>lt-peroneal</td>
<td>2.5/2.4</td>
<td>4.0</td>
<td>45</td>
<td>45.7</td>
<td>38</td>
</tr>
<tr>
<td>rt-tibial</td>
<td>12.1/9.9 (N &gt; 5)</td>
<td>4.0</td>
<td>42 (N40–60)</td>
<td>44.1 (N &lt; 45.6)</td>
<td>100 (N = 100)</td>
</tr>
<tr>
<td>lt-tibial</td>
<td>12.0/12.0</td>
<td>3.9</td>
<td>39</td>
<td>43.9</td>
<td>100</td>
</tr>
</tbody>
</table>

A, Day 8 of illness

B, Day 32 of illness

<table>
<thead>
<tr>
<th></th>
<th>M-wave distal/prox AMP (mV)</th>
<th>DL (ms)</th>
<th>MCV (m/s)</th>
<th>Minimum Latency of F-wave (ms)</th>
<th>F-wave Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rt-peroneal nerve</td>
<td>2.2/1.7 (N &gt; 2)</td>
<td>4.3</td>
<td>41 (N40–60)</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>lt-peroneal</td>
<td>3.2/2.8</td>
<td>3.7</td>
<td>40</td>
<td>45.7</td>
<td>38</td>
</tr>
<tr>
<td>rt-tibial</td>
<td>14.6/12.2 (N &gt; 5)</td>
<td>4.8</td>
<td>41 (N40–60)</td>
<td>44.1 (N &lt; 45.6)</td>
<td>100 (N = 100)</td>
</tr>
<tr>
<td>lt-tibial</td>
<td>16.4/13.3</td>
<td>3.8</td>
<td>42</td>
<td>43.9</td>
<td>100</td>
</tr>
</tbody>
</table>

*The M-wave amplitude was measured from the baseline to the negative peak. **The normal value of the minimum F-wave latency of the tibial nerve was adopted for the patient’s height of 149 cm from the reference. N: normal value or reference value. DL: distal latency, NR: non-recordable, MCV: motor conduction velocity.
An 82-year-old woman experienced an acute onset of difficulty sitting and right-dominant proximal lower-limb paralysis, followed by left Ramsay Hunt syndrome. Mild upper-limb paresis was also observed when she was transferred to our hospital, and GBS following an HZ rash should be excluded for the differential diagnosis. Islam et al. reviewed 15 reported cases of GBS following HZ rash, and found that the GBS was caused by an autoimmune mechanism after an average interval of 10 days; no CSF pleocytosis occurred in these cases. We thus diagnosed the patient VZV-associated polyradiculoneuritis, not GBS.

Since 2009, three similar cases of VZV-associated polyradiculoneuritis have been described; one by Cortese et al.\(^4\), in addition to our two previously reported cases of VZV-associated ascending quadriplegia and polyradiculoneuritis with disseminated HZ\(^3\). We compare the present case with these three cases (Table 2).

Cortese et al.\(^4\) reported the case of a 79-year-old man with flaccid paralysis of the lower limbs without HZ rash. CSF pleocytosis and a VZV DNA PCR positive result were detected in his CSF, and MRI findings showed cauda equina radiculopathy. We then encountered a 76-year-old female\(^6\) presenting with ascending quadriplegia, followed by an HZ rash on the right arm with mild meningitis; cervical and lumbar MRI revealed high-intensity lesions at the C7–Th1 and L2–S root regions. We also reported the case of a 34-year-old male\(^6\) who developed right-dominant four-limb paralysis following a disseminated HZ rash. MRI exhibited high-intensity lesions at C4–Th1 and L3–4 roots with contrast enhancements.

These cases shared the characteristic of main lesions in the spinal nerve root, and our present patient’s case was very similar to that described by Cortese et al. with lower limb paralysis and VZV PCR positivity in CSF. However, in our present’s case, lumbar MRI using 3D Nerve-VIEW imaging clearly revealed lumbar nerve root lesions, and together the patient’s findings suggested VZV-associated primary polyradiculopathy. In addition, her case was characterized by left Ramsay Hunt syndrome with an auricle HZ rash and meningitis occurring 3 days later. Ramsay Hunt syndrome is caused by VZV spread via the CSF space from VZV lumbar radiculopathy. We also speculated that our present patient’s left geniculate ganglia were in simultaneously a state of VZV reactivation.

Discussion

Table 2 Summary of the four patients with VZV-associated polyradiculoneuritis.

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age/sex</th>
<th>Underlying disease</th>
<th>HZ rash and motor paralysis</th>
<th>Neurologic symptoms</th>
<th>CSF findings</th>
<th>Nerve conduction &amp; F-wave studies</th>
<th>Spinal MRI including *3D Nerve-VIEW (Philips)</th>
</tr>
</thead>
</table>
| 1       | 79/male | Cortese et al. 2009\(^4\) | Zoster sine herpete          | Flaccid paraplegia, Meningitis | 1. ND  
2. 224/μl  
3. 374 mg/dl  
4. 35 mg/dl  
5. PCR (+) | Multifocal demyelinating neuropathy | Cauda nerve: high-intensity with enhancements |
| 2       | 76/female | Interstitial pneumonia  
Shoji et al. 2019\(^6\) | Right-forearm at same time after quadriplegia | Ascending quadriplegia, Neuralgia | 1. 140 cm  
2. 21/μl  
3. 29 mg/dl  
4. 52 mg/dl  
5. PCR (−)  
IgM Ab (+) | Right-dominant demyelinating polyradiculoneuropathy | C5–C8, L4–S2: spinal nerve root: high-intensity with enhancements |
| 3       | 34/male | Stress  
Shoji et al. 2020\(^6\) | Motor paralysis following disseminated HZ rash | Right-dominant quadriplegia, Neuralgia | 1. ND  
2. 32/μl  
3. 59 mg/dl  
4. 50 mg/dl  
5. PCR (−) | MCV of left tibial nerve decreased to 39 m/sec.  
No F-waves were detected at right peroneal nerve | *C4–Th1, L2–5: spinal nerve root: high-intensity with enhancements |
| 4       | Present Case  
82/female | | Left-auricle 3 days after paraplegia with upper limb paresis | Right-dominant paraplegia, Left Ramsay Hunt syndrome, Meningitis | 1. 110 cm  
2. 143/μl  
3. 32 mg/dl  
4. 199 mg/dl  
5. PCR (+) | M-wave amplitude of right peroneal nerve was decreased, no F-waves were detected at right peroneal nerve | *L2–5, S1–2: nerve root: high-intensity with enhancements |

*3D Nerve-VIEW (Philips) was used. Ab: antibody, CSF: cerebrospinal fluid, HZ: herpes zoster, MCV: motor conduction velocity, PCR: polymerase chain reaction, VZV: varicella zoster virus.
Although we observed increased MBP values in her CSF, myelitis was ruled out by neurological symptoms and spinal MRI findings. Serial changes in MBP value might therefore reflect subclinical radiculomyelopathy.

However, there is a report of an HZ duplex case of right Ramsay Hunt syndrome, followed by left upper-limb paresis\(^1\). Another patient with cervical HZ developed multiple cranial neuropathies with left upper-limb paresis\(^2\). These two patients were diagnosed as having multiple cranial neuropathies due mainly to VZV reactivation at the cranial ganglia, whereas our present patient and the three similar reported cases were classified as VZV-associated polyradiculoneuritis in four limbs or lower limbs. The pathophysiology of spinal ganglia and root impairment related to VZV reactivation remain to be elucidated. Further accumulation of cases of VZV neuropathies unrelated to the HZ dermatome is expected.

In summary, we treated an 82-year-old Japanese woman who developed right-predominant lower-limb paralysis with mild upper-limb paresis, followed by left Ramsay Hunt syndrome and meningitis. We diagnosed VZV-associated polyradiculoneuritis based on the patient’s clinical course, VZV DNA PCR positivity in CSF and MRI findings. We speculate that the present case and three similar reported cases may be a new subtype of VZV peripheral neuropathy.

※The authors declare there is no conflict of interest relevant to this article.

References

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