Case Report | Palliative Medicine and Palliative Care for Serious or Advanced Diseases

Femoral artery occlusion induced vasculopathy following herpes zoster: a case report

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Background: Reactivation of the varicella zoster virus (VZV) results in herpes zoster (HZ), which is a painful unilateral rash with a typical dermatomal distribution. HZ may be followed by postherpetic neuralgia (PHN), vasculopathy, myelopathy, retinal necrosis, and cerebellitis. Vasculopathy can cause ischemic stroke, aneurysms, arterial dissection, transient ischemic attack, and rarely, peripheral arterial disease (PAD). The possible mechanism is that the VZV travels to the arteries through the sensory ganglia, leading to inflammation and pathological vascular remodeling, which result in vasculopathy.

Case Description: Here, we describe a rare case of femoral artery occlusion induced vasculopathy 5 years after HZ. A 65-year-old woman visited our pain clinic with persistent pain following HZ that occurred 3 months earlier. She had several rash scars on the right thigh along with a continuous throbbing, shooting, and sharp pain. The patient was diagnosed with PHN and prescribed with medications that relieved the leg pain. The symptoms remained stationary for almost 5 years. She presented again with complaints of a paroxysmal tingling sensation in the right thigh and claudication due to increased pain, which had begun 6 months prior. She reported leg pain after walking for 10 minutes. Lumbar spine magnetic resonance imaging (MRI) revealed foraminal stenosis at the level of right L2, with no abnormality below L2. Subsequently, the patient was evaluated for vascular diseases. Lower extremity ultrasonography and computed tomography (CT) angiography revealed stenosis and thrombotic occlusions in the right superficial femoral and tibial arteries as well as the left middle femoral and tibial arteries. Surgical revascularization via percutaneous angioplasty was performed bilaterally. The leg pain was relieved after the procedure and the claudication improved.

Conclusions: Peripheral artery occlusion is a rare phenomenon following HZ. In cases involving changes in HZ symptoms, further evaluation is required for potential vasculopathy.

Keywords: Femoral; herpes zoster (HZ); occlusion; pain; case report

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Introduction

Varicella zoster virus (VZV) is an alpha herpesvirus with a double-stranded DNA genome (1). Its main targets are T lymphocytes, epithelial cells, and ganglia (1). Primary VZV infection causes varicella (chickenpox), and VZV becomes latent in the sensory ganglion of the cranial nerves or dorsal root ganglion of the spinal cord (2). VZV reactivation results in herpes zoster (HZ), which is a painful unilateral rash with a typical dermatomal distribution. HZ may be followed by postherpetic neuralgia (PHN), vasculopathy, myelopathy, retinal necrosis, and cerebellitis (3). PHN is characterized by throbbing, stabbing, or burning pain persisting for more 3 months after the onset of the rash (2,4). Pain associated with HZ and PHN can be worse than labor pain, post-surgical pain, arthritis, spinal cord injury, or chronic cancer pain (5). It adversely affects the daily lives of patients due to limited physical function and increased emotional stress, which reduce patients' quality of life (5). Vasculopathy following VZV infection results from productive viral infection within the cerebral and extracranial arteries in a unifocal or multifocal area (3,6). Vasculopathy can cause ischemic stroke, aneurysm, arterial dissection, myocardial infarction, transient ischemic attack, and rarely, peripheral arterial disease (PAD) (7-9). The possible mechanism involves the VZV travelling to the arteries through the sensory ganglia, leading to inflammation and pathological vascular remodeling, which causes vasculopathy. Increased sympathetic tone and blood pressure, as well as an altered immunological status, may contribute to vasculopathy (8). VZV vasculopathy was first reported in 1896 by evaluating cases of VZV infection that were temporally associated with stroke, especially when HZ occurred in the ophthalmic division of the trigeminal nerve. Over the past few decades, the spectrum of VZV vasculopathy has expanded to include extracranial lesions (6). This article describes a rare case of vasculopathy due to femoral artery occlusion that occurred 5 years after HZ infection. We present this case in accordance with the CARE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-24-20/rc).

Highlight box

Key findings

- We encountered a rare case of vasculopathy due to femoral artery occlusion 5 years after herpes zoster infection.

What is known and what is new?

- Varicella zoster virus reactivation may result in vasculopathy with variable clinical presentation. However, peripheral artery occlusion is rare phenomenon following herpes zoster.
- Our patient showed stenosis and thrombotic occlusion of peripheral artery of both legs and it was more severe and extensive in the same dermatome with herpes zoster.

What is the implication, and what should change now?

- In case with changes in the herpes zoster symptoms, further evaluation is needed for potential vasculopathy.

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). The study was approved by the Institutional Review Board of Samsung Medical Center (SMC; No. 2023-09-131). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of written consent is available for review by the editorial office of this journal. A database from a university pain clinic was retrospectively reviewed for the period between November 2018 and August 2023 (*Figure 1*).

A 65-year-old woman was referred to our pain clinic from the department of internal medicine due to persistent pain following HZ. Three months prior, she had developed multiple skin rashes on the right thigh with severe pain. She visited the emergency department, where she intravenously received famciclovir 500 mg along with analgesics. The rash gradually improved; however, she experienced throbbing, shooting, and sharp pain, which was rated as 8 on the numerical rate scale (NRS, 0= no pain, 10= worst pain imaginable). Allodynia, itching, and numbness were observed in the right thigh. She had a history of left breast cancer, with a history of smoking five cigarettes per day for 3 years, and had stopped smoking 10 years ago. The patient was diagnosed with PHN and prescribed with opioids, which relieved the pain (NRS 2–4). The symptoms remained stationary for almost 5 years. She presented again with complaints of a paroxysmal tingling sensation in the right thigh and claudication due to increased pain (NRS 6), which had begun 6 months prior. She reported leg pain after walking for 10 minutes. No rash was observed in the legs. Lumbar spine MRI revealed foraminal stenosis at the level of right L2, with no abnormality below L2. The ankle-brachial index (ABI) was 0.52 in the right and 0.57 in the left. Lower extremity ultrasonography and

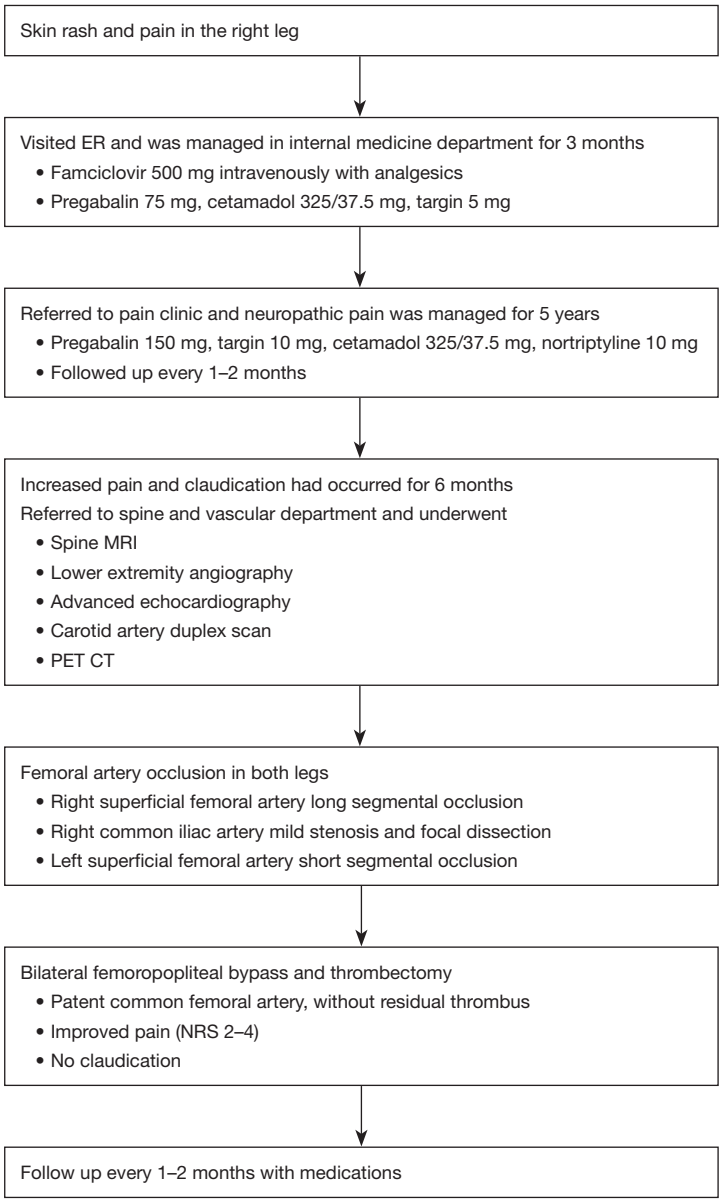

Figure 1 Case flow diagram. ER, emergency room; MRI, magnetic resonance imaging; PET, positron emission tomography; CT, computed tomography; NRS, numerical rate scale.

computed tomography (CT) angiography revealed stenosis and thrombotic occlusions in the right superficial femoral and tibial arteries as well as the left middle femoral and tibial arteries (*Figure 2A*). Her lipid profile was as follows: triglyceride, 199 mg/dL; high-density lipoprotein (HDL), 46 mg/dL; low-density lipoprotein (LDL), 132 mg/dL; cholesterol, 221 mg/dL. The blood pressure was mostly maintained within the normal range [mean blood pressure (BP): 63–67 mmHg]; however, when the pain severity increased, the blood pressure was increased temporally (mean BP: 72–79 mmHg). In the duplex scan of the carotid artery, <50% stenosis in the right carotid bifurcation, plaque in the right internal carotid artery, and left carotid bifurcation were observed. Positron emission tomography (PET) CT did not reveal metastasis and no recurrence of breast cancer was observed following breast cancer surgery. Surgical revascularization via percutaneous angioplasty was performed bilaterally. Pain was relieved after the

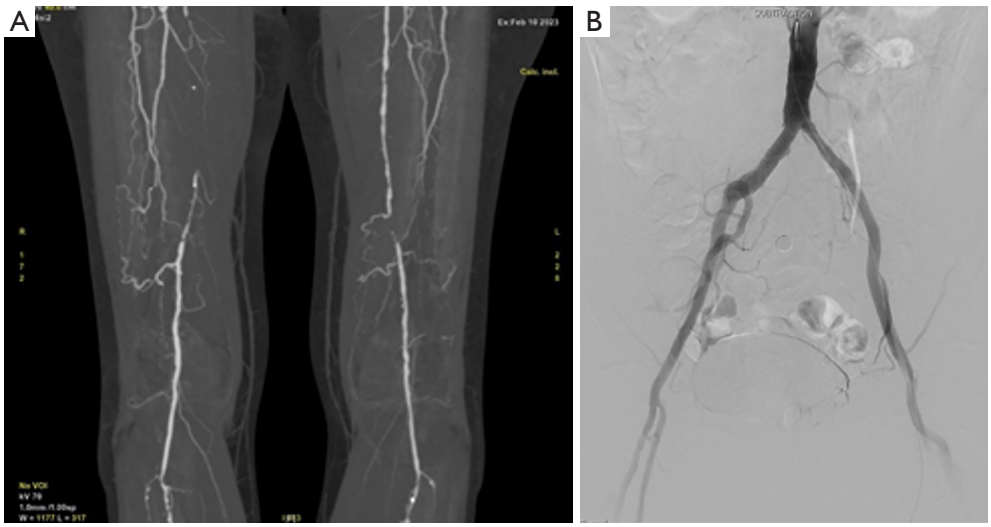

Figure 2 CT angiography. (A) Occlusions in the bilateral superficial femoral arteries; (B) arterial patency was confirmed after revascularization. CT, computed tomography.

procedure (NRS 2), with the claudication improving. The ABI increased to 0.84 in the right and 0.64 in the left leg. Follow-up ultrasonography and CT angiography showed no significant stenosis in the right superficial femoral artery and residual multifocal 40–50% stenosis with a triphasic waveform in the left superficial femoral artery (*Figure 2B*). The patient was followed-up with medications.

Discussion

Our patient developed vasculopathy due to femoral artery occlusion 5 years after HZ. We suspected that HZ may have been related to the peripheral arterial occlusion. VZV reactivation may cause vasculopathy with variable clinical presentation (10). There are several different mechanisms underlying VZV and vascular events (11,12). Reactivated VZV may travel centrally, causing infection in the arterial wall, which leads to inflammation, arterial weakening, and morphological changes, resulting in aneurysmal formation, and occlusion (1,9). There is a positive relationship of HZ or HZ ophthalmicus with cerebrovascular and cardiovascular events, which could involve VZV migration from the neurons to the cerebral and coronary vasculature, leading to vessel occlusion and ischemia (11,12). Acquired hypercoagulable state caused by an acquired protein S antibody may lead to thrombotic complications (13). Infection of cerebral arteries results in ischemic and hemorrhagic stroke, which is characterized by headache, mental status changes, and focal neurological deficits (1). A retrospective study on the risk of vascular events after HZ, which was conducted from 2007 to 2014 among adults in the United States, reported that HZ was associated with an increased risk of transient ischemic attacks and stroke (9). A clinical diagnosis of VZV vasculopathy is suspected in patients with a recent history of VZV or HZ who present transient ischemic attacks or stroke along with MRI abnormalities, especially at the gray-white matter junctions (3). The diagnostic test involves a lumbar puncture and cerebrospinal fluid (CSF) examination for the presence of anti-VZV antibodies and VZV DNA (6). Treatment comprises 10–15 mg/kg intravenous acyclovir for 14 days (6). However, there have been rare reported cases of peripheral vascular disease after HZ (14). Cases of delayed hemiparesis following primary VZV was reported; further, it was suggested that intense sympathetic stimulation combined with the production of systemic antibodies and antigen-antibody complexes might result in vasculopathy with thrombus formation (15). Cases of arterial thrombosis after HZ may involve the transient emergence of antiphospholipid antibodies, vasculitis, and atherosclerosis (16). In a case of occlusion of proximal radial artery at 2 weeks after HZ in the upper arm, peripheral artery thrombosis was diagnosed, which may have involved direct VZV transmission from the nerves outside the central nervous system (16). Our patient showed stenosis and thrombotic occlusion of the peripheral artery in both legs, which was more severe and extensive in the right side, which had a similar dermatome profile as HZ. Although we

diagnosed the patient with vasculopathy following HZ, the relationship between PAD and HZ could not be determined due to insufficient evidences.

PAD is characterized by any pathologic process that causes blood flow obstruction in the arteries (17,18). Atherosclerosis is the major pathophysiology of PAD (14). The risk factors for PAD include age, male sex, diabetes, hypertension, dyslipidemia, C-reactive protein, obesity, smoking, and renal insufficiency (17). Intermittent claudication is the hallmark of PAD and is characterized by fatigue, discomfort, cramping, or pain in the lower extremities that is caused by exercise and relieved within 10 minutes of rest (19). The ABI, which is the ratio of the highest systolic pressure in each leg to the brachial systolic pressure, is recommended for the diagnosis of PAD, with a sensitivity of 94–97% (19). The primary treatments for PAD include lifestyle modifications and medications (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, statins, and antiplatelet therapy). In lifestyle-limiting claudication showing an inadequate response to primary treatment, revascularization by bypass grafting, endarterectomy, or angioplasty with stenting may be considered (19). Lin *et al.* reported a higher risk of PAD in patients with HZ infection than in patients without HZ infection, which was attributed to two possible mechanisms (14). First, HZ can increase the level of several prothrombotic autoantibodies (13). Second, after reactivation of VZV in the ganglia, the infection spreads transaxonally to the arteries and causes pathological vascular remodeling, including disruption of the internal elastic lamina, intimal hyperplasia, and decreased smooth muscle cells in the medial layer (14). However, the exact time of PAD occurrence after HZ onset and the influence of antiviral treatment on PAD remain unclear. In our case, peripheral artery occlusion co-existed with PHN in the leg. However, it remains unclear whether PAD was a new development after HZ or whether previously existing PAD was aggravated after HZ since the interval between the onset of claudication and the HZ rash was 5 years; moreover, no CSF, coagulation, or virological analyses were performed to confirm VZV vasculopathy.

Conclusions

The co-occurrence of PAD and HZ at the same location is a rare phenomenon. Careful monitoring is required to identify vasculopathy in cases with changes in HZ symptoms.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-24-20/rc

Peer Review File: Available at https://apm.amegroups.com/article/view/10.21037/apm-24-20/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-24-20/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. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). The study was approved by the Institutional Review Board of Samsung Medical Center (SMC; No. 2023-09-131). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of written consent is available for review by the editorial office of this journal.

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