

## Case Report

### A Case of Neuralgic Amyotrophy in the Lower Extremity: A Possible Relationship with Herpes Zoster Virus Reactivation

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#### Abstract

An 82-year-old man was admitted to our hospital because of severe left lumbar pain that radiated down to the left thigh and paresis of the left lower extremity. Magnetic Resonance Imaging (MRI) revealed an extensive hyperintense signal on the left thigh and increased intensities of the cauda equine, nerve roots, and lumbosacral plexus. IgM antibodies for Herpes Zoster Viruses (HSV) were positive. We diagnosed as having Neuralgic Amyotrophy (NA), in which HSV reactivation is possibly related. We tried methylprednisolone pulse and intravenous immunoglobulin therapy followed by anti-herpes therapy. Thereafter, lumbar pain disappeared and muscle strength partially improved. Early diagnosis and treatment of NA using a detailed medical history together with appropriate imaging studies in selected patients are needed to improve the prognosis and avoid unnecessary surgery.

**Keywords:** Herpes zoster viruses; Magnetic resonance imaging; Neuralgic amyotrophy

#### Introduction

Neuralgic Amyotrophy (NA), also known as Personage-Turner syndrome, is a disease of the peripheral nervous system, characterized by sudden onset of severe neuropathic pain, usually in the upper unilateral extremity, followed a few days to weeks later by patchy

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**Citation:** Yoshioka K, Itohar T, Hayashi N, Yoshimura A (2016) A Case of Neuralgic Amyotrophy in the Lower Extremity: A Possible Relationship with Herpes Zoster Virus Reactivation. J Clin Stud Med Case Rep 3: 032.

**Received:** February 19, 2016; **Accepted:** April 11, 2016; **Published:** April 25, 2016

paresis with amyotrophy [1]. Although NA usually affects the brachial plexus, in rare cases it affects the lumbosacral plexus and causes paresis of the lower extremity [2,3]. The diagnosis of NA in the lower extremity is challenging because it is not well recognized by physicians [4], and the symptoms resemble those of lumbar diseases such as lumbar disc herniation or other causes of lumbosacral plexopathies.

The etiology of NA is not well understood, but it is assumed to be an immune-mediated neuritis of the brachial plexus that is triggered by a viral infection, vaccination, trauma, or strenuous exercise [5]. Although it could be due to causality, simultaneous occurrence suggests causal relationship between activation of herpes viruses and onset of NA [6,7]. We herein report a case of NA in the lower extremity, in which Herpes Zoster Viruses (HZV) reactivation is postulated to be involved in the development of NA.

#### Case Presentation

An 82-year-old man was admitted to our hospital because of severe left lumbar pain that radiated down to the left thigh and paresis of the left lower extremity. Three years previously, he was diagnosed as having IgG4-related disease because of swelling of the submandibular gland and pancreas, and elevation of serum IgG4 levels (>1500 mg/dl). Swelling of the mandibular gland and the pancreas disappeared following prednisolone therapy (initial dose 40 mg daily that was gradually tapered to a maintenance dose of 5 mg daily), and he had been in good health without disease recurrence.

Four weeks before admission, he experienced a sudden onset of left lumbar pain that radiated down to the left thigh and had difficulty walking. Ten days after the onset of severe pain, he noticed eruptions in the medial portion of the left knee and lower crus. By this time, he clearly noticed weakness of the muscles of left lower extremity. Vesicles were not observed, although this lack of observation was not confirmed by medical experts. He visited his family physician and was prescribed pregabalin but symptoms did not improve. He was referred to our hospital for further evaluation and treatment.

On admission, pulse rate was 92 beats/min and blood pressure was 142/92 mmHg. There were several round, scabbed skin lesions, which were not accompanied by vesicles. The remainder of the general physical examination was unremarkable. Neurologically, the cranial nerves were intact. The patella tendon reflex of the left side was absent. The tendon reflexes of the upper extremities were slightly hyperactive. In the left lower extremity, Manual Muscle Testing (MMT) revealed weakness of the quadriceps femoris (2/5) and gluteus maximus muscle (4/5), but muscle strength of the hamstrings was normal. Muscle strength of the upper extremities and right extremity were normal. No sensory abnormalities were noted.

Laboratory findings revealed mild elevation of serum IgG4 levels (217 mg/dl). Computed tomography of the whole body was also unremarkable. Although lumbar MRI revealed lumbar spondylosis, the changes were not severe enough to explain his clinical symptoms (Figure 1). MRI using STIR sequence revealed an extensive hyperintense signal on the left thigh (Figure 2). The center of distribution of the abnormal hyperintense signal was the quadriceps

femoris. In order to distinguish myositis from a deervated nerve, we performed Electromyography (EMG), which revealed active neurogenic changes in the segmental areas L3-4 of the left lower extremity (Figure 3). At this point, we thought of the possibility of NA. Gadolinium enhanced MRI showed increased intensities of the cauda equine, nerve roots, and lumbosacral plexus, mainly in the left L3-4 area (Figure 4). These findings were accordance with findings regarding the dominant nerves to the denervated muscles seen on STIR-MRI. The differential diagnosis of diseases showing similar MRI findings included Guillain-Barré Syndrome (GBS), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), sarcoidosis, invasion of malignant tumor such as malignant lymphoma, and post-infectious radiculopathy. To rule out these possibilities, further examinations were performed.



Figure 1: Lumber MRI showing mild lumbar spondylosis.

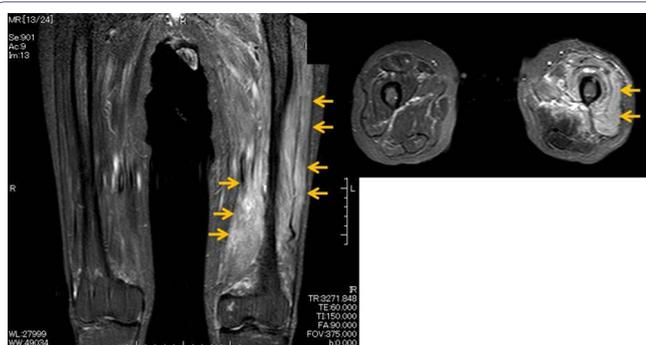


Figure 2: MRI using STIR sequence showing extensive hyperintense signal on left thigh.

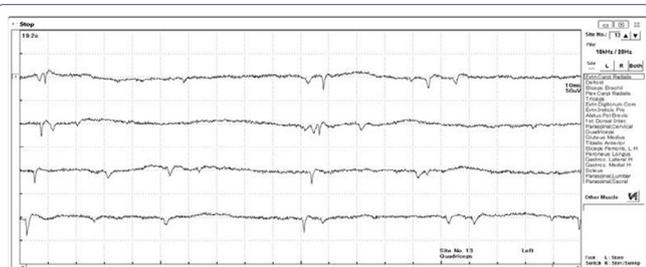


Figure 3: EMG study showing positive sharp waves at left quadriceps muscles.

The Cerebrospinal Fluid (CSF) analysis revealed mild elevation in protein level (54 mg/dl) with slight pleocytosis (54/3 mm<sup>3</sup>). Cytoalbuminologic dissociation was not observed. Cytology for CSF was negative. Angiotensin Converting Enzyme (ACE) levels (7.0 U/l) and soluble Interleukin 2 Receptor (sIL2R) levels (313 U/ml) were normal. The level of HZV antibodies was positive in the titer of 4.20

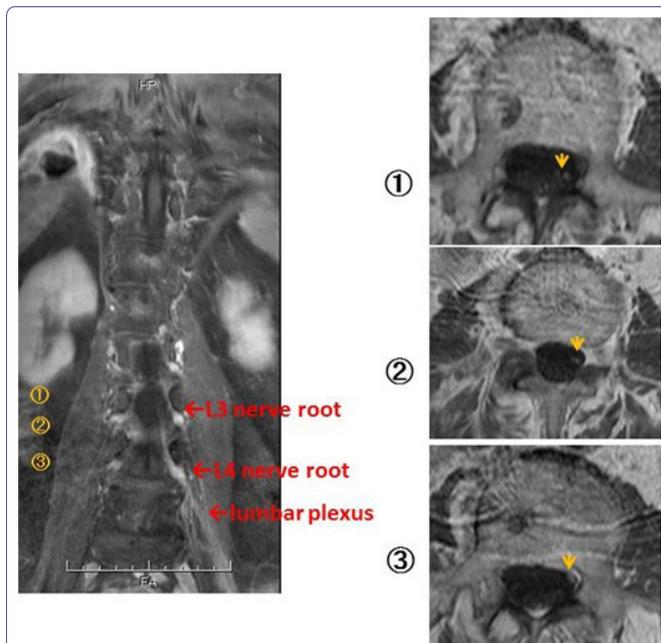


Figure 4: Gadolinium enhanced MRI showed increased intensities of cauda equine, nerve roots, and lumbosacral plexus mainly located on left L3-4 area.

(reference range <0.80). Thus, we diagnosed as having NA in the present case. The reason is discussed later.

Although 6 weeks had passed since the onset of NA, we tried methylprednisolone pulse therapy followed by Intravenous Immunoglobulin (IVIG) therapy. Thereafter, the severe lumbar pain that radiated down to the left thigh gradually disappeared. Instead, we were not able to control the severe pain inside the left knee, which we thought might have been attributable to reactivation of HSV. Valaciclovir hydrochloride together with several analgesics were given, and his pain was gradually controlled. Muscle strength gradually improved and MMT revealed mild weakness of the quadriceps femoris (3-4/5), and gluteus maximus (4-5/5). Abnormal gadolinium enhancement of the cauda equine, nerve roots, and lumbosacral plexus became disappeared (Figure 5).

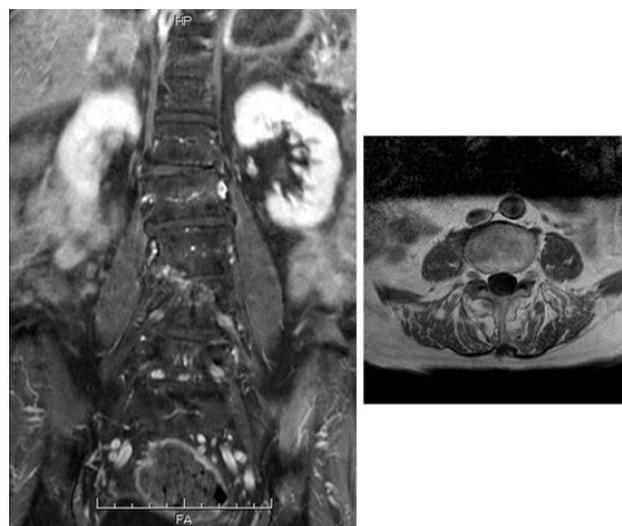


Figure 5: Abnormal gadolinium enhancement of cauda equine, nerve roots, and lumbosacral plexus became disappeared.

## Discussion

The present case experienced sudden onset of severe left lumbar pain that radiated down to the left thigh followed by paresis of the quadriceps femoris muscle. This medical history is typical of acute spinal disc herniation rather than NA. The existence of spinal canal stenosis of the lumbar spine and lack of knowledge regarding NA complicated the diagnosis. Because NA is not well recognized by many physicians, and symptoms resemble those of lumbar disc herniation, it is speculated that misdiagnosis is frequent. The diagnosis of NA depends on a medical histories and exclusion of other diseases, as no specific imaging diagnosis exists. This may be one reason NA has a low recognition rate among physicians.

Evaluation of the peripheral nervous system depends on clinical history, physical examination, nerve conduction study, and EMG. West et al., reported that an increased STIR signal was seen in denervated muscles after peripheral nerve injury as early as 4 days after clinical symptoms, which is several weeks earlier than EMG changes become manifest, and the signal changes may be caused by an increase in extracellular fluid [8]. Furthermore, the MRI signal changes are reversible when the recovery of motor function occurs as a result of muscle innervation. In the present case, we could visualize the distribution of the denervated muscles using MRI with STIR sequence and validated the physical and electrophysiological studies. Matsuda et al., reported a similar case of NA, in which skeletal muscle MRI was useful for detecting denervated muscles [9]. Thus, it seems that skeletal muscle MRI using STIR is useful for localization of denervated muscle in NA.

van Alfen et al., analyzed 15 patients with NA affecting the brachial plexus and reported that MRI findings were abnormal in 3, showing focal T2 hyperintense areas in two patients and focal thickening of the plexus in 1 patient [5]. Furthermore, Fukushima reported that STIR-MRI often shows hyperintense signal abnormalities on the affected side of the proximal brachial plexus [10]. However, MRI findings of NA affecting the lumbosacral plexus have rarely been reported. Ishii et al., reported a case of idiopathic lumbosacral plexopathy, which seems synonymous with NA affecting the lumbosacral plexus, in which gadolinium-enhanced MRI showed increased intensities of lumbar plexus [11,12]. Unoda et al., reported a case of NA, in which gadolinium-enhanced MRI showed increased intensities of the cauda equine [3]. In the present case, gadolinium enhancement MRI showed increased intensities of the cauda equine, nerve roots, and lumbosacral plexus mainly located in the left L4 area, which were accordance with findings regarding the dominant nerves to the denervated muscles on STIR-MRI. Thus, it seems that the combination of STIR-MRI and gadolinium-enhanced MRI is useful for visualization of affected nerves and resulting denervated muscles in patients with NA.

The differential diagnosis of a disease that shows abnormal gadolinium enhancement includes GBS, CIDP, sarcoidosis, invasion of malignant tumor such as malignant lymphoma, and post-infectious radiculopathy. Antiganglioside antibody, which is associated with certain forms of GBS and CIDP, is reported to be positive in some patients with NA [13]. Thus, differences between NA and GBS are difficult to discern. However, the medical history and the CSF analysis were not compatible with the diagnosis of GBS or CIDP in the present case. It has been reported that sarcoidosis may present with peripheral nerve manifestations [14,15]. However, such cases usually have another manifestation of neurosarcoidosis, such as brain parenchymal

lesions, leptomeningeal involvement, and cranial nerve involvement. In the present case, the diagnosis of sarcoidosis was unlikely because the lesion was limited to the peripheral nerve and ACE levels were normal. Malignant lymphoma could not be completely ruled out because a biopsy was not performed. However, it was unlikely because cytology for CSF was negative and sIL2R levels were normal.

Our case presented with eruptions, which were already scabbed on admission and vesicular rash was not observed by medical experts. However, we thought the possibility of HZV because IgM antibodies for HZV were positive. Motor paresis due to HZV in the extremities is rare it usually occurs several days to weeks after manifestation of the vesicular rash [16]. While sensory disturbances are usually present in patients with motor paresis due to HZV, they are less prominent in patients with NA. Although Ismail et al., reported a case of pure motor HZV induced brachial plexopathy, they denied the possibility of NA because severe pain was lacking. The present case experienced sudden onset of left fulminant pain followed by muscle weakness without apparent sensory disturbance. Based on the above, we consider that the paresis in the present case was caused by NA and not by motor paresis due to HZV. Although it could be due to casualty, simultaneous occurrence suggests causal relationship between activation of herpes viruses and onset of NA [6,7]. Gariani et al., reported a 86 years old man with acute shoulder pain, followed by left limb monoparesis and a herpetic rash on the left upper limb and thoracic region [6]. Goaster et al., reported a 50 years old man, who has unusually high titers of anti-HSV antibodies without neutralizing ability, developed NA. Because the patient was cured by anti-herpes therapy, they postulated the herpes viruses are causally related to the development of NA [7]. Thus, we speculate that reactivation of HZV is causally related to the onset of NA.

Formerly, the prognosis of NA has been considered to be good, and patients were thought to recover without specific treatment. However, recent reports show that the functional prognosis is not as good as has been assumed [5]. Recently, glucocorticoid [17], IVIG [18], and the combination of glucocorticoid and IVIG [19] have been reported to hasten the recovery of NA if treatment begins in the early phase of the disease (within 1 month). In the present case, we tried a combination of glucocorticoid and IVIG followed by anti-herpes therapy 6 weeks after the onset of symptoms. The patient showed partial improvement but it may represent the natural disease course. As Goaster et al., proposed [7], anti-herpes therapy should have done in the earlier stage of the disease.

In summary, we reported a case of NA in the lower extremity, in which HZV reactivation is postulated to be involved in the development of NA. As the functional prognosis of NA is not as good as has been assumed, early diagnosis and treatment of NA using a detailed medical history together with appropriate imaging studies in selected patients are needed to improve the prognosis and avoid unnecessary surgery.

## Conflict of Interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

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