

Delayed Diagnosis of Herpes Zoster Infection due to Long-Term Pregabalin Treatment for Lumbar Spinal Canal Stenosis: A Case Report

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Learning Point of the Article:

Prescription of multiple analgesic agents, including pregabalin, might conceal the neuropathic pain associated with herpes zoster infection and may hamper early presentation and timely inception of the antiviral therapy, possibly leading to the development of severe late complications such as postherpetic neuralgia.

Abstract

Introduction: Lumbar spinal stenosis is a common disease among elderly adults, and pregabalin is increasingly used for pain relief in this disease. However, little is known about whether pregabalin may cause any undesirable outcomes when used conjointly with other medications in elderly people. We report a case of herpes zoster infection, the initial symptom of which was obscured due to the use of a combination of pregabalin, tramadol, and acetaminophen for lumbar spinal canal stenosis.

Case Report: In February 2018, a 72-year-old Japanese man presented with eruption without pain on his right shoulder. As an itching sensation and pain gradually emerged, he visited the clinic 10 days after the initial appearance of the eruption. He was diagnosed with lumbar spinal canal stenosis, in 2014, and had been prescribed a combination of tramadol, acetaminophen, and pregabalin for pain relief. He was diagnosed with herpes zoster infection, and valacyclovir was prescribed for 7 days. His symptoms were relieved on the 10th day after the initial presentation.

Conclusion: The use of multiple analgesic agents, including pregabalin, may conceal pain associated with herpes zoster infection and delay its early diagnosis, possibly leading to a worse outcome of the disorder.

Keywords: Pregabalin, herpes zoster, lumbar spinal stenosis.

Introduction

Lumbar spinal canal stenosis is a disorder that can cause pain, numbness, and intermittent claudication in the lower back or extremities due to nerve compression and inhibition of circulation as the spinal canal narrows [1]. The prevalence of the disorder is positively associated with age and increases from 1.9% during the 40s to 10.8% during the 70s in the general population [2]. With the worldwide trend of aging, lumbar spinal canal stenosis has emerged as one of the most common diseases in orthopedics. The representative symptom of lumbar spinal canal stenosis is pain, and analgesic agents are commonly used as the first choice for its management. Although prostaglandin E1, aspirin, and nonsteroidal anti-inflammatory

drugs are predominantly used, pregabalin, an agent that is especially effective for neuropathic pain, was approved in Europe and the United States, in 2004, and in Japan, in 2010. It has been suggested that pregabalin can alleviate the pain caused by lumbar spinal canal stenosis and can improve the quality of life [3]. Its use has increased rapidly due to its marked efficacy, from USD 1.8 billion in 2007 to USD 4.9 billion in 2016 [4]. Due to its synergistic interactions with other classes of analgesic agents, this agent is likely to be administered conjointly with other analgesic agents [5]. However, little is known regarding whether such drug use would lead to any undesired outcomes [6]. Here, we report a case of an elderly patient with herpes zoster infection, the main symptom of which was obscured due

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to the use of multiple analgesic agents, including pregabalin, for lumbar spinal canal stenosis.

Case Report

A 72-year-old Japanese man presented with eruption without pain on his right shoulder. The eruption appeared 10 days before the consultation, and the McGill Pain Questionnaire (MPQ) score was 0 when retrospectively scored. Although the patient did not initially sense any pain or itching, the pain gradually emerged in the following days, which led him to seek assistance at a nearby clinic. His MPQ score was 2 when he presented to the clinic. History taking revealed that he had been diagnosed with lumbar spinal canal stenosis 4 years earlier. A conservative treatment was chosen for its management, yet strong pain in his lower back and left knee persisted; thus, he was prescribed a combination of tramadol hydrochloride (37.5 mg), acetaminophen (325 mg) (1 tablet/day), and pregabalin (150 mg/day). At approximately the same time, pravastatin sodium (10 mg/day) was started for hyperlipidemia. The patient had no history of herpes zoster subunit vaccination, immunodeficiency, depression, physical trauma, chronic lung or kidney disease, or malignancy. At initial presentation, a scabbing eruption was noted on his right shoulder, corresponding to C5–6 dermatomes. The eruption was confined to this area, and no lesions were detected on the opposite shoulder or other areas. Although rapid diagnostic and antibody tests were not performed, based on these observations, the patient was diagnosed with moderate herpes zoster infection. Valacyclovir (1000 mg/day) was prescribed for 7 days. Although mild pain persisted, he was free from the pain 9 days after consultation, with MPQ score 0. On the 11th day after consultation, the eruption disappeared and only pigmentation remained. The eruption was not severe and no late complications were detected on the 46th day from consultation. The patient's previously prescribed medication, including pregabalin, was not changed.

Discussion

This case suggests that the concomitant use of analgesic agents, including pregabalin, may mask the pain associated with herpes zoster infection and can delay diagnosis and treatment of the disease. Herpes zoster is a disease induced by the reactivation of endogenous latent varicella zoster virus within sensory ganglia, and pain and eruption are its representative symptoms. However, our patient did not perceive pain when the eruption initially occurred. Pregabalin is specifically effective against neuropathic pain [7] as the agent suppresses excessive excitation of nerve cells by suppressing the inflow of calcium

ions [8]. Further, it has been suggested that pregabalin can reduce the pain associated with acute herpetic neuralgia [9], another type of herpes infection. Moreover, in our case, tramadol, which has a synergistic effect with pregabalin, was conjointly prescribed. Thus, it is reasonable to assume that joint use of pregabalin and other analgesic agents may have concealed the pain associated with herpes zoster in this case. Delayed medical consultation for herpes zoster can lead to devastating consequences. It is a well-recognized consensus that antiviral therapy should be started within 72 h after the appearance of initial symptoms indicative of herpes zoster [10]. A premise of this statement is that early treatment not only reduces ongoing pain, it also promotes early healing of the eruption and reduces acute pain in herpes zoster. Furthermore, such timely treatment potentially decreases the incidence and severity of postherpetic neuralgia, one of the critical long-term consequences of herpes zoster [11]. Fortunately, our patient did not experience adverse outcomes associated with the disease despite delayed administration of valacyclovir. One plausible explanation is that the patient did not have any critical conditions associated with the development of herpes zoster, namely immunosuppressive status, cancer, and other chronic diseases, despite his older age and statin use [12]. As shown in this case, patients with herpes zoster may delay their initial medical consultation unless pain is clearly perceived. Thus, proper education should be provided for patients with chronic pain who are newly starting combined analgesic therapy that includes pregabalin. Since atypical herpes zoster can be diagnosed more easily with the recently implemented herpes zoster virus antigen kit [13], it has become increasingly important to promote early presentation for herpes zoster in high-risk populations. No universal treatment to prevent postherpetic neuralgia after the development of herpes zoster is currently available [14]. Thus, herpes zoster vaccine may be a reasonable option for high-risk patients, considering its high efficacy in preventing herpes zoster among elderly adults [15].

Conclusion

Our case suggests that the use of a combination of analgesic agents including pregabalin may conceal the pain associated with herpes zoster infection and delay its early diagnosis. These risks should be suspected in patients using multiple analgesic agents. Herpes zoster vaccination can be an effective preventive measure in patients at high risk for developing this condition.



Clinical Message

Prescription of multiple analgesic agents might conceal neuropathic pain associated with herpes zoster infection and delay its early diagnosis. Thus, proper education about taking multiple oral analgesic agents should be provided for patients with chronic pain who may receive combined analgesic therapy that includes pregabalin.

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