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Extremely prolonged prodromal pain due to herpes zoster mimicking atypical facial pain

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Herpes zoster (HZ) is caused by reactivation of the varicella-zoster virus (VZV), which remains dormant in cranial and spinal root nerves after the initial chicken pox infection. The prodromal period of dermatomal pain before vesicle eruption, described as a burning, itching or shooting sensation, is clinically significant. Its mean duration is about 5 days and the mean severity of pain is about 6 on a VAS scale of 0 to 10. The prodrome of HZ may be severe and prolonged in aged or immunosuppressed patients. Herein, we present an 88 year old man had prodromal facial pain for 3 months before the appearance of typical herpes zoster vesicles. He was initially seen by a dentist, an ENT doctor, a neurologist, and a pain physician. Physical examination and diagnostic tests during this period, including brain MRI and MRA, did not identify a definitive cause of the pain, and he received an initial diagnosis of tension type headache with temporomandibular joint syndrome and sternocleidomastoid myofascial pain. Eruption of vesicles in the right ear duct then appeared, and he was diagnosed with herpes zoster oticus, and was successfully treated with acyclovir and prednisone. The case suggest that HZ should be considered in aged or immunosuppressed patients after exclusion the other differential diagnosis and pain treatment with pregabalin attempted if other treatments have limited efficacy in reducing neuralgia, even without a concurrent skin rash.

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Conflict of Interest

The author declares no conflict of interest.

Author Contributions

Yi-Chun Chen is first author of the manuscript.

Introduction

Herpes zoster (HZ) is caused by reactivation of the varicella-zoster virus (VZV), which remains dormant in cranial and spinal root nerves after the initial chicken pox infection. Re-emergence of the virus occurs when cell-mediated immunity decreases, during aging or following use of immunosuppressive drugs. The reactivated virus travels down to the nerve endings and causes prodromal pain, and then acute pain and vesicle eruption along the dermatome supplied by the affected nerve. In 10 to 25% of patients, HZ also causes post-herpetic neuralgia,1, 2 a condition that is more common and severe in older patients.3-5

During reactivation, the virus sometimes spreads to other ganglia and produces additional symptoms in the innervated areas. It only rarely travels upward into the brain and brain vasculature, leading to more generalized symptoms. About 20 to 25% of HZ episodes involve the cranial nerves, primarily the trigeminal nerve. Only about 1% of episodes involve the facial nerve, thus causing Ramsay Hunt syndrome.6

The prodromal period of dermatomal pain before vesicle eruption, described as a burning, itching or shooting sensation, is clinically significant. Its mean duration is about 5 days and the mean severity of pain is about 6 on a VAS scale of 0 to 10. Prodromal pain is more severe in aged or immunosuppressed patients and is associated with the severity of acute pain.7

The patient described here had intractable atypical prodromal facial pain for three months before the appearance of a vesicular rash indicative of HZ in the right ear.

Case report

An 88-year-old man presented to the ER with a three-month history of short-lasting, one-sided headache, right ear retroauricular pain, and a sore throat. He lived at home and had poor activities of daily living, and a history of type II diabetes, hypertension, coronary artery disease, dissecting abdominal aneurysm, previous stroke, bladder cancer (treated with surgery and radiation), and cervical and lumbar spine surgery for a herniated disk. He had no history of rhinorrhea, eye redness or discharge, and no history of fever, nausea, vomiting, unilateral limb weakness, slurred speech, facial palsy or consciousness disturbance.

The patient was previously taken to a dental and otolaryngology clinic, but no pathology was seen. He then visited a neurology clinic and received a brain MRI, on suspicion of malignancy or stroke. The MRI showed brain atrophy and an old lacunar infarction, but no metastasis, current infarction, or enhancement of the facial nerve.

Due to the intractable pain, he was then brought to the ER and hospitalized for further evaluation. A lumbar puncture was performed to rule out malignancy, but no malignant cells were seen. A magnetic resonance angiography (MRA) ruled out an AV fistula, and a sinus X-ray ruled out sinusitis. Examination of the CSF showed no abnormal values and was negative for Cryptococcus, acid-fast bacteria, aerobic bacteria, and anaerobic bacteria. No neurophysiological tests were performed. All tests and accompanying blood and urine work-ups were negative. The patient was initially diagnosed as having a tension-type headache complicated with right temporomandibular joint syndrome and sternocleidomastoid myofascial pain. He was prescribed tramadol (50 mg PO BID) and celecoxib (200 mg PO QD) at discharge.

However, his symptoms persisted and he returned to the ER because of vomiting and epigastric pain, thought to be side effects of the analgesic drugs. A pain

physician was consulted who suggested atypical facial pain as the diagnosis. Pregabalin (75 mg PO BID) was then prescribed to replace the tramadol and celecoxib.

After one week of pregabalin, the patient's pain had abated and vesicles typical of HZ broke out over the right ear and tongue (Figure 1). Treatment with oral acyclovir (400 mg PO Q6h) and acyclovir ointment was then initiated. The patient reported the a decline in pain after use of pregabalin and acyclovir (from 8 to 4 on a pain VAS), but he still had postherpetic neuralgia.

Atypical Ramsay Hunt syndrome without motor involvement was highly suspected as the diagnosis, and the 3 month period of prodromal pain was rare and impressive.

Discussion

The present patient is an unusual case of HZ oticus. The patient's condition was similar to Ramsay Hunt syndrome, except that an extremely long period of facial pain preceded vesicular eruption and there was no facial paralysis. Table 1 lists other conditions that may resemble in HZ oticus. The patient's combination of erythematous vesicles on his ear and tongue excludes other potential causes of skin and oral involvement. The distribution of the patient's pain differed from that seen in trigeminal neuralgia, and the physical examination and imaging results excluded other possible diagnoses.

The common presentation of HZ oticus is Ramsay Hunt syndrome. This syndrome is due to reactivation of the varicella virus in the facial nerve, and its symptoms include ear pain, ipsilateral facial paralysis, and vesicle eruption on the face and external ear and ear canal.6,8,9 Symptoms such as vertigo, nausea, and vomiting sometimes occur due to an involvement of the trochlear nerve10 or vestibular nerve.11 Other cranial nerves are also occasionally involved.8, 12, 13 Our patient did not have the facial paralysis or vesicle eruption that is typical following reactivation of the facial nerve, and there were no indications of involvement of the cranial nerves, other than the facial nerve.

Prodromal pain in HZ occurs on one or more skin dermatomes supplied by the infected nerves. It is typically described as muscle or toothache-like in origin, but may lead to a headache, iritis, pleurisy, brachial neuritis, cardiac pain, appendicitis or other intra-abdominal diseases, or sciatica. Typical prodromal pain before vesicle eruption in HZ lasts for up to 14 days,1 although it is possible for pain to precede the rash by longer periods.14 A previous case report described a 58 year-old patient in Norway who had symptoms of prodromal pain that lasted 7 months prior to the diagnosis of HZ.15 Our patient had prodromal pain for 3 months before vesicle eruption, and its non-specific nature led to an extended series of investigations and provisional diagnoses.

Older HZ patients are more likely to have prodromal pain,7 and more severe prodromal pain is associated with more vesicular lesions and more severe pain during the course of the disease.2 However, our patient, who was 88 years-old and with a very long period of prodromal pain with a VAS pain severity score of 8/10 (higher than typical for patients with HZ), had relatively few skin lesions. The presence of postherpetic neuralgia is consistent with reports that this condition is more common in older HZ patients.3,4

The notable feature of this case is the prolonged course of prodromal sensory phenomena without a definite diagnosis until HZ oticus became evident. However, a cardinal symptom of HZ is neuropathic pain,2 and the patient's response to pregabalin, an antiepileptic drug used to treat neuropathic pain and known to be effective for acute herpetic pain, led the author to suspect HZ. Consistent with the long time

before the appearance of HZ vesicles, the severity of HZ appeared to be much more moderate than typical Ramsay Hunt syndrome. In particular, the patient only had a few vesicles in the orifice of his auditory canal, and did not have facial palsy, taste loss, or vesicles in his throat or tongue. These clinical features suggest that host immunity may have been robust, despite the patient's age, or that a viral deficit was present that led to a dissociation between viral reactivation and effective multiplication, leading to a restricted dermatome involvement and nerve dysfunction. The guidelines for Taiwan and other Asia-Pacific countries (but not India) recommend HZ vaccination for individuals after age 50 or 60 years-old, but the HZ vaccination rates in Taiwan and these other countries remain low.2

A limitation is that this was a clinical diagnosis of VZV, and real-time polymerase chain reaction testing was not used to rule out other types of herpes viruses. It was also not possible to completely exclude unknown contributions to the prodromal headache symptoms, although all tests for possible causes had negative results.

Conclusion

The prodrome of HZ may be severe and prolonged in aged or immunosuppressed patients. HZ should be considered and pain treatment with pregabalin attempted if other treatments have limited efficacy in reducing neuralgia, even without a concurrent skin rash.

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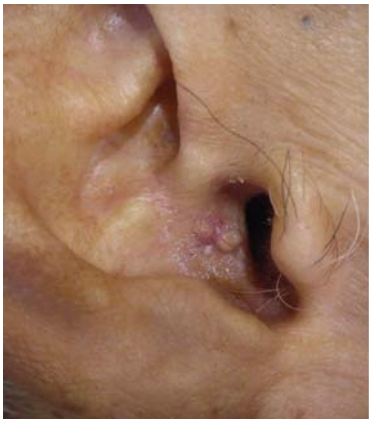
Table 1. Differential Diagnosis of Herpes Zoster Oticus

	Herpes zoster oticus	***Differential diagnosis***
Skin involvement	An erythematous vesicular rash in the ear canal	Auricular hematoma; Auricular perichondritis; Otitis externa; Cholesteatoma; Contact dermatitis; Ear foreign body; Mastoiditis
Oral involvement	Taste loss in the front two-thirds of the tongue; An erythematous vesicular rash in the tongue, and/or hard palate	Dental caries
Distribution	Pain in the ear	Glossopharyngeal neuralgia; Trigeminal autonomic headache; Atypical facial pain; Tympanic membrane rupture; Otitis media; Otic barotraumas; Otomycosis; Bullous myringitis; CVA; temporal arteritis
Trigger	Decreased cell-mediated immunity resulting from carcinoma, radiation therapy, chemotherapy, or HIV infection; Physical stress and emotional stress	
Numbness during pain attack	Involvement of the trigeminal nerve can cause numbness of the face	Trigeminal neuropathic pain; Bell palsy; Tick paralysis
Associated neurological symptoms	Facial palsy; Vestibulocochlear nerve is in proximity to the geniculate ganglion, it may also be affected, and patients may also suffer from tinnitus, hearing loss, and vertigo	Labyrinthitis; Meniere's disease; Sudden sensorineural hearing loss; CNS tumor; Anesthesia nerve blocks; Brainstem pathology like tumor or vascular or inflammatory disorder; SLE
Eye involvement	Dry eyes	Tolosa–Hunt syndrome; temporal arteritis

Figure legend

Figure 1 Herpes in Patient's Right Ear Duct



長達三個月帶狀皰疹前驅痛以非典型臉痛表現病例報告

陳怡君、林峯盛、孫維仁

帶狀皰疹（HZ）是由水痘 - 帶狀皰疹病毒（VZV）的再激活引起的，水痘 - 帶狀皰疹病毒在最初的水痘感染後仍然在顱神經和脊髓神經中休眠。囊泡形成前的皮膚疼痛的前驅期，被描述為灼燒，瘙癢或射擊感，具有臨床意義。其平均持續時間約為 5 天，疼痛的平均嚴重程度約為 6(VAS 等級 0~10).HZ 的前驅症狀可能在老年人或免疫抑制患者中嚴重且持續時間延長。在這裡，我們提出一個 88 歲的男性在典型的帶狀皰疹囊泡出現前 3 個月有前驅面部疼痛。他最初是由牙醫，耳鼻喉科醫生，神經科醫生和疼痛醫生看到的。在此期間的身體檢查和診斷測試，包括腦部 MRI 和 MRA，沒有確定疼痛的確切原因，首次診斷為伴有顳頜關節綜合徵和胸鎖乳突肌肌筋膜疼痛的緊張型頭痛。然後才出現右耳道中的皰疹被診斷患有帶狀皰疹，並且成功地用抗病毒藥物和類固醇治療。該病例表明，排除其他鑑別診斷後，如果其他治療方法在減少神經痛方面效果有限，即使沒有併發皮疹，也應考慮普瑞巴林 (pregabalin) 在老年人或免疫抑制患者中的應用。

關鍵字： 帶狀皰疹，神經痛，老年

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