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Headaches due to giant cell arteritis following herpes zoster ophthalmicus in an elderly patient

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Abstract

Herpes zoster ophthalmicus (HZO) with post-herpetic neuralgia (PHN) and giant cell arteritis (GCA) are two diseases more commonly seen in the elderly population. Each has potentially serious and preventable visual complications by differing mechanisms. Treatments for the two diseases differ. Antiviral medications are used in HZO and high-dose corticosteroids in GCA. These two entities could potentially coexist in the same patient, leading to a complicated diagnostic scenario where a potentially treatable disease could be overlooked. Here, we report a patient who was suffering from PHN following zoster ophthalmicus who developed GCA within a time frame suggesting a potential pathogenic association with the reactivation of latent varicella zoster virus (VZV). This association could be either direct with viral vessel infiltration leading to the arteritis or by an indirect dysimmune route. A pathophysiological association with VZV leading to the development of GCA is proposed.

Keywords

Giant cell arteritis, herpes zoster ophthalmicus, headache, dysimmune

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Introduction

Herpes zoster ophthalmicus (HZO) with post-herpetic neuralgia (PHN) and giant cell arteritis (GCA) are two diseases more commonly seen in the elderly population. These two entities could potentially coexist in the same patient, leading to a complicated diagnostic scenario where a potentially treatable disease could be overlooked. Here, we report a patient who was suffering from PHN following zoster ophthalmicus who developed GCA within a time frame suggesting a potential pathogenic association with the reactivation of latent varicella zoster virus (VZV). The importance of recognizing this association and the potential pathophysiological implications are discussed.

Case report

An 80-year-old woman presented to the out-patient neurology clinic complaining of right upper facial pain in the distribution of the first division of the trigeminal nerve (V1), right eye photophobia, and a right-sided headache. The patient had been diagnosed at an outside clinic 2 months prior to presentation to our clinic with HZO after developing a painful vesicular rash in the right V1 distribution along with corneal involvement without visual compromise. She was treated with an appropriate course of oral valacyclovir and an ophthalmic prednisone suspension.

The vesicular rash improved, but the patient was left with neuropathic pain in the V1 distribution and persistent photophobia consistent with PHN. A new right-sided headache began 4–6 weeks after the onset of HZO. She described this as being distinct from the neuropathic pain. This new pain was located in the right tempo-parietal area and was described as a dull constant ache over the entire area. There was also associated scalp tenderness without any scalp nodules or necrotic areas appreciated. Temporal artery pulsations were normal and the arteries appeared to be normal in consistency. She denied any visual loss or distortions and the vision examination was normal. She did not have symptoms suggestive of polymyalgia rheumatica.

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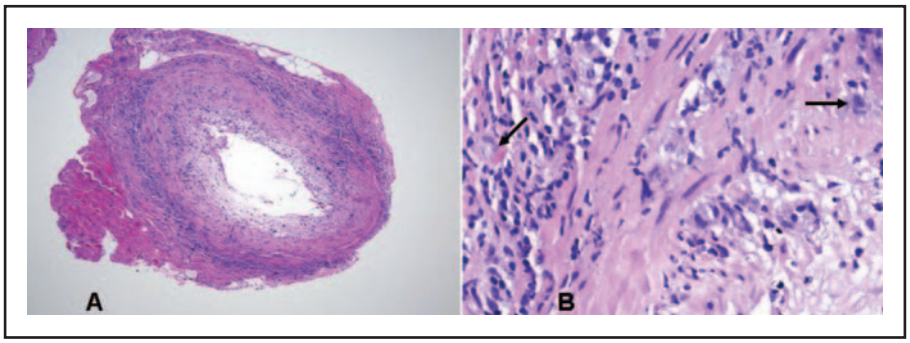

Figure 1. (A) Low-power magnification haematoxylin and eosin (H&E) section demonstrating lymphocytic infiltration of the vessel wall with disruption of the internal elastic lamina. (B) High-power magnification H&E section demonstrating lymphocytic infiltration and the presence of multinucleated giant cells (arrows).

Initial evaluation included magnetic resonance imaging (MRI) of the head with contrast along with laboratory studies. The MRI was normal and did not show any areas of abnormal contrast enhancement. Serum inflammatory markers were elevated with an erythrocyte sedimentation rate (ESR) of 77 mm/1 h and C-reactive protein (CRP) level of 50.9 mg/dl. Given the patient's age, unilateral headache, scalp tenderness and elevated inflammatory markers, GCA was suspected and a neuro-ophthalmology consultation was arranged for a right temporal artery biopsy. The formal eye examination was normal with no evidence for visual loss or corneal scarring. A right temporal artery biopsy was performed demonstrating typical vessel wall lymphocytic infiltration with giant cells present consistent with the diagnosis of GCA (Fig. 1).

Oral prednisone was started at a dose of 60 mg daily. Pregabalin was provided for symptomatic relief of the PHN pain. She was then seen back in the neurology clinic 1 month after initiation of prednisone therapy. The right-sided headache had resolved within a few days of starting prednisone and the inflammatory markers were reduced to normal limits (ESR 9 mm/1 h, CRP < 3.0 mg/dl). The PHN pain was persisting but had improved with pregabalin.

Further examination of the temporal artery biopsy specimen was requested with polymerase chain reaction (PCR) for VZV, but unfortunately could not be performed on the available tissue for technical reasons.

Discussion

The reactivation of VZV leading to shingles is typically easily diagnosed in the presence of the typical painful dermatomal vesicular rash. Many patients experience the persistent neuropathic pain of PHN following resolution of the rash. This case was complicated by the presence of GCA, which could easily have been overlooked given the PHN pain. Severe visual consequences could have resulted without the initiation of corticosteroids in this case. GCA should be strongly considered in any older patient (> 50 years old) with a new-onset localized headache with elevated inflammatory markers (ESR and CRP) even when another potential explanation exists for the head pain such as in our patient. The threshold for obtaining a temporal artery biopsy should be low given the relatively non-invasive nature of the procedure.

The cause of GCA is currently unknown, but pathological findings of multinucleated giant cells suggest an infectious, particularly viral cause (1). The disease typically responds rapidly to corticosteroids, suggesting a dysimmune process. A known rare complication of herpes zoster reactivation, particularly with HZO, is a granulomatous angiitis (GA) affecting the intracranial circulation leading to a variety of neurological complications secondary to cerebral ischaemia (2). The neurological complications typically develop weeks to months following the initial rash (3). This delay in the development of neurological symptoms makes diagnosis difficult. Autopsy cases have shown the arterial lesions to be focal and chiefly affect large vessels at the base of the brain or their meningeal branches ipsilateral to the zosteriform rash (4). Less is known about the role VZV may have in the development of extracranial vasculitis. The pathology of GCA and GA are similar with lymphocytic infiltration of the vessel wall with giant cell formation, but distinct differences exist, such as the relative sparing of the vessel media and elastica in GA, whereas all vessel layers are typically involved in GCA (5). Several authors have investigated the potential relationship between VZV and GCA, but results have been conflicting. Norborg et al. examined 10 temporal artery biopsy specimens positive for GCA and found no causal relationship between VZV and GCA (1). On the other hand, Mitchell and Font found VZV viral particles by PCR in one-quarter of biopsy-confirmed GCA cases and in none of the control cases, suggesting an association, but the virus was either present in very low quantities, abortively

replicating, or was latent (5). Another study by Alvarez-Lafuente et al. did not find an association with VZV or human herpes virus 6, but did find that Parvovirus B19 was present in more GCA specimens than controls by PCR analysis of biopsy specimens (6). Thus, the association between VZV (or other viruses) and GCA remains indeterminate. The temporal association in our case suggests that VZV may have played a role in the development of GCA by either a direct or indirect method. Further, larger scale pathological studies of temporal artery biopsy specimens for the presence of VZV are needed to determine if an association between VZV and GCA exists.

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