New disease

Shingles with secondary asymptomatic CNS involvement!

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Summary

A 32-year-old married Asian woman, previously fit and well, presented with a 3-day history of interscapular back pain followed by a 1-day history of frontal headache and a few episodes of vomiting. She did not have photophobia or neck stiffness. On examination, there was evidence of herpes zoster infection involving the right T3 dermatome. There were no signs of meningeal irritation, cognitive impairment or any neurological deficit. As it is uncommon to have reactivation of herpes zoster infection at a young age, HIV serology was requested to exclude immunodeficiency state. While awaiting serology, a lumbar puncture was performed to exclude opportunistic infections of the central nervous system as she had transient headache and vomiting at the onset. The cerebrospinal fluid showed an elevated level of protein, an increase in lymphocytes and a strongly positive PCR for varicella zoster. The HIV test was negative. Oral acyclovir was changed to intravenous therapy and, a week later, she was discharged with uneventful recovery.

BACKGROUND

Shingles or cutaneous herpes zoster (HZ) is commonly seen in the elderly or in immunocompromised patients due to reactivation of latent varicella zoster virus (VZV). Rarely can it spread to the central nervous system (CNS) leading to meningitis, encephalitis, myelitis, vasculitis or mixed forms. Such patients present with a history that is suggestive of meningeal involvement or cognitive impairment.

We report a case where an immunocompetent young patient developed shingles with asymptomatic CNS invasion by VZV requiring intravenous acyclovir therapy with complete recovery. None or very limited information is available in the medical literature on secondary asymptomatic CNS involvement following cutaneous HZ.

CASE PRESENTATION

A 32-year-old Asian housewife with two children presented with a 1-day history of stable frontal headache associated with nausea and a few episodes of vomiting. Three days earlier, she felt upper back pain with localised rash at the pain site. She denied photophobia or neck stiffness. Her only significant medical history was mild asthma, well controlled with occasional use of a salbutamol inhaler and never required steroids. There was no history of migraine. She had chicken pox in childhood. General physical as well as systemic examinations were entirely normal (apart from a few rhonchi), with no signs of meningeal irritation. An examination of the upper back confirmed typical shingles rash involving the right T3 dermatome.

INVESTIGATIONS

The patient's white cell count was $12.6 \times 10^9/l$, neutrophils $10.9 \times 10^9/l$ and C reactive protein 2.8. Fasting blood glucose was 5.8 mmol/l. Her renal function, liver function, calcium and urinalysis were normal. HIV serology was negative. An examination of her cerebrospinal fluid (CSF) revealed normal sugar, protein 0.51, white cells 27 (100% lymphocytes) and negative gram stain. A strongly positive

PCR for varicella zoster and a negative PCR for herpes simplex virus 1 and 2 were noted.

TREATMENT

On admission, the patient was given oral acyclovir which was changed to intravenous acyclovir following a positive PCR for varicella zoster.

OUTCOME AND FOLLOW-UP

The patient made an uneventful recovery.

DISCUSSION

Cutaneous HZ is a common disease occurring at all ages, but the incidence strongly increases with age. It is caused by re-activation of VZV that has remained dormant in sensory ganglia following a primary varicella infection (chicken pox). As the virus travels along the sensory nerves, it causes inflammation resulting in pain and rash. Occasionally, it can cause myelitis, meningoencephalitis or encephalitis either as a result of the virus travelling centripetally along the posterior root to infect the spinal cord, meninges and brain¹ or as a result of vasculopathy.² Unless a patient is immunosuppressed, complications of HZ in the CNS are very rare in young adults.¹ Shingles in young adults may be the first manifestation of underlying HIV infection.³

Although neurological complications of shingles are well known, guidelines on management of patients with shingles and neurological symptoms are sparse.⁴ HZ meningitis, meningoradiculitis and encephalitis can occur in the absence of rash, but no clear evidence is available to suggest the incidence of CNS involvement in cases of uncomplicated shingles. Subclinical aseptic meningitis has been reported long ago in 40–50% of patients with HZ and headache.⁵ In another study involving 50 immunocompetent patients with HZ, abnormal CSF was detected in 28 of 46 patients (61%) without any clinical signs of meningeal irritation, encephalitis or myelitis.¹ There was strong evidence of VZV in the CSF in 14 of 46 patients (35%), either in the form of a positive PCR or as anti-VZV

antibodies. A prospective study by Steiner *et al*⁶ to evaluate CNS involvement in the acute phase of HZ infection showed clinical evidence of spinal cord involvement (long tract signs, sensory level, pyramidal limb weakness and/or sphincter involvement) in 12 of 24 patients without any clinical symptoms. This study suggested that the mechanisms responsible for CNS involvement could be immune-mediated or infectious. None of these patients underwent CSF examination and clinical signs improved on follow-up examination without any specific treatment.

Although cases of uncomplicated shingles can be associated with lymphocytic pleocytosis and moderately elevated protein levels in the CSF,^{1 7 8} there is paucity of literature and there are no recommendations for managing such cohorts of patients. Therefore, in practice, CSF examination is not routinely performed in cases of uncomplicated shingles. In this case, the young age of the patient with no obvious risk factors and transient associated headache prompted the clinicians to consider CSF examination. As the CSF showed elevated protein levels and lymphocytic pleocytosis, it was considered appropriate to treat the patient with intravenous acyclovir while awaiting PCR result, which later reported as positive. Currently, no large studies clarify how often shingles is associated with asymptomatic CNS involvement and whether PCR-positive CSF can be associated with adverse neurological outcome if untreated. It is unclear whether all asymptomatic patients with PCR-positive CSF require intravenous antiviral therapy and whether such a treatment would prevent neurological complications. On the other hand, intravenous acyclovir is a potentially harmful drug with nephrotoxic properties. Therefore, intravenous acyclovir therapy should be reserved only for patients with a high-risk profile. It is also not known whether the CSF should be re-examined after treatment to ensure PCR is negative for VZV.

Cases of uncomplicated shingles are usually managed in primary care and do not require CSF examination. However, younger patients with no risk factors and associated headache may be referred for CSF examination to rule out asymptomatic CNS involvement.

Learning points

- ▶ Cutaneous herpes zoster (HZ) is a common disease occurring at all ages, but incidence strongly increases with age.
- ▶ Secondary asymptomatic central nervous system (CNS) involvement is not widely documented in the literature.
- ▶ Shingles may be associated with secondary asymptomatic CNS involvement, with the cerebrospinal fluid (CSF) showing evidence of positive PCR for varicella zoster.
- ▶ CSF examination is recommended in cases of uncomplicated shingles in patients who have a high-risk profile and headache.
- ▶ In such a cohort of patients, intravenous acyclovir therapy should be reserved for those with PCR-positive CSF for varicella zoster.

Competing interests None.

Patient consent Obtained.

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