

A concerned young woman with a recurrence of genital herpes

BASIL DONOVAN MD, FACHSHM, FAFPHM, FRCPI, FRCP

A 25-year-old woman experienced herpes simplex virus encephalitis during her first episode of genital herpes. Six months later, genital herpes recurs. Is she at risk of recurrent encephalitis?

Case scenario

Eight months ago, 25-year-old Josie had her first episode of genital herpes simplex virus type 2 (HSV-2) infection (Figure). She was treated within 48 hours of symptom onset with an immediate dose of 1500 mg oral famciclovir, followed by 500 mg twice daily. Despite this treatment, Josie developed HSV encephalitis within five days of the rash appearing and was hospitalised. After discharge, Josie continued famciclovir for a further six months then ceased the medication; within a week she developed genital herpes again and resumed famciclovir.

Josie is concerned that if she ceases the famciclovir again she could have a reactivation of encephalitis. Is this correct and if so, is this only if she has an outbreak of genital herpes?



Commentary

Josie's case raises some interesting issues. Of particular note, HSV encephalitis is usually caused by herpes simplex virus type 1 (HSV-1), while HSV-2 usually causes meningitis (but I doubt that matters to Josie). Central nervous system (CNS) involvement by HSV-1 or HSV-2 can begin within hours of or may even precede the genital symptoms. HSV encephalitis is a much more severe disease than HSV meningitis: encephalitis usually results in a neurological deficit, whereas meningitis rarely does. CNS infection should be treated as soon as possible with high-dose intravenous aciclovir. Josie appears to have been fortunate that she has not incurred any neurological deficit.

The likelihood of recurrent disease

HSV-2 meningitis recurs infrequently (in fewer than 10% of patients with an initial episode of HSV-2 meningitis) and encephalitis probably even less often. This rarity of recurrences means that recruiting into sufficiently powered trials of secondary prophylaxis with antivirals is very difficult and probably not possible for HSV-2 encephalitis. Given the rarity of recurrent HSV-2 CNS disease, long-term suppressive antiviral therapy is probably not indicated for this purpose. But, of course, suppressive therapy may be required anyway until the recurrent genital disease settles. Recurrent genital disease is typically concentrated in the first 12 to 24 months after the primary episode.

Advice for Josie

The good news is that Josie has already had her first, almost inevitable, recurrent episode of genital herpes with no suggestion of any recurrence of encephalitis. The first genital recurrence is the highest risk time for CNS disease recurrence, which involves a local reactivation of the infection. As Josie experienced the first

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Professor Donovan is Professor and Head of the Sexual Health Program at The Kirby Institute, University of New South Wales, Sydney, and is a Senior Specialist at Sydney Sexual Health Centre, Sydney Hospital, Sydney, NSW.



Figure. A case of primary genital herpes.
Image courtesy of Dr Stephen Davies, Sydney.

recurrence without CNS disease I believe that she is probably in the clear. That said, if I was Josie I would remain a little nervous. I would suggest she keep some antivirals on hand at least to manage genital recurrences, because there may be times such as during travel where she has difficulty accessing health services.

Managing recurrent encephalitis

Any recurrence of HSV encephalitis will probably produce CNS symptoms similar to those experienced in the original episode, but initially symptoms can be much milder or atypical. Josie could take a double-dose of antiviral medication promptly to try to head off any suspected, recurrent CNS disease. As with genital disease, the antivirals will be most effective in treating CNS disease if they are taken immediately.

Josie needs to be aware that CNS involvement may not necessarily be associated with genital symptoms. The different elements of HSV-related disease – fatigue, stress/irritability, neuritis, CNS involvement and genital lesions – are only loosely related to each other. If Josie experiences CNS symptoms that continue to progress after taking a double-dose of oral antivirals, she should go to the emergency department

and may require intravenous antivirals. Recurrent CNS symptoms would be an indication for long-term suppressive therapy with antiviral drugs.

Conclusion

Josie's case serves to remind us that suspected primary genital herpes is a medical emergency. Up to 10% of people with primary genital herpes will develop CNS disease (usually 'aseptic meningitis') if treatment is delayed. Even if the diagnosis of genital herpes is uncertain, antiviral therapy should be started immediately and swabs should be taken for pathology. Valaciclovir and famciclovir are safe drugs and can always be stopped if the polymerase chain reaction test of the swab is negative for HSV or if another diagnosis becomes apparent.

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