Herpes Zoster Ophthalmicus with Delayed Cerebral Infarction and Meningoencephalitis

Mark S. Freedman and Ronald D. Macdonald

ABSTRACT: Herpes zoster ophthalmicus can be complicated by a delayed ipsilateral cerebral angiitis which may cause infarction and a smoldering meningoencephalitis. We describe such a case treated successfully with steroids and acyclovir. It is important to consider the diagnosis of this disorder early since therapeutic intervention may prevent an otherwise high morbidity and mortality. Steroids may have to be continued for some time after clinical resolution, using the ESR as a guideline for decreasing dosages.

RÉSUMÉ: Herpès zoster ophtalmique compliqué tardivement d'un infarctus cérébral et d'une méningoencéphalite. L'herpès zoster ophtalmique peut se compliquer d'une angéite cérébrale ipsilatérale tardive qui peut provoquer un infarcissement et une méningoencéphalite évoluant à bas bruit. Nous en décrivons un cas que nous avons traité avec succès au moyen de stéroïdes et d'acyclovir. Il est important d'envisager ce diagnostic tôt dans l'évolution de cette maladie, car une intervention thérapeutique précoce peut prévenir la morbidité et la mortalité sévères qui y sont attachés. On doit parfois maintenir la thérapie au moyen des stéroïdes pendant quelque temps après la disparition des signes cliniques, en se servant de la vitesse de sédimentation globulaire comme guide pour ajuster la posologie.

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Herpes zoster involvement of the ophthalmic branch of the trigeminal nerve can be complicated by local spread affecting ocular components, and less frequently by cranial nerve palsies.[1] A delayed syndrome of ipsilateral angiitis leading to cerebral infarction has been well documented.[2-9] Mortality has been claimed to be as high as 20%, especially if there are diffuse CNS symptoms suggestive of underlying meningoencephalitis.[7,8]

There has been much enthusiasm generated by the efficacy of the newer anti-herpetic drugs in both complicated and uncomplicated varicella-zoster infections,[10-13] but their potential benefit in treating granulomatous angiitus with encephalitis is not known.

We report a case of Herpes zoster ophthalmicus (HZO) complicated by delayed cerebral angiitis, ipsilateral cerebral infarction, and meningoencephalitis, which was successfully treated with steroids and acyclovir.

Case Report

A 73 year old left handed woman was admitted 8 weeks after the onset of right V_1 Herpes Zoster because of neurological complications. She had ocular involvement with corneal scarring and uveitis leading to secondary glaucoma which required initial hospitalization elsewhere. She was discharged but soon re-admitted because of anorexia, lassitude, dehydration and severe pain. A partial right third nerve palsy, left sided central facial weakness and arm incoordination, and slight gait ataxia were then noted. Over two weeks she was intermittently confused and paranoid with visual hallucinations, and then became quite obtunded.

There was no history of hypertension, diabetes or heart disease and she was a non-smoker and a non-drinker.

Examination demonstrated hypopigmentation of the right V_2 dermatome, and opacified right cornea and conjunctival hyperemia. She was confused, disoriented, paranoid and intermittently obtunded. Speech was normal. Remote memory was poor but immediate recall quite good. Her abstractions were poor. Visual acuity was reduced to counting fingers at 10 ft. O.D. and 20/50 OS. Her right pupil was fixed and dilated. There was a right ptosis and exotropia but no ophthalmoparesis. There was complete anesthesia in the right V_1 territory. A left upper motor neuron facial weakness was prominent. Slowed rapid fine finger movements in the left hand, and left leg drift were noted. Muscle stretch reflexes were symmetrical and both plantar responses were flexor. There was no limb or trunk ataxia and sensation was intact.

Routine hematological and biochemical tests were normal except the ESR (Westergren) which was 43 mm/hr (0-20 mm/hr normal). A lumbar puncture demonstrated clear fluid with a glucose of 3.2 mmol/L (serum 6.0 mmol/L) and a protein of 0.55 g/L. There were 29 x 10^6 white cells/L, no RBC's and the differential was of mononuclear predominance. No viral particles were seen on electron microscopy of CSF and antibody titres to herpes simplex and herpes zoster were less than 1:8 and 1:8 respectively. Anti-nuclear factor, rheumatoid factor, VDRL and

From the Department of Neurology, The Wellesley Hospital and University of Toronto
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Reprint requests to: Dr. R.D. Macdonald, The Wellesley Hospital, 160 Wellesley St. East, Toronto, Ontario M4Y 1J3 Canada

serum complement were all normal. A CT scan revealed a hazy hypodense region in the right internal capsule or corona radiata region compatible with infarction. An EEG demonstrated slowing of the background and intermittent bilateral dysrhythmia especially over the anterior head regions, but more prominent on the right where it spread posteriorly. The patient would not consent to angiography.

We felt that this was a case of HZO with delayed cerebral infarction, with meningo-encephalitis. She was treated with a 10-day course of acyclovir 500 mg/m^2 every 8 hours along with 50 mg daily in divided doses of I.V. methylprednisone. The steroids were then changed to oral prednisone which was tapered slowly but then increased again as the ESR dramatically changed (Figure 1). She was followed by repeat EEG's and CT scans. She refused a repeat lumbar puncture.

Within 48 hours of treatment there was a marked improvement in her mental state. She was more alert, fully oriented, and the hallucinations and paranoid delusions had cleared. By 10 days, both she and her family felt that she had re-attained her pre-morbid state. There were no adverse effects of the acyclovir other than a mild increase in the urea and creatinine, which promptly returned to baseline following cessation of therapy.

Although her clinical state remained quite steady, the ESR rose suddenly when the steroid dosage was lowered, but fell quickly again in response to increasing dosage (Figure 1). Repeat EEG's showed a gradual improvement in the background rhythms, with however, a persistent mild right temporal dysrhythmia. Neuropsychological testing confirmed her left-handedness and revealed considerable dysfunction in visuospatial skills including a mild left visual field neglect.

She was discharged one month after admission with only a mild right ptosis and left facial weakness. Her family physician weaned her to 5 mg daily of prednisone over a three-month period, then maintained the dosage for an additional six months. She remained asymptomatic over two and a half years of follow-up.

Discussion

There have been several recent reviews of HZO with delayed contralateral hemiparesis, which has long been recognized as a distinct clinical entity.[4,7-9] To date, there have been only 51 well documented cases in the English literature.[8] We feel that our case is another typical example. The history, clinical findings, neuropsychological, CSF, EEG, and CT abnormalities were all supportive of the diagnosis.

Our patient had no history of, nor any major risk factor other than age, for cerebrovascular disease. She also demonstrated no neck bruits or evidence of vascular disease outside the brain to suggest a thromboembolic etiology for cerebral infarction.

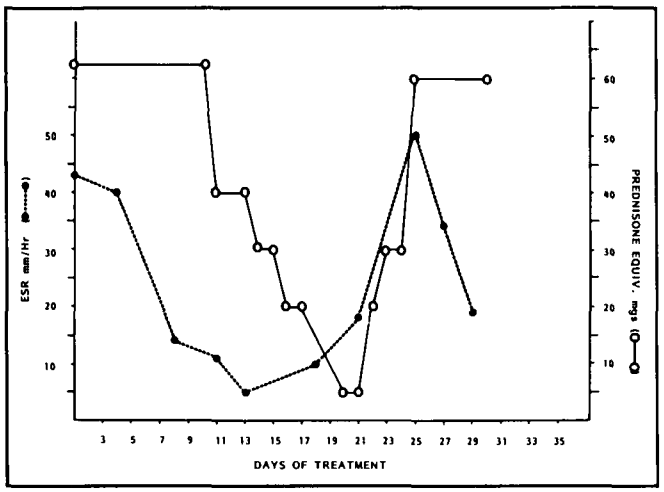

Figure — The response of the ESR to alteration in steroid dosage is depicted. Early tapering resulted in a sudden increase in the ESR which decreased promptly in response to steroid pulsing.

Angiography should not be necessary for clinical diagnosis given a typical clinical picture and CT scan.[14,15]

The highest mortality in this disorder was reported in patients having diffuse CNS symptomology, such as stupor, somnolence, disorientation, confusion or memory deficits;[8] the mortality approaching 20%. Our patient demonstrated some, if not all, of these symptoms and improved remarkably on steroids and acyclovir. Such a regimen has been used previously but with variable results. Hilt et al[4] treated two of their patients with acyclovir and steroids, and although one died and the other did well, they concluded that the treatment did not alter the course of the disease. Menkes et al[6] reported a patient treated with a 5-day course of acyclovir and six weeks of prednisone with no change clinically, but this patient was also noted to have coexistent sarcoidosis. In addition, he was not treated until two months after the time of the original infarct when he presented with several more infarcts ipsilateral to his HZO.

Given that patients with zoster arteritis who have an encephalopathy as well as a stroke appear to be at the greatest risk of death,[7] it is important to recognize the diagnosis and begin treatment early. Recent evidence suggests that the pathogenesis is via viral spread intracranially. This can occur either by contiguous spread from the affected gasserian ganglion to involve the meninges and neighbouring blood vessels[5,9,16] where viral particles have been seen[17,18] or via tracking along the intracranial trigemino-vascular branches of V_1[19], terminating in the adventitia of ipsilateral cerebral arteries including ICA, ACA, MCA, and SCA vessels.[20-22] It is therefore possible that a potent antiviral agent could interfere with the pathogenesis of the angiitis and more directly abate the process.

There has been much success recently with the use of acyclovir in the treatment of acute herpes zoster infections, the effectiveness mostly dependent upon early administration.[10-13] There is, however, little experience in the treatment of zoster-induced angiitis with acyclovir. We recommend that therapy be initiated with both high dose steroids and acyclovir as soon as the diagnosis of cerebral angiitis as a late sequela of HZO is suspected, and that oral steroids be continued for at least six months following the cessation of acyclovir. The sedimentation rate may prove to be a good non-clinical indicator to follow as steroid dosages are altered.

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