



# A case of Myelomeningoradiculitis caused by Herpes Simplex Virus Type 2

S. Buechner\*, I. Florio\*, R. Binazzi, G. Tabiaddon\*

\* Department of Neurology, Regional General Hospital, Bolzano, Italy

^ Department of Infectious Diseases, Regional General Hospital, Bolzano, Italy



## INTRODUCTION

- > 47-year-old immune-competent woman.
- > Since 1 week progressive perineal pain associated to dysuria, and headache with photophobia, and mild fever; since 2 days hypo- and dysesthesia in both legs and the inferior abdominal region, which quickly extended to both foot and the right thorax.
- > **Medical history:** at the age of 27 viral meningitis; since the age of 34 recurrent episodes of headache with photophobia and fluctuating fever; these episodes usually lasted several weeks and regressed completely after corticosteroid treatment.

## INVESTIGATIONS

- > **Neurological examination:** hypoesthesia thoracic and sacral region and both legs with sensory level (D8-D9 at the right side, L1 at the left side); diminished deep tendon reflexes of the lower limbs; urinary retention and constipation.
- > **Brain MRT with gadolinium:** unremarkable.
- > **Spinal cord MRT with gadolinium:** multiple swollen lesions, hyperintense on T2-weighted images (figures 1+2); no enhancement.
- > **CSF:** increased proteins (95 mg/dl) and pleocytosis (700/mmc) of lymphocytes and monocytes; cytological examination: possible Mollaret-like cells (figure 3); PCR highly positive for Herpes simplex virus (HSV-1/2).



Figure 3

## DIAGNOSIS

Myelomeningoradiculitis caused by HSV-1/2.

## TREATMENT

- > Intravenously acyclovir 10 mg/kg t.i.d. for 14 days, ceftriaxone 2 g/day for 3 days and methylprednisolone 1 gr/day for 5 days followed by tapering.
- > Intravenous treatment followed by oral valacyclovir 1 gr t.i.d. for 7 days.

## OUTCOME

- > Headache disappeared quickly, sensory deficits improved significantly.
- > Interestingly, cutaneous bumps and blisters appeared in the right S1 dermatome some days *after* the beginning of the intravenous antiviral treatment.
- > **CSF control after 2 week:** 10/mmc cells; PCR for HSV-1/2 negative.
- > **Neuroradiological follow-ups:** improvement with nearly complete regression of the spinal cord lesions (figures 4+5); mild meningeal enhancement.
- > **Type-specific serological testing:** antibodies IgG anti-HSV-2 positive.
- > 1 week after treatment termination: reappearance of the cutaneous HSV infection, therefore restart with oral antiviral therapy (valacyclovir).
- > Since more than 6 months: antiviral prophylaxis with valacyclovir 500 mg b.i.d.

## OPEN QUESTION: PROPHYLACTIC ANTIVIRAL TREATMENT

- > Recurrence in up to 30% of patients during the first year after herpetic meningitis or radiculomyelitis.
- > Prophylactic treatment might reduce frequency, severity and duration of recurrences.
- > Most data derive from recurrent meningitis - data are highly variable:
  - > Antiviral therapy until PCR of HSV-2 in liquor has become negative?
  - > Intermittent or continuous antiviral prophylaxis?
  - > Duration of oral maintenance treatment (months - years)?
  - > Dosage of oral maintenance treatment (acyclovir 400 - 1000 mg/day)?
  - > Relapses despite antiviral prophylaxis.

## CONCLUSIONS

HSV-2 infection of the nervous system can cause recurrent meningitis and radiculomyelitis, also in immunocompetent adults. Neurological complications may occur without herpetic mucocutaneous disorder. Treatment with acyclovir should be started as soon as possible, however, the duration of the suppressive prophylactic therapy has still to be clarified.

## REFERENCES

- Berger J.R., Houff S. *Neurological Complications of Herpes Simplex Virus Type 2 Infection*. Arch Neurol 2008; 65(5)
- Nakajima H., Shoji H. *Herpes Simplex Myelitis: Differences in Clinical Manifestations between HSV Type 1 and Type 2*. J Clin Neurosci 2012; 15(11): pp 253-254.
- Burgmann K., Schibli A. et al. *Fussabdruecke im Liquor*. Schweiz Med Forum 2012; 12(11): pp 253-254.
- Gilden D.H., Mahalingam R. et al. *Herpesvirus Infections of the Nervous System*. Nat Clin Pract Neurol. 2007; 3(2)
- Kallio-Laine K., Seppänen M. et al. *Recurrent Lymphocytic Meningitis Positive for Herpes Simplex Virus Type 2*. Eur J Clin Microbiol Infect Dis 2013; 38(12): pp 2053-2057.
- Ganzenmueller T., Karaquelle D. et al. *Prolonged detections of HSV-2 DNA in CSF despite antiviral therapy in a patient with recurrent meningitis*. J Clin Microbiol Infect Dis 2013; 38(12): pp 2053-2057.
- Steiner I., Benninger F. *Update on Herpes Virus Infections of the Nervous System*. Curr Neurol Neurosci Rep 2013; 13(12): pp 1273-1281.
- Poulikakos P.J., Sergi E.E. et al. *A case of recurrent benign lymphocytic (Mollaret's) meningitis and review of the literature*. J Clin Microbiol Infect Dis 2013; 38(12): pp 2053-2057.
- Jacobi C., Wildemann B. *Infektionen des Nervensystems durch Herpesviren*. NeuroTransmitter 2010; pp 42-46.
- Roth K., Ferreira V.H., Kaushic C. *HSV-2 vaccine: current state and insights into development of a vaccine that targets the latent virus*. J Clin Microbiol Infect Dis 2013; 38(12): pp 2053-2057.
- Garcia-Moncó J.C. *Acute viral encephalitis: Herpesvirus and Enterovirus*. Book "CNS Infection", 2014, chapter 10:

## BEFORE TREATMENT



Figure 1 T2-weighted



Figure 2 T2-weighted

## AFTER TREATMENT



Figure 4 T2-weighted



Figure 5 T1-weighted with gd

## Herpes Simplex Virus Type 2 (HSV-2)

- > **Primary HSV-2 infection:** herpes genitalis; in immunocompetent adults usually asymptomatic (~ 80%).
- > **HSV-2 latency:** dorsal spinal nerve root of lumbo-sacral ganglia; possible throughout the whole CNS axis.
- > **Most important neurological complications in adults:**
  - > Acute aseptic meningitis (in 36% of woman with primary HSV-2 genital infection, in 13% of men);
  - > Myelitis (ascending in immunosuppressed individuals) / Radiculomyelitis (Elsberg syndrome);
  - > Encephalitis (> brainstem) (> immunosuppressed individuals);
- > Neurological complications may be more frequent in HSV-2 infections without preceding HSV-1 infections.
- > There is no efficient vaccine for HSV-2.

## Mollaret's meningitis

- > **Definition:** benign self-limiting recurrent acute aseptic meningitis, where CSF-analysis often reveals large, mononuclear cells with an indistinct cytoplasm (= Mollaret cells) within the first 24-48 hours.
- > HSV-2 is NOT the only responsible virus of Mollaret's meningitis, but the most frequent (until 80%).

An inefficient virus kills its host. A clever virus stays with it. James Lovelock (British scientist).