

Herpes simplex virus type 1 reactivation following a severe purulent meningitis in ICU

Réactivation du virus herpès simplex type 1 suite à une méningite purulente grave en réanimation

Herpes simplex virus (HSV) is the most common cause of sporadic viral encephalitis and may present with severe forms needing to be managed in intensive care unit (ICU). This causative agent can be latent in humans and reactivated due to several factors.

We report a 19-year-old male patient with no significant medical history who was incarcerated; presented to emergency room with a worsening headache, fever, projectile vomiting and altered mental status. There was an actual history of undertreated community acquired pneumonia (CAP) since few days. On admission, he was febrile at 39 °C and neurological examination showed a Glasgow coma scale score of 6/15 without focal abnormalities. Non-enhanced brain computed tomography (CT) scan was normal. The lumbar puncture showed a purulent CSF, pleocytosis (White Blood Cell (WBC) count of 4800/mm³ with 90% neutrophils), elevated protein concentration (6.6 g/l; normal < 0.45 g/l) and low glycorrachia (< 0.01 g/l). The soluble bacterial antigen of streptococcus pneumoniae was negative. CSF culture was defective and HSV PCR was negative. Bacterial meningoenzephalitis was retained and treatment with high dose ceftriaxone and dexamethasone was empirically initiated. The patient was then admitted in ICU and mechanically ventilated. An association of Vancomycin and Fosfomycin was added when a methicillin-resistant staphylococcus aureus (MRSA) was isolated from both ear's pus draining and respiratory samples. The brain magnetic resonance imaging (MRI) showed ventriculitis as well as right hemisphere cortex thickening with diffusion restriction that suggested pre-suppurative encephalitis. The clinical course was originally favorable with resolution of symptoms and successful extubation (at day 6). Follow-up CSF examination at 9 days of treatment showed a reduction of pleocytosis (12 cells/mm³), normal protein (0.3 g/l) and glucose concentration (0.87 g/l). On the 12th day after admission, there was an

unexpected worsening: his temperature rose to 38.5 °C, became drowsy (GCS 13/15) with focal neurological deficit (left hemiparesis). He also presented an oro-facial vesicular cutaneous eruption with skin vesicles on the anterior face of the chest. A

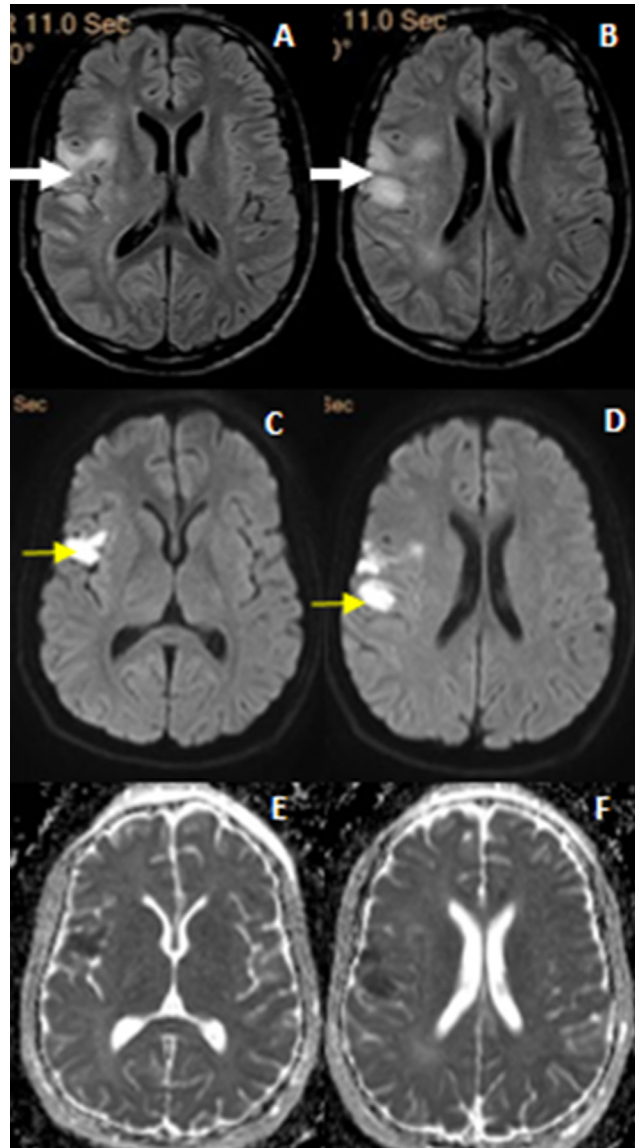


FIGURE 1

A and B. Axial FLAIR MRI showing high signal cortical and subcortical right frontal and temporal areas (white arrows). Their signal is high on DWI MRI (yellow arrows) (C and D) with low ADC (E and F)

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second brain MRI showed focal right frontal and temporal areas with high signal on FLAIR and DWI sequences. The ADC was low and no enhancement has been found. Vascular sequences (2D-TOF, 3D-TOF and 3D T1 sequence with gadolinium enhancement) didn't show any arterial or venous thrombosis (figure 1). A new CSF analysis showed again increased protein level (1.2 g/l) with normal glucose concentration and pleocytosis (96/mm³ with 93% neutrophils); CSF analyzed by end-point PCR was highly positive for HSV. HSV-1 was identified using sequencing of DNA polymerase. The diagnosis of herpes simplex 1 encephalitis was retained; based on clinical, imaging and microbiological data. Intravenous acyclovir was added to the antibiotic treatment (15 mg/kg/8 h) for 21 days. Skin vesicles recovered in few days without scars. A favourable outcome without neurological sequelae was obtained and the patient was successfully discharged.

Comments

Concurrent viral and bacterial central nervous system infection is an uncommon association. In this case, we illustrate the possibility of HSV-1 reactivation in CSF during treatment of bacterial meningitis. This association has already been reported in pneumococcal meningitis. [1] In a post-hoc analysis of a prospective randomized cohort, Weerkamp et al. showed that cutaneous clinical manifestations of herpes reactivation occurred in 40 of

phase of decreased immunity which became hyporesponsive, called "immune paralysis or paralysed immune system", [3] leaving the patient susceptible to secondary infections and allowing latent viruses to reactivate.

Second, psychological stress is one of contributing factors of reactivation of HSV. Padgett et al. demonstrated that the use of social stress in mice provides a good model in which to investigate the neuroendocrine mechanisms that underlie behaviorally mediated reactivation of latent herpes viruses. [4] Offence commission and incarceration background represented significant source of stress that could contribute to HSV reactivation in our patient.

Third, it is already known that patients hospitalized with invasive pneumococcal disease can be superinfected with respiratory or encephalitic virus. [5] In analogy with these findings, our patient had an invasive staphylococcal pneumonia and otitis, and the evidence of bacterial encephalitis (with an ear infection gateway) even though CSF culture's was defective; so we hypothesized that MRSA invasive infections could also be superinfected with encephalitic virus.

Conclusion

Only few cases of reactivation of herpes simplex virus type 1 in bacterial meningitis had been reported in the literature. Several risk factors supporting HSV reactivation could be: immune paralysis due to bacterial encephalitis, psychological stress situation and coinfection with staphylococcal pneumonia. This possibility should be envisaged and confirmed by clinical, imaging and microbiological data.

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Glossary

HSVE	Herpes simplex virus encephalitis
HSV-1	herpes simplex virus type 1
CSF	cerebrospinal fluid
PCR	polymerase chain reaction
CAP	community acquired pneumonia
CT	Computed tomography
WBC	White Blood Cell
CRP	C-reactive protein
ICU	intensive care unit
MRSA	methicillin-resistant staphylococcus aureus
MRI	magnetic resonance imaging
FLAIR	fluid attenuated inversion recovery
DWI	diffusion weighted imaging
ADC	apparent diffusion coefficient

301 patients (13.3%) with bacterial meningitis. Unfortunately, there was no CSF sample analysis in this study, so incidence of meningeal reactivation following a bacterial meningitis could not be clearly determined currently. [2].

Many contributing factors of HSV reactivation have been studied. First, the immunity response to bacterial infection can have a

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