Varicella-zoster reactivated vzv infection, in whom cerebrospinal

Varicella-zoster virus(VZV) is a human neurotropic virus, member of the Herpesviridae family.

Ithas the ability to remain dormant in cranial and dorsal root ganglia 1. Twoclinical syndromes are caused by this virus. The primary infection (chickenpox)usually occurs during childhood and is extremely contagious, characterized byfever, malaise, and a vesicular rash 2. Reactivation of VZV results in herpeszoster (shingles), with dermatomal distribution of pain and rash.

and it isusually a disease of older or immunocompromised people 1, 2. Central nervoussystem (CNS) involvement may occur during primary infection or reactivation, and may include meningitis, encephalitis, meningoencephalitis, vasculopathy, myelitis, Guillain-Barré syndrome, and retinal inflammatory disorders 1, 2. Here, we present thecase of a previous healthy immunocompetent 37-year-old man with asepticmeningitis without rash as a result of reactivated VZV infection, in whomcerebrospinal fluid (CSF) analysis revealed hypoglycorrhachia. A 36-year-old Caucasianmale presented to our hospital with a 4-day history of persistent frontalheadache and low-grade fever, with no other symptoms. He had an episode ofvaricella infection in his childhood, but no history of zoster. The rest of hismedical history was unremarkable.

Apart from paracetamol, no other medicationshad been taken in the previous days. He was an active smoker with a10-pack-year history, with no use of alcohol or illicit drugs. His familyhistory was insignificant. He was married, lived in an urban area, worked as arefrigerant, and with no contacts with

animals. Initially, the patientwas evaluated by an otolaryngologist, without findings from the ear, nose andthroat examination, but neck stiffness was noted, and the patient was referredto the emergency room.

On examination, he was alert and oriented. His bodytemperature was 36 °C, and the rest of the vital signs werealso normal. Neck stiffness was present, but no other neurologicalabnormalities were detected. The remainder of the clinical examination, including skin, respiratory and cardiovascular system, was normal. A chest x-ray and acomputed tomography of the head and sinuses were carried out and showed noabnormalities. Laboratory tests revealed a white blood cell (WBC) count of 6.

1 x 109 /L (neutrophils: 61. 3%, lymphocytes: 24. 5%, monocytes: 11. 7%, eosinophils: 2. 2%, basophils: 0. 3%) and aplatelet count of 149 x 109 /L. The serum biochemical parameters of kidneyand liver function were normal.

C-reactive protein and erythrocytesedimentation rate levels were within normal range also. Blood and urineculture were drawn and serology for human immunodeficiency virus (HIV) wasobtained. A lumbar puncture (LP) was performed in the emergency room and yieldedclear cerebral spinal fluid (CSF), with 400 x 106/L WBC (94%lymphocytes), 25 x 106/L red blood cells (RBC), an elevated totalCSF protein of 177 mg/dL, and a low CSF glucose of 45 mg/dL (serum glucose of 90mg/dL), with a CSF to serum glucose ratio of 0. 5. Gram stain, Ziehl–Neelsenstain and Indian ink stain were negative, while CSF cultures were sent.

CSFvolume was insufficient for performing polymerase chain reaction (PCR) studies. The patient was started on intravenous ceftriaxone and acyclovir

and he wasadmitted to the internal medicine department with the diagnosis of probableaseptic meningitis. On day 3 ofhospitalization, the patient continued to be afebrile, while the headache andthe neck stiffness had resolved. Blood, urine and CSF cultures obtained onadmission did not demonstrate any bacterial growth, and ceftriaxone was stopped. The HIV serology was negative too. A second LP was performed in order tocollect a CSF sample for neurotropic viruses' PCR and assess the need forcontinuing acyclovir treatment. Repeated LP revealed WBC count of 667 x 106/L(93% lymphocytes), RBC count of 30 x 106/L, total protein level of94 mg/dL, and a glucose level of 38 mg/dL (serum glucose of 94 mg/dL), with aCSF to serum glucose ratio of 0. 4.

CSF cytology did not yield any malignantcells. The PCR analysis of the CSF herpes simplex virus (HSV) I and II wasnegative, but VZV DNA was detected. The patient received a total of 8 days ofintravenous acyclovir and he was discharged with instructions for an additional6-day course of oral valacyclovir and for performing a magnetic resonanceimaging (MRI) of the brain as an outpatient. On his follow-up visit two weekslater, the patient was in a good health condition, while the MRI showed noabnormalities. VZV meningitis is anuncommon complication of herpes zoster 3. Nevertheless, VZV represents one ofthe commonest etiological agent for aseptic meningitis 4-6. The progress ofthe technology has allowed a more detailed attribution of central nervoussystem (CNS) disorders to VZV.

PCR and other molecular amplification methodsare characterized by high sensitivity and specificity in detecting viral DNA inCSF, and have become essential tools in the diagnostic armory 1. In contrastwith VZV encephalitis or

meningoencephalitis, VZV meningitis is associated witha favorable clinical outcome in immunocompetent hosts, and the need fortreatment with antiviral agents in these patients is controversial 6. It is well establishedthat aging causes a multitude of changes in the immune system leading tonumerous defects, and to a subsequent vulnerability to pathogens 7. Additionally, disease-related or iatrogenic immunosuppression have deleterious effects onhost defense 8. Defects in specific functional compartments of the immunesystem are associated with susceptibility to specific infectious agents 8. Herpes zoster is most frequent in the elderly and in immunocompromised patients1, 2.

The reason relies on the fact that VZV-specific, cell-mediated immunitydeclines with age or immunosuppression, and it is the adaptive T cell responsethat is crucial for preventing the reactivation of the latent virus 7-9. Arecent study demonstrated that the incidence of herpes zoster was twice as highin immunocompromised than in immunocompetent hosts, and that higher incidenceswere observed among individuals with severe immunosuppression 10. Higherincidences were also observed among women and older patients 10. Herpes zoster is manifestedby a unilateral dermatomal rash, which is painful and/or pruritic. It starts aspapules and quickly evolves into vesicles or bullae.

Occasionally, a dermatomaldistribution of pain and/or pruritus occurs in the absence of an antecedent skineruption. This condition is known as zoster sine herpete 1. The dormant virus has also the ability, during itsreactivation, to travel from the ganglia to the central nervous system, withoutconcurrent skin manifestations 11. Indeed, in cases of VZV meningitis, therash can be

absent in a significant proportion of patients 5, 12-14. The CSF analysis in viralmeningitis typically includes lymphocytic pleocytosis, a slightly elevatedprotein level, and a normal glucose level. A CSF hypoglycorrhachia is definedas CSF glucose less than 45 mg/dL, and is usually detected in bacterial, tuberculous, and fungal meningitis 15. Less common causes ofhypoglycorrhachia include acute syphilitic meningitis, Mycoplasma pneumoniae meningitis, primary amebic meningitis, meningeal cysticercosis, carcinomatous meningitis, subarachnoid hemorrhage, sarcoidosis, rheumatoid meningitis, and lupus myelopathy 16. Viruses that may cause lowCSF glucose levels when they invade meninges are mumps and, occasionally only, HSV, enteroviruses, lymphocytic choriomeningitis virus and VZV 13, 14, 16.

It mustbe emphasized that CSF glucose level may be falsely low in case of concurrenthypoglycemia. A serum glucose must be drawn before the LP, and a CSF to serumglucose ratio must be calculated. A normal ratio is around 0. 6, and ratios lessthan 0. 5 are considered abnormal 15. We report anunusual presentation of VZV meningitis in previously healthy young adult, without a rash and with hypoglycorrhachia. Only few similar cases have beenpreviously reported 17-19.

Mayo and Booss 17 reported four young adult patientswithout exanthem and with clinical and serological diagnosis of VZV meningitis. Three of them had low CSF glucose, and the other patient an abnormal CSF toserum glucose ratio, while all had a favorable outcome. Habib et al.

18presented an immunocompetent 26-year-old woman who was diagnosed with VZVmeningitis using PCR in CSF, without a rash and with low CSF glucose and CSF toserum glucose ratio. The patient was successfully treated with intravenousacyclovir. Pasedag et al. 19 reported an 18-year-old previously healthy manwith molecular and serological diagnosis of VZV meningitis, presented with hypoglycorrhachiaand treated successfully with acyclovir and valacyclovir.

Finally, three othersimilar cases exist in the literature concerning three patients under the ageof 16 years, all with a benign course 20-22. In conclusion, ourcase emphasizes the importance of considering reactivated VZV as a cause ofaseptic meningitis in young and immunocompetent individuals, even in theabsence of an exanthem. It is also highlight the fact that VZV meningitis canbe accompanied by hypoglycorrhachia. The widespread use of molecular methods inCSF analysis allows the prompt recognition of CNS involvement during the courseof this viral disease and the early initiation of treatment.