A 45-year-old female patient presented with fever, confusion, nuchal rigidity, and vomiting to the emergency department of our hospital. She had a runny nose for the three days prior to admission and frontal headache. Her past medical history was significant for hypertension and allergy to penicillin. The patient was on nifedipine, monoxidine, and irbesartan per os. On examination, she was febrile with a temperature of 38.3°C. Her blood pressure was 140/90 mmHg, pulse 100 per minute regular and 14 respirations per minute. She was confused and stuporose.

A computed tomography of the brain was normal. Subsequently, she underwent a lumbar puncture. Examination of the cerebrospinal fluid revealed 550 cells/mm³, 78% lymphocytes, 56 mg/dl glucose levels (serum glucose levels: 111 mg/dl), protein 111.8 mg/dl. Gram stain of the cerebrospinal fluid (CSF) was negative, as was culture of the CSF.

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Diagnosis
The patient was empirically commenced on treatment with acyclovir intravenously in adjusted doses for mild renal failure (serum creatinine: 1.5 mg/dl). Polymerase chain reaction (PCR) testing to detect genetic material of DNA viruses and RNA viruses was performed in the CSF. Immunophenotype of the CSF was performed and revealed CD3+ (97%), CD4+ (69%) predominance while CD19+ and CD20+ were detected in much smaller proportions (3% and 2% respectively).

Serum IgG antibodies against cytomegalovirus (CMV) were positive in a titer of 1:11212 (positive=1:558), whilst IgM were negative. PCR testing on peripheral blood mononuclear cells to detect CMV-DNA was not performed. Wright agglutination and serology against Brucella spp and Listeria monocytogenes were negative. HBsAg, anti-HCV and anti-HIV were negative. Serum immunoglobulin levels were normal.

Results of PCR were available after a few days, CMV DNA was detected while PCR was negative for HSV1, HSV2, VZV, EBV, HHV-6, adenoviruses, enteroviruses, influenza type A and influenza type. PCR for Mycobacterium tuberculosis was negative. In accordance with these results, treatment was changed to ganciclovir. A repeat lumbar puncture showed 29 cells/mm³ (98% lymphocytes) and a decrease in CSF protein (74.6 mg%). The patient made an uneventful recovery and when last seen at follow up (30 days after discharge) was in excellent health.

Teaching points
- Cytomegalovirus (CMV) is a pathogen mainly associated with significant morbidity and mortality in patients with immunosuppression [1]. Nevertheless immunocompetent patients suffer as well from the devastating consequences of the virus' neurotropism [2, 3]. The neurotropism of CMV is well known in immunodeficient patients [4, 5].

- CMV meningitis is a well-documented infection in immunocompromised patients. However, there are only a few reports in the scientific literature describing CMV meningitis in immunocompetent adults.

- CMV leads to considerable morbidity and mortality in immunosuppressed patients. However, the virus may occasionally cause significant diseases in patients without, at least, apparent immunosuppression. CMV has a noteworthy neurotropism in immunodeficient patients [4, 5]. In addition, intrauterine infections cause affliction of the central nervous system of the embryos with catastrophic consequences [6]. Infants and children are not spared by the consequences of CMV associated diseases of the brain either [7]. In contrast CMV meningitis is considered a rarity in immunocompetent patients. Only a couple of dozen patients have been described in the literature [8-11]. Probably the disease is underdiagnosed, as polymerase chain reaction (PCR) testing, often necessary to document the disease, of the cerebrospinal fluid is not ubiquitously available. Nevertheless, the use of PCR is increasingly employed in various centers around the world and has facilitated the diagnosis of CMV meningitis [12, 13]. Serology may be positive but it has to be explained in the context of a high prevalence of seropositivity for CMV in the general population. In our patient, the presence of serum anti-CMV IgG in the absence of anti-CMV IgM indicates a previous primary CMV infection. CMV can establish latency in the central nervous system (CNS); then, the absence of serum anti-CMV IgM with presence of CMV in the CSF, should be an index of local (CNS) reactivation. A PCR performed on peripheral blood mononuclear cells to detect CMV-DNA could add important additional information in such a clinical setting to rule out CMV viremia.
It is not clear whether CMV meningitis is a self-limited disease or a disease with potential catastrophic consequences for the patient [8]. It has been argued that the toxicity associated with ganciclovir treatment exceeds the therapeutic benefit for the patient, and thus should probably be withheld. In our opinion, until large prospective studies will clarify the issues one has to carefully consider the disease burden that follows this CMV infection of the CNS. We think that as treatment is available, (a not so common scenario in viral meningitis), treatment is probably warranted for a disease with the severity of meningitis. However, one may criticize this view, due to the lack of evidence for the effectiveness of antiviral treatment of CMV meningitis in the immunocompetent patient. In addition, there are no adequate data regarding the proportion of CMV cases to the total cases of lymphocytic meningitis in immunocompetent patients. Finally, one should take under consideration the adverse effects of antiviral treatment.

In conclusion, in immunocompetent patients with acute meningitis with predominance of lymphocytes, CMV meningitis has to be included in the differential diagnosis and has to be ruled out with PCR testing of the cerebrospinal fluid. Until prospective trials will clarify whether the disease needs treatment or not, we would suggest to treat with ganciclovir, as lifelong aftermath of CMV involvement of the central nervous system can be disastrous.

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References