

A Case of Mumps Virus Reinfection Manifesting as Severe Meningitis that Mimicked Tuberculous Meningitis

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Abstract

It is known that mumps is an acute and highly contagious systemic viral infection that occurs in childhood, the hallmark of which is parotid gland swelling. Although mumps infection in the central nervous system (CNS) is uncommon among adults in association with vaccinations generally administered in developed countries, CNS involvement can occur without parotitis. Here, we report such a case of severe meningitis due to reinfection by the mumps virus. Based on our findings, we propose that mumps meningitis can mimic tuberculous meningitis in regard to clinical symptoms and course, as well as laboratory test results of cerebrospinal fluid. Follow-up investigations that include key cytokines such as IL-6, IFN- γ , and TNF- β in the CSF are important for differential diagnosis.

Keywords: Mumps meningitis; Tuberculous meningitis; IL-6; IFN- γ ; TNF- α

Introduction

While mumps is not uncommon in childhood, it is rare in adults, especially those living in well-developed countries where mumps vaccines are usually administered [1]. However, optimal dosing and vaccination timing have not been established, thus outbreaks still occur among children as well as young adults in Western countries [1,2]. A mumps viral infection is characterized by parotid gland swelling (31% to 65%), while other clinical presentations such as aseptic meningitis (1% to 10%) and encephalitis (0.1%) are rarer [3]. Without parotitis or hyperamylasemia, a differential diagnosis may include infection by *Staphylococcus aureus*, a gram-negative bacterium, and atypical mycobacteria [3], as cerebrospinal fluid (CSF) samples from affected individuals often contain a substantial number of polymorphonuclear cells [4]. Here, we report a case of mumps meningitis due to reinfection in a Japanese adult that mimicked tuberculous meningitis.

Case Report

A 53-year-old female with a history of mumps infection in childhood was admitted to our hospital because of a 2-day history of high fever, vomiting, severe headache, and sensation of chills. Her daughter had contracted mumps 2 weeks prior. The body temperature of the patient was 38.7°C, though salivary glands were not swollen or tender. A neurological examination revealed the presence of meningeal irritation signs, while other findings were normal. Peripheral blood testing showed a white blood cell (WBC) count of 8900/ μ l and neutrophils at 77.0%. The levels of C-reactive protein, amylase, and aminotransferases in serum were normal. An enzyme immunoassay (EIA) for the IgM antibody specific to mumps virus revealed the titer was 0.07 (positive >0.8), while the IgG antibody titer was 8.6 (positive >1.2). An atraumatic lumbar puncture yielded hyper-cellular CSF containing 370/ μ l WBC (368/ μ l mononuclear cells, 2/ μ l neutrophils)

and red blood cells (RBC) at 4/ μ l, along with elevated levels of protein (64 mg/dl) and β 2 microglobulin (3.6 mg/L), and a normal level of adenosine deaminase (ADA) (2.7 U/L). The EIA titers for anti-mumps IgM (0.01) and IgG (0.51) antibody levels in the CSF, as well as the IgG antibody specific to herpes simplex virus (HSV) indicated negative for infection. Cultures of the CSF sample for bacteria, mycobacterium tuberculosis (TB), and fungus were all negative. PCR analyses for HSV and TB DNA were also negative. Cytological screening of CSF cells revealed no malignancy. Gadolinium-enhanced magnetic resonance imaging of the brain showed only diffuse leptomeningeal enhancement in T1-weighted images. There were no radiological findings indicating the presence of encephalitis or basal meningitis. The patient was diagnosed as having aseptic meningitis with a probable viral etiology.

Conservative treatment was given with an intravenous drip infusion of 10% glycerin and empirical administration of acyclovir started on the day of admission (Day 1). However, intermittent vomiting associated with severe headache and high fever persisted. On Day 3, findings of a CSF sample obtained by a follow-up lumbar puncture had worsened, i.e., WBC 556/ μ l (all mononuclear), RBC 3/ μ l, protein 74 mg/dl, β 2 microglobulin 5.9 mg/L, and ADA 5.3 U/L. Measurement of cytokines in the CSF using an immunoassay system also revealed markedly elevated IL-6 (263 pg/ml), and slightly elevated IFN- γ (8.5 IU/ml) and TNF- α (8 pg/ml) levels. For suppression of excess inflammatory reactions in the CSF, dexamethasone (3.3 mg/day) was started, and headache and vomiting showed improvement. On Day 8, a follow-up CSF examination using an atraumatic lumbar puncture only showed slight improvement, such as WBC 342/ μ l (335/ μ l mononuclear, 7/ μ l neutrophils), RBC 2/ μ l, protein 46 mg/dl, and β 2 microglobulin 4.0 mg/L. On the other hand, the CSF levels of IL-6 (15.3 pg/ml), IFN- γ (0.6 IU/ml), and TNF- α (3.0 pg/ml) were decreased, while ADA was further elevated to 5.5 U/L. Since an ADA level of 6 U/L or greater in the CSF has been proposed to strongly support a diagnosis of tuberculous meningitis [5], we considered the possibility of this disorder in our patient, as dexamethasone may have suppressed the natural immune response to TB. Thus, we re-checked this possibility by examining a CSF sample obtained on Day 15, after discontinuation of that drug. However, CSF cultures for TB and a PCR

assay for the TB antigen were again negative. Furthermore, findings of this CSF sample showed other improvements, including fewer WBC (138/ μ l, all mononuclear) and decreased levels of β 2 microglobulin (4.6 mg/L), ADA (3.1 U/L), and IL-6 (4.8 pg/ml). In contrast, CSF protein level alone remained increased to 61 mg/dl.

On Day 18, PCR analysis of the first CSF sample (Day 1) showed it to be positive for mumps RNA. Serologic testing for mumps performed on Day 18 demonstrated remarkable elevation of the specific IgG titer in serum (372) and the CSF (106). Based on these results, we made a definitive diagnosis of mumps meningitis due to reinfection. The clinical condition of the patient rapidly improved and complete recovery was noted on Day 21.

Discussion

It has been reported that severe mumps cases are characterized by elevated levels of IL-6 and IFN- γ in plasma [6], while another study also noted that IL-2 and IFN- γ were increased in serum of patients with acute mumps infection, thus indicating an important role for Th1 cells in this disease [7]. Likewise, inflammatory processes occurring in meninges during mumps meningitis seem to be similar, as IFN- γ , IL-2, and IL-6 levels are significantly elevated in the CSF of affected patients, while TNF- α in the CSF does not show an elevated level [8], though an increased level of that cytokine is a feature of patients with tuberculous meningitis [9].

Conclusion

In the present case, we found it necessary to consider the latter possibility because of persistent severe headache and vomiting, along with the progressive course associated with elevation of ADA and TNF- α level in the CSF. Therefore, we consider it important to emphasize that reinfection by the mumps virus can potentially cause severe meningitis without parotitis and may mimic tuberculous

meningitis. Careful neurological and radiological follow-up examinations, as well as repeated analyses of CSF samples using detailed immunological measurements in addition to routine studies are necessary for proper diagnosis and avoiding unnecessary treatment.

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