Case Report

Parotitis associated with Crimean Congo hemorrhagic fever virus

Selçuk Kaya *, Gurdal Yılmaz, Barış Ertunç, İftihar Koksal

Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Karadeniz Technical University, 61080 Trabzon, Turkey

Article Info

Article history:
Received 8 August 2011
Received in revised form 10 October 2011
Accepted 14 October 2011

Keywords:
Crimean Congo Hemorrhagic Fever
Parotitis

ABSTRACT

Background: Crimean Congo Hemorrhagic Fever (CCHF) is a potentially fatal tick-borne viral disease, the course of which may accompanied by various clinical findings.

Objectives: We describe a picture of non-suppurative parotitis developing in association with CCHF virus.

Study design: A 48-year-old patient presenting to our hospital with lethargy, hemorrhage and pain and swelling below the left ear was diagnosed with CCHF through IgM antibody and polymerase chain reaction positivity in serum investigated for CCHF virus. A picture of non-suppurative parotitis developed on the 3rd day of admission.

Results: Other causes of parotitis were excluded with the help of serological tests, and the case was regarded as one of CCHF-associated parotitis. The patient was put on adjuvant therapy, an improvement in clinical findings was observed and he was discharged in a healthy condition on the 5th day.

Conclusions: Ours is the first case in the literature of parotitis seen during CCHF. CCHF should be considered in differential diagnosis in addition to other frequently encountered viral agents in patients from endemic regions presenting with a picture of non-suppurative parotitis.

© 2011 Elsevier B.V. All rights reserved.

1. The significance of this case

Our case is important as the first in the literature of parotitis developing in association with CCHF.

2. Crimean Congo Hemorrhagic Fever (CCHF)

Crimean Congo Hemorrhagic Fever (CCHF) is a tick-borne disease caused by Nairoviruses of the family Bunyaviridae and transmitted to human beings by bites from infected ticks or by direct contact with viremic animals/humans.1,2 CCHF has a wide global distribution, with an increasing prevalence over the last decade, Turkey being one of the countries in which it is endemic.3–6

Following a brief incubation period, the disease begins with symptoms such as sudden-onset fever, shivering, muscle-joint pain, nausea-vomiting, headache, vertigo, back-stomach ache and lethargy-fatigue.3,4,7 Hemorrhage associated with direct/indirect viral effect on the vascular endothelium and even disseminated intravascular coagulation and shock may be observed.9 Cardiovascular and respiratory symptoms such as hypotension, relative bradycardia and tachypneoa, as well as conjunctivitis and pharyngitis, are some of the findings frequently seen in the early stage.8 Hepatomegaly and splenomegaly may be observed in around half of cases, while delirium, confusion, cerebellar findings and various central nervous system dysfunctions ranging as far as coma can be seen in some patients.8

3. Case description

A 48-year-old male presented to our hospital in June 2011 with weakness over the previous 15 days, bleeding from the mouth, pain and swelling below the left ear for the preceding 2 days. The patient lived in a village in the district of Gümüşhane/İran and had a history of several previous contacts with ticks. He had no previous history of major disease. At initial presentation his general condition was average, and he exhibited full consciousness, orientation and cooperation. Body temperature was 36 °C, respiration rate 24/min, heart beat 100/min and arterial blood pressure 100/70 mmHg. At physical examination, we determined a focus of hemorrhage in the oropharynx, bilateral facial and conjunctival hyperemia and mild swelling in the left parotid region.

At laboratory analysis, serum white blood cell (WBC) count was 2300/µL (4.800–10.800), hemoglobin (Hb) 11.5 g/dL (12–17), platelet (Pit) count 27.000/µL, sedimentation 33 mm/h (0–20), C-reactive protein (CRP) 0.85 mg/dL (0–5) and procalcitonin (PCT) 0.5 ng/mL (<0.5). Peripheral blood smear revealed a lymphomonocytic series predominance of 40–50%. In terms of biochemical parameters, serum aspartate transaminase (AST) was 332 U/L (10–38), alanine transaminase (ALT) 145 U/L (10–41), lactate dehydrogenase (LDH) 1838 U/L (240–480), creatinine phosphokinase (CPK) 4321 U/L (20–200) and amylase 165 U/L (28–100). The fact the patient came from an endemic region and had hemorrhagic
symptoms, a typical facial appearance and elevated bicytopenia, serum CPK, myoglobin, AST and ALT levels at laboratory examinations suggested CCHF, and a CCHF IgM, polymerase chain reaction (PCR) was planned for serum CCHF. For this purpose, serum and/or plasma samples from patient are submitted to the Refik Saydam National Hygiene Center, Virology Reference and Research Laboratory in Ankara, Turkey with an official “possible case report form”. TaqMan-based real-time PCR was performed as described by Yapar et al. CCHF IgM was detected by ELISA prepared with inactivated native CCHF viral antigens grown in Vero E6 cells on serum samples following recommendations of the Centers for Diseases Control and Prevention (CDC, Atlanta, USA), respectively. Both of the results were positive for CCHF virus infection.

The swelling below the left ear at admission became increasingly evident over days 2–3, and the patient developed non-suppurative parotitis (Picture 1). Computed tomography of the neck revealed inflammation and secondary thickening in the left parotid gland and sternocleidomastoideus. Three or four hypodense areas, the largest of which was 1 cm in diameter, in the parotid gland were evaluated as reactive lymph glands (Fig. 1). No material was obtained at fine needle aspiration of the parotid gland performed for diagnostic purposes. Serum antibody tests were performed for other causes of non-suppurative parotitis, such as mumps, influenza, parainfluenza cytomegalovirus, coxsackie, echo virus, RSV, HIV, hantavirus, dengue virus and toxoplasmosis, but no positive findings were obtained. Specific serological tests for monospot and EBV and brucella tube agglutination tests were also negative. Saliva sample of patient could be sent to reference laboratory at the second week of the disease. Although the result was negative by real-time PCR for CCHF virus, we thought that this could be possible by reason of latest stage of the acute disease. Finally, we concluded that since all known causes of parotitis had been excluded, this parotitis might be CCHF-associated.

In addition to adjuvant therapy aimed at CCHF, the patient was also given symptomatic treatment for parotitis, such as analgesic and antipyretic drugs, and was discharged on day 8 once a significant improvement in clinical and laboratory findings had been established.

4. Other similar and contrasting cases in the literature

Aksoy et al. reported an epididymo-orchitis in a 53-year-old male patient diagnosed with CCHF. Toth et al. described an acute bilateral parotitis case in a 55-year-old immunocompetent patient diagnosed with dengue virus. Pettersson et al. were detected hantavirus-specific IgA in saliva and viral antigen in the parotid gland in patients with hemorrhagic fever with renal syndrome.

5. Discussion

Since CCHF clinically resembles Ebola Hemorrhagic Fever (EHF) it is also known as “Asian Ebola virus”. Both are generally seen in countries without such modern medical facilities as biosafety level 4 laboratories, so it is not easy to perform pathophysiological investigations regarding these diseases. If other viral hemorrhagic fevers are excluded, clinical course, laboratory findings, pathological findings and immune responses to the virus are similar for both viruses, and there are also thought to be similar mechanisms involved in the pathogenesis of the disease caused by the two viruses. Several animal studies have meant that the pathogenetic mechanisms in EHF have been investigated in greater detail compared to CCHF. While the pathogenesis of CCHF is still not completely understood, the endothelium and mononuclear phagocyte system are the virus’s main target. As with EHF, the general pathogenetic characteristic of the infection is thought to stem from suppression of type 1 interferon response as a result of necrosis of dendritic cells and macrophages that would initiate antiviral response, and immune response defect developing in the host as a consequence. Together with this damage, the virus spreads to organs with a similar structure containing macrophage and dendritic cells, such as the liver, spleen and lymph nodes. Proinflammatory cytokines, chemokines and other mediators released from infected cells cause vascular permeability, rapidly increasing systemic inflammation, and widespread intra-vessel coagulation.

At the same time, the virus causes multifocal necrosis by spreading to the parenchymal cells of organs such as the liver, spleen, adrenal cortex and macrophage, dendritic cell destruction leads to widespread damage in such lymphoid tissues. Since the parotid gland is an organ that harbors many lymphoid structures in and around it, we thought that in our case the CCHF virus led to a parotitis picture with the inflammation it caused by spreading directly to the parotid gland lymph structures.

Clinically, parotitis may be encountered in suppurrative or non-suppurative forms. In suppurrative parotitis, bacteria such as Staphylococcus aureus and oral aerobes/anaerobes are the agents involved and are more frequently encountered in debilitated, dehydrated and elderly patients who have undergone surgery, while in non-suppurative parotitis the most frequent cause is mumps, although influenza, parainfluenza, coxsackie, echo viruses, CMV, HSV, HIV, EBV, lymphocytic choriomeningitis virus, hemorrhagic
fever viruses such as hantavirus, dengue virus, *Mycobacterium tuberculosis* and other atypical microbacteria may also, rarely, cause parotitis. Clinical findings are very similar among the hemorrhagic fever viruses which caused by parotitis. So serologic and molecular tests are essential for the differential diagnosis of them. In one study, a 55-year-old, previously healthy, white man presented after experiencing malaise, hyporexia, frontal headache, retro-orbital pain, and fever for 3 days. He also complained of generalized arthralgias, myalgias, and severe low backache. Bilateral symmetric preauricular swelling, which lifted the earlobe forward and obscured the mandible angle. Dengue virus was detected in the saliva and serum of the patient by PCR. At the same time, many of the other possible reasons of parotitis were excluded in the patient and he was accepted as parotitis associated with dengue virus. In our case, hemorrhage developed following a 2-week period of weakness, and the parotitis picture emerged after these symptoms. Findings such as no risk factor being determined in terms of bacterial parotitis, no fever or purulent discharge at follow-up, low serum WBC, and CRP being almost negative were evaluated more in favor of viral parotitis. Although the patients was at advanced age for mumps, since non-suppurative parotitis cases most frequently have viral causes and are endemic in Turkey, he was investigated for mumps with serum antibody tests, but no result in favor of acute infection was determined. The fact that diagnosis was confirmed as CCHF suggested that the possibility of other viral etiologies due to viral interference appeared remote. Nonetheless, other rarely seen viral agents that can cause non-suppurative parotitis were excluded by aiding serologic and molecular tests, and since the patient had confirmed CCHF by PCR positivity, we diagnosed CCHF-associated parotitis. There is no doubt that, if it is possible, the most definitive diagnosis can be achieved by the PCR of the fine needle biopsy material in such patients but unfortunately that is not possible to do it for every patient especially with high bleeding risk. The detection of PCR in saliva is another approach for this purpose. But it should keep in mind that, PCR positivity in saliva does not submit a definitive proof related to parotitis which is to be developed with these viruses in fact. Because PCR positivity in saliva is possible finding for the patients with hemorrhagic fever virus infections. So detection of PCR in saliva had been only used as an alternative tool for the diagnosis of CCHF virus infections just as in some studies. And on the other hand, PCR positivity can be develop even in the absence of parotitis in hemorrhagic fever patients. So clinical findings of parotitis are very important in a laboratory confirmed hemorrhagic fever virus patient for put on the diagnosis of parotitis which associated with hemorrhagic fever virus.

**Conflict of interest**

The authors have no conflict of interest to report.

**References**