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Lymphocytic choriomeningitis virus infection following occupational ocular exposure

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SUMMARY

A man in his mid-20s presented to the occupational health service following an ocular projection with a concentrated solution of lymphocytic choriomeningitis virus (LCMV clone-13). Subsequently, a regular clinical and biological follow-up was initiated. 7 days after exposure, the patient developed influenza-like symptoms. During the acute phase, specific RT-PCR testing of blood plasma was negative for LCMV. Symptomatic treatment was administered, and the symptoms resolved after a few days. The patient remained asymptomatic in the following weeks. Serological follow-up detected a seroconversion 6 weeks after exposure, indicating a recent infection. The occupational health service's protocol, comprising clinical monitoring and serological surveillance, facilitated the detection of seroconversion. This case underscores ocular mucosal exposure as a route of occupational LCMV transmission, which is often not considered. It served as an opportunity to review and enhance prevention measures and laboratory protocols within the biosafety level P2 facility.

BACKGROUND

Lymphocytic choriomeningitis virus (LCMV), a member of the Arenaviridae family, is transmitted by the common house mouse. Human infections primarily result from direct contact with body fluids or inhalation of aerosolized droplets of contaminated body fluids.[1] While LCMV infection is usually asymptomatic or results in a mild self-limited illness in immunocompetent adults, it can lead to severe disease such as meningitis.[2] Research laboratory workers can be exposed to LCMV while handling infectious material or infected mice. Previous studies or case reports have primarily documented acute infection after percutaneous inoculation of the virus.[3–6] Here, we report a documented lab-acquired LCMV infection following ocular exposure. This mode of contamination warrants consideration when devising prevention strategies, particularly in research laboratory settings.

CASE PRESENTATION

A man in his mid-20s presented to the occupational health service following an ocular projection that occurred 2 days prior when he was working in a research laboratory. The exposure involved a concentrated solution of LCMV variant clone-13 used to infect mice. The incident happened while he was injecting a solution containing an LCMV concentration of 10^7 plaque forming units (PFU)/mL into the tail vein of a mouse. The syringe contained 200 µL of solution and was fitted with a hollow needle. While injecting, he felt a resistance and withdrew the needle without releasing the pressure on the syringe, resulting in a splash of solution on his face, including on his right eyelid and right eye, as he leaned forward to improve visibility. According to the laboratory safety concept (biosafety level 2), he used a biosafety cabinet II for all manipulations involving group 2 biological agent and should have been wearing protective glasses in case of a risk of liquid projection. He was not wearing protective glasses, considering that the window of the protective Plexiglas hood provided sufficient protection. Immediate first aid measures were taken by thoroughly washing the face and eyes for 5 min. The estimated volume of the splash was approximately 50 µL, corresponding to 5×10^5 PFU.

A regular clinical and biological follow-up was initiated in accordance with the occupational health service protocol, scheduled at 1, 2, 3, 6 and 12 weeks post exposure, as well as in the event of symptoms. 7 days after the exposure, the patient developed influenza-like symptoms with chills, fever (39.5°C), fatigue, myalgia, headache with mild photophobia, dizziness, sensation of blurred vision at the periphery of the visual field, difficulty swallowing, nausea and painful swelling in the right submandibular region. He presented to the emergency room 2 days after the onset of symptoms. The clinical examination, including a neurological assessment, was normal except for the presence of a right submandibular lymphadenopathy.

INVESTIGATIONS

At the emergency room, blood tests revealed mild leucopenia (3.4×10^9/L) and mild thrombocytopenia (124×10^9/L). There were no signs of an inflammatory syndrome, and the HIV serology was negative. Specific RT-PCR test conducted on blood plasma for LCMV, Epstein-Barr Virus (EBV), cytomegalovirus (CMV) and SARS-CoV-2 were negative. Following discussion with the patient, a decision was made not to perform a lumbar puncture given the low probability of complications in the event of viral meningitis.

DIFFERENTIAL DIAGNOSIS

The additional laboratory tests made it possible to rule out other viral infections considered in the differential diagnosis (HIV, EBV, CMV, SARS-CoV-2).

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TREATMENT

In the absence of neurological clinical abnormalities and that of a specific treatment for LCMV infection, he was discharged with paracetamol and ibuprofen.

OUTCOME AND FOLLOW-UP

The symptoms resolved after a few days and the patient was on sick leave from work for a total of 4 days. The follow-up was resumed at the occupational health service with a clinical evaluation at 1, 2 and 3 weeks post exposure and serological testing for LCMV at 1, 2, 3, 6 and 12 weeks post exposure. The patient did not develop any additional symptoms during the follow-up period. Serological testing was performed in a specialised laboratory in France using a seroneutralization assay in cell culture with replicative virus, which measures the serum's ability to neutralise the growth of the virus. While this method cannot differentiate IgM and IgG antibodies, it is highly specific. Initial samples returned negative results. However, 6 weeks post exposure, seroconversion was detected, with a rise in specific LCMV antibodies to a titre of 1:20 (negative reference<1:20) and then increased again to a titre of 1:320 at 12 weeks post exposure. These results strongly indicate a recent infection, with seroconversion occurring in the absence of an alternative diagnosis.

DISCUSSION

This symptomatic case of an LCMV infection followed an accidental occupational ocular exposure to a small amount (approximately 50 µL) of a solution containing a high concentration of LCMV (estimated dose received of 5×10^5 PFU). Previous case reports of occupational contamination of LCMV have primarily described percutaneous transmission or inhalation of biological fluids.[3–6] Several decades ago, a laboratory worker infected herself following a conjunctival injury caused by glass powder contaminated with LCMV.[7] To the best of our knowledge, we report the first documented case of seroconversion for LCMV following ocular exposure through a mucosal contact.

Since 2015, other cases of accidental LCMV exposure involving research laboratory workers have been reported to our occupational health service. These cases included a bite from a previously infected mouse which had already partly eliminated the virus as well as three needle prick injuries; the first from a needle soiled with blood from a previously infected mouse, the second from an empty needle immediately after administration of the LCMV containing solution to a mouse and the third from a needle coupled to a syringe containing a concentrated solution of LCMV. Of these four cases, all except the latter remained asymptomatic with no seroconversion during the follow-up period. In asymptomatic cases, we presume that the inoculum was significantly lower compared with a direct contact with a solution of LCMV, as seen in needle stick injuries or ocular splashes.[4 8]

While laboratory safety protocols and first aid measures are clearly defined, precise monitoring guidelines after occupational exposure to LCMV are currently lacking. Prophylactic vaccines, postexposure prophylaxis and specific treatments for LCMV are not yet available. Treatment primarily focuses on symptomatic relief and the efficacy of ribavirin in improving outcomes for patients with LCMV infection remains unclear.[9] Our occupational health service has established a standardised procedure for managing occupational injuries involving LCMV exposure, which includes clinical evaluation and serological monitoring. Additional LCMV RT-PCR testing is warranted if symptoms develop. Typically, LCMV RT-PCR performed during the acute phase of symptoms is a sensitive and appropriate diagnostic tool for detecting an LCMV infection,[10] but the kinetics and magnitude of serum viraemia in human infection are unknown.[4] However, in the case we present here, the diagnosis was not initially confirmed. The patient developed aspecific influenza-like symptoms and the RT-PCR test on blood plasma showed a negative result at that time. The negative finding could result in a viral load below the detection threshold of this RT-PCR assay. Furthermore, the fact that the patient did not develop a secondary phase of symptoms, such as meningitis, supports the observation that LCMV infection is generally asymptomatic or mild, self-limited illness.[2]

Serological monitoring revealed seroconversion for LCMV at 6 weeks post exposure, with a subsequent increase in antibody titre between the 6 and 12 weeks postexposure samples, confirming an LCMV infection. With no alternative exposure to LCMV identified, we concluded that the infection resulted from the accidental exposure. The follow-up protocol, which included serological monitoring, effectively detected the seroconversion, unlike RT-PCR, which failed to detect the acute infection.

Despite appropriate risk assessment and safety protocols in research laboratories, LCMV infections still occur among laboratory workers.[5 6 11] In the case presented here, the hood was not sufficiently lowered and a risk of splash of liquid existed when approaching the mouse's tail. Current prevention measures were reassessed and reinforced by adding the use of protective glasses when performing intravenous inoculation of mice, even when working in a biosafety cabinet.

Laboratory workers require comprehensive education on the various transmission modes and clinical presentation of LCMV infection, along with regular training in safe handling procedures of LCMV or infected animals with LCMV. Additionally, well-defined emergency procedures in the event of an accidental exposure should be readily accessible and prompt communication with the occupational health service is imperative.

In conclusion, this case highlights the significance of ocular mucosal inoculation as a route of accidental occupational transmission of LCMV, which is rarely considered in the literature. Occupational acute LCMV exposures are likely underreported, and workers may lack adequate awareness of the risk of infection and/or seroconversion. Despite LCMV infection being typically asymptomatic or mild and self-limiting, a better understanding of the various transmission routes is essential to enhance prevention efforts in research laboratories.

Learning points

- Seroconversion for lymphocytic choriomeningitis virus (LCMV) can occur through a mucosal contact.
- Occupational acute ocular LCMV exposures are likely not considered, and laboratory workers are insufficiently informed about the risk of infection and seroconversion.
- Better understanding of the different routes of transmission is crucial to improve infection prevention efforts in research laboratories.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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