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Case Report

A Case of Disseminated Adenovirus in an Immunocompetent Individual

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Abstract

Background: Adenovirus infections are typically associated with minor respiratory, gastrointestinal, and conjunctival symptoms, with severe cases being more common in immunocompromised individuals. However, our case report details a rare instance of an immunocompetent patient suffering from disseminated adenovirus resulting in bacteraemia, acute respiratory distress syndrome and encephalitis.

Case Presentation: A previously healthy 49-year-old male presented with symptoms initially suggestive of heat stroke, but rapidly deteriorated developing respiratory distress and fluctuating consciousness. Extensive diagnostic evaluation eventually revealed disseminated adenovirus, infections notably in cerebrospinal fluid and blood. Supportive management commenced in the intensive care unit. Cidofovir and intravenous immunoglobulins were administered, and the patient was monitored closely for potential complications.

Conclusion: This case emphasises the importance of not underestimating the potential severity of adenovirus infections in otherwise healthy individuals.

Introduction

Typically, adenovirus causes minor upper and lower respiratory infections, gastrointestinal tract infections and conjunctivitis. Young children are more susceptible to severe adenovirus infections due to their immature humoral immunity (1) as well as immunocompromised patients. It is rare for immunocompetent adults to suffer from severe infections. Here we report a case of interest of an immunocompetent patient in which disseminated adenovirus infection led to acute respiratory distress syndrome and encephalitis. This is meant to highlight the importance of not overlooking adenovirus in healthy individuals.

Case Presentation

A 49-year-old male with no past medical history presented to the emergency department with a history of diarrhoea, lethargy, fever and slurred speech. His temperature was 39.6 oC, blood pressure was 131/94mmHg with a pulse rate of 103 bpm, saturations of 95% on room air and respiratory rate of 24 breaths/min. The impression was initially one of heat stroke as this event occurred during a heat wave, with temperatures reaching over 40oC. The patient was referred to the intensive care unit in view of respiratory distress and fluctuating consciousness. As the patient's oxygen requirements increased, with saturations of 94% on 15 L/min on a normal face mask and mottling of lower limbs, a CT pulmonary angiogram was performed. This revealed bilateral multifocal, patchy areas of ground glass changes and consolidations with differentials including organising and eosinophilic pneumonia. Piperacillin/tazobactam was started. Initially, a trial of high-flow nasal oxygen was started however he continued to deteriorate requiring intubation after one hour. Neurology input recommended a lumbar puncture to exclude encephalitis. The adenovirus RT-PCR from CSF was positive. An MR head was also performed which showed no evidence of significant intracerebral pathology and venous sinuses appeared patent.

There was no information on the serotype of adenovirus. The adenovirus RT-PCR from EDTA blood was detected with more than 10,000 copies/ml. On the fourth day of ITU admission, the infectious disease team prescribed cidofovir 5mg/kg with intravenous fluids administered before and kept on maintenance fluids after as probenecid was unavailable. Renal function was monitored judicially and fortunately never suffered an acute kidney injury. On sedation breaks the patient was not waking up appropriately and an EEG was taken on the fifth day. This showed encephalopathy with no seizure activity. Blood cultures repeated on this day were positive for Staphylococcus hominis and was hence kept on antibiotics for a total of fourteen days. Repeat adenovirus titre from blood EDTA on day 12 showed 64,5000 copies/ml and thus a second dose of cidofovir was repeated one week after the first dose was given. Probenecid was available and given. This same day he was started on 45g of intravenous immunoglobulins daily for a total of 6 days. The highest fraction of inspired oxygen the patient required was 0.65. This was weaned over ten days and the patient was successfully extubated to non-invasive ventilation the day after the second dose of cidofovir. He was found to be dysarthric, otherwise well. Over the following days, the patient became more oriented and appropriate, improving steadily and was discharged from ITU. Adenovirus RT-PCR in blood was not detected 11 days following the second dose of cidofovir. The patient was eventually discharged to a rehabilitation centre.

Discussion

Adenovirus commonly presents with a self-limiting respiratory, gastrointestinal, or conjunctival infection. 67 serotypes have been identified and classified into 7 species (2) with serotypes 3, 4, 7 and 21 accounting for the more severe infections (3). It is spread via aerosolized droplets or faecal-to-oral pathways (4). Many infected are asymptomatic however it most commonly causes flu-like symptoms. The incubation period is between 2 to 14 days (4) meaning symptoms may not present up to 14 days after contact with the virus. Disseminated adenovirus is when two or more organs are affected which is uncommon in immunocompetent patients (5).

Positive cultures of adenovirus may be observed in nasal swabs, throat swabs, bronchoalveolar lavage fluid, eye swabs or scrapings, stool samples, urine samples or tissue biopsies such as in hepatitis. PCR

of blood or CSF samples may also reveal adenovirus. However, not all positive cultures correlate with significant disease (2). Taking quantitative viral load measurements would help identify invasive diseases and aid in management when taken repeatedly (2).

Treatment for adenovirus is limited. There is currently no available adenovirus vaccine for the public and there are no approved anti-viral agents for treating adenovirus (6). Cidofovir is a cytosine nucleotide analogue which acts by inhibiting viral DNA polymerases (7). It has a broad-spectrum antiviral action against herpes, papilloma and pox viruses (8). Cidofovir is not FDA-approved for the treatment of adenovirus (4) however its use has been reported to be successful in management. It is given intravenously with standard doses being 5mg/kg weekly or fortnightly or 1mg/kg twice weekly. The main concern limiting use is its nephrotoxicity as well as myelosuppression and uveitis (7). More than 90% of cidofovir is recovered unchanged in urine over 24 hours (9). To minimize nephrotoxicity, intravenous pre-hydration and oral probenecid are advised to be given alongside. Probenecid is a sulphonamide derivative inhibiting inorganic acid transport in the distal renal tubule, used more commonly as a uricosuric agent in the treatment of gout (10). It also reduces the renal clearance of cidofovir since it blocks its active tubular secretion. The standard dose of probenecid is 2g 3 hours before cidofovir then 1g at 2 and 8 hours after cidofovir (8). The challenge arises when choosing which patients would benefit from cidofovir as a treatment option for adenovirus. It seems reasonable to consider this drug in immunocompetent patients with disseminated disease, with high viral loads in blood, persistent lymphopenia or immune deficits (7). Intravenous immunoglobulins are typically used to manage immunodeficiency and autoimmune states. They may also be used as specific therapy against infections (11). Intravenous immunoglobulin therapy has been shown to suppress adenoviral replication through neutralisation by viral antibodies. Early administration has been shown to decrease the use of mechanical ventilation in immunocompetent children (12).

When reviewing the medical literature, case studies from Singapore, China, and Chicago were found to describe rare cases of disseminated adenovirus in immunocompetent patients. In the cohort from Singapore, 4 cases are reported of rapidly worsening respiratory failure with multi-organ dysfunction requiring ECMO (3). The adenovirus serotype identified in all 4 patients was 7. The patients were treated with cidofovir 5mg/kg except one with 2mg/kg in view of kidney disease. This was given together with probenecid after adequate hydration in all but one patient as unfortunately treatment was withdrawn. The 3 surviving patients all required dialysis for acute kidney injury (3). In a case report from Chicago (5) an immunocompetent female tested positive for adenovirus on respiratory and stool PCRs. She was treated with cidofovir 3mg/kg along with probenecid successfully. From China, a prospective study showed that 5 immunocompetent patients with high fevers and respiratory failure suffered from adenovirus serotype 55 infection leading to acute respiratory distress syndrome. Four out of the five had not survived, none of which were given cidofovir (13). Our case of disseminated adenovirus infection successfully managed with cidofovir treatment aligns with and contributes to this growing body of evidence from the literature.

Conclusion

This case highlights the significance of adenovirus infections, even in healthy and immunocompetent individuals as they can pose a life-threatening risk. Monitoring viral load could offer valuable insight into the severity, response to therapy and prognosis of the disease (13). The high mortality rate associated with this condition, even with respiratory support, marks ECMO as a potential intervention to consider (3,13). Additionally, early administration of cidofovir in immunocompetent patients could be beneficial (1).

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