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Treatment of Severe Adenovirus Infection with HAdV-B21 in a Young Obese Male with Normal Immunity

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Abstract

Background: Adenovirus infections typically present mild to moderate symptoms in immunocompetent individuals. However, the emergence of severe adenovirus pneumonia, particularly with rare serotypes like Human Adenovirus B21 (HAdV-B21), in patients without underlying immunodeficiency challenges existing clinical paradigms and calls for novel treatment strategies.

Case Presentation: We report a case of severe adenovirus infection with HAdV-B21 in a 32-year-old severely obese yellow Asian race male with normal immunity. The patient was admitted with severe respiratory distress, including fever, cough, sputum production, and dyspnea, requiring invasive mechanical ventilation. The oxygenation index was critically low at approximately 62mmHg. Traditional therapeutic interventions, including prone ventilation, hormonal anti-inflammatory therapy, and ribavirin antiviral therapy, were employed, leading to a successful outcome without needing extracorporeal membrane oxygenation (ECMO).

Intervention and Outcome: The combined use of hormonal anti-inflammatory therapy and ribavirin antiviral treatment was pivotal in the patient's recovery. This approach facilitated the improvement of the patient's oxygenation index and eventual weaning from mechanical ventilation. The patient fully recovered, with adenovirus nucleic acid turning negative on the 13th day of treatment.

Conclusion: This case underscores the potential for severe adenovirus pneumonia in immunocompetent adults, especially with rare serotypes like HAdV-B21. The successful recovery of our patient highlights the efficacy of a combined hormonal and antiviral treatment strategy in managing severe adenovirus infections, offering valuable insights for future clinical management.

Keywords: ***Severe adenovirus infection; HAdV-B21; Immunocompetent adult; Ribavirin; Hormonal anti-inflammatory therapy; Mechanical ventilation***

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1. Highlights

- A rare case of severe HAdV-B21 infection in an immunocompetent adult.
- Successful use of combined ventilation, anti-inflammatory, and antiviral therapy.
- Significant improvement in oxygenation index and full recovery.
- Negative conversion of adenovirus nucleic acid confirmed recovery.
- Provides insight into managing rare severe adenovirus infections.

2. Introduction

Adenoviruses constitute a diverse group of pathogens capable of causing a wide array of human diseases, ranging from mild respiratory illnesses to severe, life-threatening conditions. These non-enveloped, double-stranded DNA viruses are known for their stability in the external environment, facilitating transmission and causing outbreaks in communal settings such as military barracks and healthcare facilities [1]. In immunocompetent individuals, adenovirus infections typically manifest as self-limiting conditions affecting the respiratory tract, gastrointestinal system, or conjunctiva. However, severe forms of the disease, including pneumonia, can occur, particularly in immunocompromised patients or in the context of novel or re-emergent adenovirus serotypes. The rarity of severe adenovirus infections in individuals with normal immunity makes each case significantly contribute to our understanding of the virus's pathogenic potential and clinical management [2].

The epidemiology of adenovirus infections reveals a complex landscape of more than 50 serotypes, each associated with different clinical presentations and varying degrees of severity [3]. Human Adenovirus B21 (HAdV-B21) is particularly interesting due to its uncommon occurrence and the lack of data regarding its epidemiology and clinical impact. HAdV-B21 has been sporadically reported in the literature, with cases often presenting severe symptoms and a higher risk of progression to acute respiratory distress syndrome (ARDS). This serotype's ability to cause severe disease in otherwise healthy adults highlights a critical gap in our understanding of adenovirus pathogenesis and the need for enhanced surveillance, diagnosis, and treatment strategies. Existing literature predominantly focuses on common serotypes, such as types 3 and 7, leaving a knowledge void around the clinical management of rarer serotypes like HAdV-B21 [4].

Current challenges in treating adenovirus infections underscore the necessity for novel therapeutic approaches and a better understanding of the virus's behavior in immunocompetent hosts. The lack of specific antiviral treatments approved for adenovirus infections necessitates a reliance on supportive care and broad-spectrum antivirals, which may not be optimally effective against all serotypes. The case of severe HAdV-B21 infection described in this report addresses this gap by illustrating the successful management of a rare and severe adenovirus infection in an immunocompetent adult. Through this case, we explore the efficacy of combined hormonal anti-inflammatory and ribavirin antiviral therapy, shedding light on potential treatment avenues for similar future cases. This contribution is poised to enrich the existing knowledge on adenovirus infections, providing valuable insights into the epidemiology, clinical presentation, and management of rare serotypes like HAdV-B21 in the general population.

3. Case Report

A 32-year-old yellow Asian race male with a body weight of 140 kg and no known underlying immune deficiencies presented with a 15-day history of intermittent cough and sputum production without apparent cause. Four days before hospital admission, the patient experienced a worsening of symptoms, characterized by repeated fever peaks. In response, he self-administered amoxicillin and anaxine without notable improvement. Subsequently, he sought treatment at a local clinic, where he received an unspecified antibiotic infusion. Persisting symptoms prompted a visit to a local health center, where a chest X-ray was performed, though details remain unspecified. Due to deteriorating respiratory function, the patient was administered high-flow oxygen inhalation (F 60L/min, FiO2 100%) and commenced using moxifloxacin and imipenem for anti-infection at a local hospital. Despite these measures, the patient's condition did not significantly improve, necessitating endotracheal intubation the same afternoon. Arterial blood gas analysis post-intubation revealed pH 7.26, PCO2 66.0 mmHg, PO2 62.0 mmHg, K+ 4.30 mmol/L, Na+ 134 mmol/L, and Lac 1.0 mmol/L. Laboratory tests indicated PCT 0.15 ng/ml, IL-6 59.91 pg/ml, and normal white blood cell count. Staining and microscopy for acid-fast bacilli, Pneumocystis carinii, nucleic acid tests for influenza A and B viruses, and novel coronavirus returned negative results.

Upon transfer to our facility due to insufficient oxygenation, the patient's oxygenation index was approximately 60mmHg, indicative of severe pneumonia, type II respiratory failure, and severe acute respiratory distress syndrome (ARDS), with an APACHE II score of 21, correlating to a mortality risk of 75.68%. The patient's family declined ECMO treatment due to financial constraints. Bronchoscopic alveolar lavage revealed bilateral airway mucosal hyperemia and edema without evidence of sputum obstruction. Following lavage (FIG. 1), cultures and smears were obtained for further analysis. Treatment was initiated with azithromycin and moxifloxacin for anti-infection, and an intravenous injection of methylprednisolone 60 mg was administered for its anti-inflammatory effects, alongside prone ventilation, low tidal volume ventilation, plateau pressure limitation, fluid rebalance, and lung re-expansion strategies.

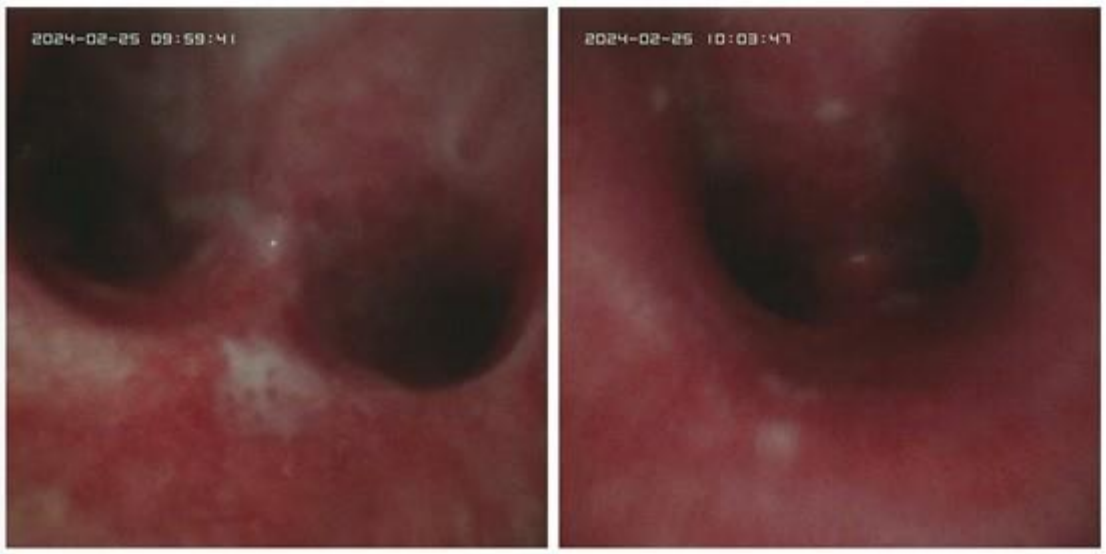

FIG. 1. **Airway condition under fiberbronchoscopy on the first day of admission.**

On the second day post-admission, the oxygen concentration was reduced to 50%, with an improved oxygenation index of approximately 120 mmHg. A subsequent chest CT scan (FIG. 2 A-D) and adenovirus nucleic acid test confirmed a strong positive result for adenovirus with a high titer. Ribavirin therapy was initiated at a dosage of 0.5 g every 12 hrs. A follow-up chest CT on day 9 of treatment showed significant improvemen (FIG. 2 E-H). The methylprednisolone dosage was tapered to 30 mg intravenously, and by day 10, the patient's oxygenation index had stabilized around 300 mmHg, allowing for successful ventilator weaning and tracheal intubation catheter removal. By day 13, adenovirus nucleic acid tests returned negative, marking the patient's recovery and subsequent discharge.

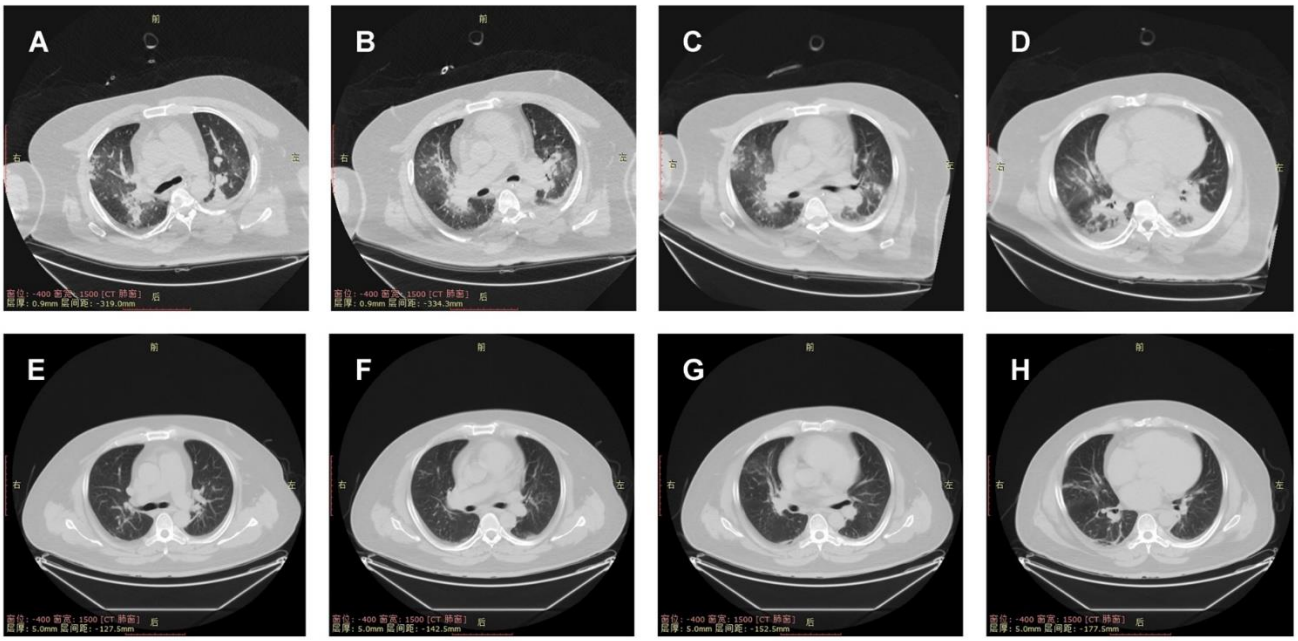

FIG. 2 **Chest CT on day 1(A-D) and day 9 of admission(E-H).**

This case emphasizes the effectiveness of a multidisciplinary treatment approach, including using ribavirin and corticosteroids, in managing severe adenovirus infection, specifically HAdV-B21, in an immunocompetent adult. The intervention strategy, underscored by timely antiviral and anti-inflammatory therapies, contributed significantly to the patient's recovery, underscoring the potential for such regimens in similar cases.

4. Discussion

Adenoviruses constitute a significant etiology of viral pneumonia, contributing to approximately 2% of all community-acquired pneumonia cases [5-6]. While predominantly observed in pediatric populations, adenovirus pneumonia can also affect healthy adults, particularly those residing or working in confined or densely populated settings, such as military environments [6]. The precise mechanisms underlying the susceptibility of immunocompetent adults to adenovirus infection remain elusive. However, it is hypothesized that environmental factors, such as suboptimal sanitary conditions observed at the patient's workplace—a

construction site—may play a contributory role in the pathogenesis [7]. Notably, adenoviruses exhibit resilience against a wide array of environmental disinfectants, yet their viability can be effectively neutralized by solutions containing 95% ethanol.
In cases of severe adenovirus pneumonia, the predominant symptoms include sputum production and dyspnea, with approximately 90% of patients exhibiting fever and over 90% presenting with cough. Notably, fewer than 30% of patients display neurological or gastrointestinal symptoms [8]. This case aligns with these findings, manifesting fever, cough, and sputum at disease onset, alongside white blood cell counts and procalcitonin levels within normal ranges, and a presence of lymphocytopenia, consistent with descriptions in the literature. Adenoviruses exhibit tissue tropism, with their clinical manifestations varying according to the infecting serotype. The HaV-B21 serotype, initially identified in a patient with conjunctivitis, has been linked to respiratory infections in children. However, cases of respiratory failure and severe acute respiratory distress syndrome (ARDS) associated with HaV-B21, particularly the B21a subtype, are relatively rare but have been noted for their severity and potential lethality [9-10].

For accurate diagnosis of adenovirus pneumonia, etiological evidence is essential. Although virus isolation and serotyping are considered the definitive standard for adenovirus diagnosis, their application in early clinical settings is limited due to the time-consuming nature of these methods. Currently, the most prevalent clinical diagnostic technique is antigen detection. This method involves analyzing patients' nasopharyngeal secretions, nasopharyngeal swabs, sputum, and bronchoalveolar lavage fluid using the immunofluorescence assay to detect the adenovirus capsid hexon antigen. Notably, the detection rate peaks 3-5 days prior to symptom onset, and in severe cases, the virus may remain detectable for over two weeks [11]. Polymerase chain reaction (PCR) assays offer a quantitative approach to viral detection. Carmen Andrea Pfortmueller highlighted in her 2019 case report the utility of quantifying viral load in alveolar lavage fluid and plasma via PCR to inform clinical management and prognosis assessment [12]. Macrogenome sequencing presents significant benefits for identifying pathogens in patients with critical infections. For infections with non-specific pathogens, early identification and subsequent targeted therapy are critical to improving patient survival rates.

Currently, the management of severe adenovirus pneumonia lacks specific treatments, with care predominantly supportive. The therapeutic efficacy of pharmacological interventions remains underexplored due to the scarcity of large-scale, controlled clinical studies. Cidofovir, approved by the US FDA for treating severe adenovirus pneumonia, is not available in China, and its clinical efficacy in this context remains uncertain. A 2019 Swiss study reported the deaths from multiple organ failure of two patients with severe adenovirus pneumonia despite receiving ECMO-supported cidofovir treatment [12].

While there have been instances of successful outcomes attributed to cidofovir, discerning whether these results stem from the drug's action or other therapeutic influences remains challenging. Ribavirin, a guanosine analog with in vitro efficacy against both DNA and RNA viruses, is indicated for cytomegalovirus infections according to the Chinese pharmacopeia. Jie Gu's 2021 meta-analysis identified ribavirin as the second most frequently administered medication following cidofovir for adenovirus pneumonia (15/228, 6.6%) [13]. Byung Woo Yoon's 2017 report detailed a successful treatment of adenovirus pneumonia with oral ribavirin in a 39-year-old male [14].

Additionally, a 2022 observational study by Shen K involving 52 pediatric patients with adenovirus pneumonia found that ribavirin monotherapy significantly shortened the duration of non-respiratory symptoms [15-16]. In this case, the patient's oxygenation showed no significant improvement until ribavirin was administered three days post-admission, at which point a substantial enhancement in oxygenation was observed, highlighting ribavirin's potential effectiveness in this patient.

In the initial phase of severe infections, both pro-inflammatory and anti-inflammatory responses are activated concurrently. The dominant response significantly influences the prognosis of critically ill patients. Glucocorticoids serve an essential anti-inflammatory function in managing severe adenovirus pneumonia by moderating the excessive immune reaction during the infection's early stages and diminishing pulmonary exudation. Concurrently, current guidelines for managing severe acute respiratory distress syndrome (ARDS) endorse the early application of glucocorticoids and immunoglobulin therapy. In the case discussed, timely administration of glucocorticoid therapy was crucial in reducing pulmonary exudation, and the adoption of a prone position proved pivotal for the obese patient to navigate through the most critical phase on the night of admission.

5. Conclusion

In conclusion, severe adenovirus pneumonia is associated with a high mortality rate, with treatment predominantly reliant on supportive measures. In scenarios lacking ECMO support, the emphasis on prone position ventilation and ARDS ventilation strategies becomes central to care, while early intervention with glucocorticoids, immunoglobulins, and antiviral therapy serves as complementary approaches.

6. Acknowledgements

Not applicable.

7. Author Contribution

Xun Zhang and Shili Zhong collected all information about this case and was the major contributor in writing the manuscript. Shifeng Shao, Hong Xiao, Zhen Wang performed all examinations and treated the patient. and Shili Zhong read the first draft of the manuscript and made changes that contribute to the final version. All authors read and approved the final manuscript.

8. Availability of Data and Material

Not applicable.

9. Declarations

9.1 Funding

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9.2 Ethics approval and consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

9.3 Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal

9.4 Competing interests

The authors declare no competing interests.

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