



Outbreak of adenovirus type 55 infection in Israel



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ABSTRACT

Background: Different types of adenoviruses are associated with diverse diseases and with varied disease severity. Adenovirus 55 could be associated with severe respiratory infections.

Objectives: Here, we report on an adenovirus 55 outbreak in two psychiatric institutions in Israel. The objective of this study was to investigate the adenovirus 55 outbreak.

Study design: We studied the clinical parameters of the patients and sequencing analysis of certain parts of the virus gene was performed.

Results: We identified the first patient who developed symptoms (the index case) and we showed that while both patients and staff members of the institutions were infected, the disease in the psychiatric patients was more severe. We attributed these differences to their mental and underlying health conditions.

Conclusions: It is important to monitor for adenovirus infection in the community, especially in mental health institutions to allow appropriate medical care.

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1. Background

Human adenoviruses (HAdV) are double-stranded DNA viruses that belong to the *Adenoviridae* family. There are 51 adenovirus serotypes, determined by neutralization assays, which are grouped within seven species (A–G). In the last years, with the use of sequencing and phylogenetic analysis, the name “types” with the correspondent subsequent numbers started to be used [1]. Potential types (even up to number 67), have been proposed by some authors although this statement has not been widely accepted in the adenovirus community [2,3]. Certain serotypes and types are more commonly associated with specific disease syndromes, epidemiological settings and demographic risk groups. Serotypes 1, 2, 3, 5, 6 and 7 primarily cause respiratory illness [4], while serotypes 40 and 41 mainly cause gastroenteritis [5]. An association between specific types/subtypes and disease severity has been demonstrated [6–9]. Although most infections are self-limited,

adenovirus infections might be severe and even fatal particularly in immunocompromised individuals [10–14,15–17]. In the immunocompromised host, adenovirus can cause severe localized disease or disseminated disease with multi-organ failure [10,11,14]. The fatality rates among such patients range between 50–80% [2,10,11,18].

Adenovirus type 55 is a relatively recently identified pathogen, evolved from recombination between adenovirus 11 and 14 [19,20]. It was first described as serotype 11a and later re-labelled as type 55 because of its recombinant genome [19–22]. Adenovirus 55 has been responsible for outbreaks in military camps [23,24] and has been recognized as a cause of community-onset pneumonia, responsible, in some cases, for severe disease that required hospitalization [25,26].

2. Objectives

We report an outbreak of adenovirus 55 infection that occurred among mentally ill patients in two different psychiatric institutions in the Tel Aviv District, Israel. Out of seventeen suspected (demonstrating influenza-like symptoms) individuals, 9 were infected with

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adeno 55. Out of the 9 confirmed cases, seven required hospitalization, three were hospitalized in intensive care unit. The objective of this work was to investigate this outbreak.

3. Study design

3.1. Ethics

The institutional review board (IRB) of the Sheba Medical Center approved this anonymous retrospective analysis (Helsinki number 1003-14-SMC); informed consent (either written or verbal) was not required.

3.2. DNA extraction and sequencing

Nasopharyngeal and throat swabs (medical wire) were obtained from all 9 patients (two patients were admitted to the Emergency Room but did not require hospitalization). Each sample was obtained at the day of ER/hospitalization. The results were discrepant. DNA extraction was performed using NucliSENS easyMAG (bioMérieux, Marcy l'Etoile, France) semiautomated extractor and eluted in 55 ml elution buffer [27].

Real-time PCR was performed, as previously described, using TaqMan Chemistry on the ABI 7500 instrument [28]. For sequencing we performed additional PCR reaction according to the method previously described [29,30].

The following primers were used
HAdV55 Forward fiber: (position 30,626–30,645)
GAAATTTCTCCAGCAGCA

HAdV55 Reverse fiber: (position 31,921–31,940) AGATTG-GCTCGCTCTGAAAC

HAdV55 Forward penton: (position 13,515–13,534) GAT-GATAGCAGCGTGTGGA

HAdV55 Reverse penton (position 15,442–15,461) CACGGGAT-GTTGGGTAGAAC

For hexon amplification nested PCR was used: Forward1 (position 19,135–19,160) TICTTTGACATTCGIGGIGTICTIGA-3 and Reverse1 (position 20,009–20,030) CTGTACIGCCTGRTTCCACA.

Forward2 (position 19,165–19,187) GGYCCYAGYTTAARCCC-TAYTC and

Reverse2 (position 19,960–19,985) GGTTCTGTCCCCAGAGART-CIAGCA.

The PCR products were purified using the Qiagen High Pure PCR Product Purification Kit (RocheH Diagnostics GmbH, Mannheim, Germany) and sequenced using the ABI PRISM Dye Deoxy Terminator cycle sequencing kit (Applied Biosystems, Foster City, CA). Reaction mixtures were analyzed on the Applied Biosystems model 3100 DNA automatic sequencing systems. The Sequencher 5.0 program (Gencodes Corporation, Ann Arbor, MI) was used to compare the nucleotide sequences. Phylogenetic trees were prepared by nearest neighbor joint analysis using Clustal 6 with 1000 bootstraps, and trees were visualized using TreeView or NJ plot software.

4. Results

4.1. Description of the outbreak

In early June 2013, the Tel Aviv District Health Office (TADHO) was notified of an outbreak of pneumonia among mentally ill patients. At the time of the notification, four mentally ill patients had been hospitalized with pneumonia (Fig. 1), two of whom were residents of a hostel for mental health patients in Tel Aviv, Israel (Cluster A, designated P for patient, 30.5.2013, Fig. 1). The hostel is a special care home which helps rehabilitate psychiatric patients

by providing guidance and support by a trained team of counselors, social workers and nurses. The hostel offers private as well as group counseling to help patients cope with community life. The patients participate together in group activities twice a week (English and music lessons are among the classes that are offered). The tenants share daily activities, such as eating and watching television together.

The hostel is located in the center of Tel Aviv which helps its residents integrate the community and even find a suitable job in the city, according to their capabilities.

The two other hospitalized patients were residents of the same open ward of a psychiatric hospital in the Tel Aviv district, Israel (Cluster B, 1.6.2013, Fig. 1). Three of the four hospitalized patients were transferred to the intensive care unit (ICU) and required respiratory assistance.

The severe nature of the disease prompted the TADHO to conduct an epidemiologic investigation of current cases and active surveillance of any new case of respiratory tract infections (RTI) in the two institutions.

At the beginning of the investigation, a staff member in Cluster A (designated W for worker, 31.5.2013, Fig. 1) also showed symptoms of RTI. He had sought medical care and was diagnosed with pneumonia for which he received ambulatory treatment. Meanwhile, in Cluster B, three residents (designated P for patient, 4.6.2013, Fig. 1) and one staff member (5.6.2013) had symptoms of RTI, three of which had sought medical care and had radiologically confirmed pneumonia. They were each treated by their general practitioner.

Respiratory samples (nasopharyngeal and throat swabs) taken from the four hospitalized patients tested positive for adenovirus 55. The remaining residents of the two psychiatric facilities were closely monitored for any appearance of RTI and respiratory samples were taken from symptomatic patients only, all of which proved positive for adenovirus 55. Later in the month (starting from 9.6.2013, Fig. 1), seven additional cases were identified (six from cluster A and one from cluster B, Fig. 1), two of whom (one from cluster A and one from cluster B) were hospitalized, and both found positive for adenovirus infection.

A common link between the two institutions, namely, the index case (colored yellow in cluster A and B, Fig. 1) was identified. He was a resident of the hostel, who had suffered a surge of his psychiatric condition, resulting in his hospitalization (Fig. 1, cluster A) in the psychiatric ward involved in the outbreak in late May (29.5.2013, cluster B, Fig. 1). At the time of the hospitalization, he fell ill and had high fever and cough. An X-ray was performed and revealed right lower lobe pneumonia. On May 30, his psychiatric condition had been stabilized and he returned to the hostel. He visited the psychiatric ward to receive treatment twice in early June. On June 5, his mental condition worsened and he was admitted to the psychiatric ward once again, while still suffering from respiratory symptoms.

Overall, 17 suspected patients were involved in the outbreak, ten from cluster A (including the index case) and seven from cluster B. Seven patients were hospitalized. Overall, adenovirus infection was detected in eight patients. Four of the 17 suspected patients were staff members (3 in cluster A and 1 in cluster B, designated W, Fig. 1). Mean age was 56 years, and most patients were men (11 out of suspected 17 patients).

4.2. Patient symptoms and treatments

A total of nine patients visited the emergency room, seven of whom were hospitalized. The symptoms of the suspected and the confirmed patients are shown in Table 1. One patient was diagnosed with conjunctivitis, one patient had diarrhea and all nine patients that visited the ER had radiologically confirmed pneumonia. A total of four patients were admitted to the ICU with respiratory deterioration and required mechanical ventilation. Median time

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