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Outbreak report

AN OUTBREAK OF ADENOVIRUS TYPE 8 KERATOCONJUNCTIVITIS IN A NURSING HOME IN MADRID

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This work describes and analyses an outbreak of epidemic keratoconjunctivitis which occurred in 2001 and 2002 in a nursing home for the elderly in Leganes (an area of Madrid). This is the first such published case in Spain with these characteristics and this serotype identification.
Sociodemographic characteristics, epidemic curve and attack rates are described. Comparisons of the data were carried out using a chi2 test for qualitative variable and t-test for quantitative. Factors associated with the illness are explored by means of contingency tables and logistic regression models.
One hundred and two cases were detected, with an attack rate of 36.4% for residents, and 12.9% for workers, not considering spatial or professional differences. The epidemic curve showed an interpersonal transmission pattern. Multivariate analysis identified the following risk factors in the residents: able to wander freely through the building, urinary incontinence and use of shared bathroom. In 34.6% of the conjunctival samples, adenovirus serotype 8 was detected with identical genomic sequence.
Establishment of hygienic sanitary guidance adapted for the cleaning of such establishments and contact with residents as well as early diagnosis and good coordination of human and material resources are key factors in the prevention and control of these outbreaks in closed communities.

Introduction

The clinical manifestations of epidemic keratoconjunctivitis (EKC) were recognised for the first time in 1889 by Austrian investigators (1,2). Adenoviruses are a well recognised cause of keratoconjunctivitis, producing a characteristic sub epithelial punctate keratitis and follicular conjunctivitis which can be seen by examination of eye using a slit lamp (ophthalmic anterior segment microscope or biomicroscope) (3). The more frequently implicated adenoviral serotypes in EKC, corresponding to subgroup D, are 8, 19 and 37 (4). The incubation period is between one and 30 days. The infectious period ranges from 3 days before, to 14 days after onset of symptoms. The described inefficiency of ammoniacal compounds in inactivating adenoviruses, and their good viability on environmental surfaces, improve the epidemic potential of these viruses (5).

Transmission is via person to person spread and fomites. Hands of healthcare personnel, medical devices (such as instruments used in eye examination) and products contaminated by adenoviruses have been implicated in the transmission within healthcare environments (6-10). Described adenoviral EKC outbreaks usually been in specific environments: hospitals, ophthalmology units, emergency services facilities, factories, schools, residences, and camps (5,6,7,8). Factors associated with community outbreaks are the use of pools

(5,6,7,8). Factors associated with community outbreaks are the use of pools, overcrowded conditions, poor hygiene rules , shared use of personal objects and direct physical contact (4). Outbreak control recommendations are based on hand and general hygiene and appropriate disinfection of surfaces.
Only one published study was found which analysed a community outbreak in Spain (11). Our report is the first in Spain to describe the specific serotype identification and the diffusion of an EKC outbreak in a nursing home for the elderly (from December 2001 to March 2002) in Leganes (south of Madrid). The identification of possible risk factors associated with its occurrence and the assessment of the measures adopted for its control are described.

Methods
The case definition used during the investigation is as follows:
"A resident or worker of the establishment having worked at least one day, or a relative of theirs who after 12 December 2001 and before 11 April 2002, was identified with characteristic subepithelial punctate keratitis by slit lamp ophthalmological examination or presented with redness of the eye with one or more of the following: photophobia, foreign body sensation, discomfort, pain, decreased visual acuity or discharge, with a clinical course of longer than 24 hours".
Description of the nursing home:
The establishment concerned is an assisted nursing home with 220 residents located in Leganes (a city located south of Madrid). There are 3 floors divided into 11 modules (groupings of rooms). All the rooms are singles, apart from 16 double rooms which are shared by married couples. There are both individual and shared use bathrooms, depending on the structure of each module. The workforce consists of 140 workers: 96 care staff and 44 non-care staff.

Epidemiological investigation of the outbreak
Clinical and epidemiological information were collected on all residents and workers using a specific questionnaire regardless of whether or not they were cases or not. The following variables were collected: date of onset of symptoms, whether a resident or worker, floor and room number (residents), presence or absence of ability to move around the building freely (referred to as autonomy (residents)), dependence type (residents), cognitive deterioration (residents), age, sex, symptoms, complications, referral, treatment and evolution.
Dependence was scored according to ability to carry out everyday tasks such as to smarten oneself up, get dressed, feed oneself, wash and use the toilet without help and presence of urinary incontinence. Information on the presence or absence of cognitive deterioration was collected from medical records.
Cases were all those who met the definition of case, and non-cases were all residents who did not. An epidemic curve was drawn. Overall and specific attack rates in residents (by floor, module and bathroom distribution) and staff were calculated and compared in contingency tables. Differences with regard to age and sex in residents and workers between cases and non-cases were explored. The chi2 test or the exact Fisher test for the comparison of categorical variables and the t-test for quantitative variables were used.
The association in residents between illness and autonomy, incontinence, food, toilet, bathroom and dress dependence, cognitive deterioration, and availability of private bathroom were explored in contingency tables and using forward stepwise method in logistic regression model with probability criteria for entry of 0.05 and for removal of 0.10, and classification cutoff of 0.5. The OR (odds ratio) and its 95% confidence interval was obtained to estimate its association and confusion for age and sex were controlled in the logistic regression.

Laboratory investigation:
Conjunctival fluid samples taken from 26 symptomatic patients were analysed for bacterial and viral isolation in a laboratory using the usual tests. Genome amplification techniques based on polymerase chain reaction (PCR) provide a rapid and sensitive alternative for adenovirus detection in clinical samples. Clinical samples were amplified with specific nested PCR designed on the hexon protein gene (12) . After amplification, direct sequencing of purified products in both directions was made using 2ml of DNA dilution in a mixture containing 4ml of BigDye terminator Reaction Mix (ABI Prism BigDye Terminator Cycle Sequencing Kit; Perkin-Elmer Applied Biosystems) and 20 pmol of each sense or anti-sense inner primers to a final volume of 10 ml. Phylogenetic analysis was performed on a fragment of hexon protein coding region of the adenovirus genome. The analysis of sequences was made by pairwise alignment of the query sequence with every adenovirus sequence deposited in the database (GenBank).

Results
Between 12 December 2001 and 10 March 2002, a total of 102 cases associated with this outbreak could be identified: 80 residents, 1 person attending the daycare centre, 18 workers and 3 family members.

The global attack rate was 27.2%: 36.4% in residents and 12.9% in workers (p<0.001). In this last group attack rate was 15.8% in care staff and 6.7% in non-care staff (p=0.178). No significant differences could be observed between cases and non-cases with regard to age and sex in residents and workers (Table 1). Attack rates by floor, module and the distribution of bathrooms for room in residents did not present significant differences (Table 2).

Table 1
Attack rates and socio-demographic characteristics of EKC in residents and workers. Madrid, Spain 2001-2002

	No. of cases	No. of non-cases	Attack rate (%)	P (χ^2 test)
Total*	98	262	27.2	
Residents	80	140	36.4	<0.001**
Mean age	*84.3*	*83.6*		*0.507*
Female (%)	*74.1*	*76.3*		*0.724*
Workers	18	122	12,9	
Mean age	*33.4*	*38.1*		*0.136*
Female (%)	*88.9*	*72.4*		*0.218*
Care staff	15	80	15.8	0.178***
Non-care staff	3	42	6.7	

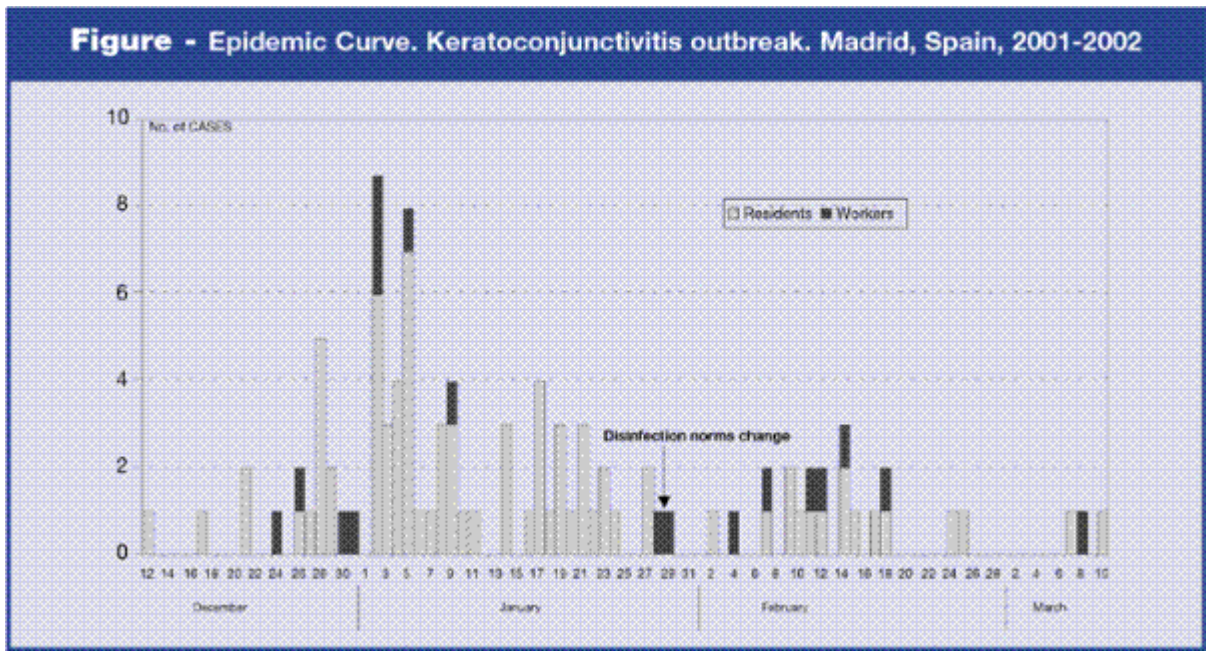
* One person affected attending in the day-care centre and three family members of workers are not included in the table.
** Between attack rates of the residents and workers.
*** Between attack rates of the care staff and non care staff.

Table 2 - Attack rates (%) on resident by place of stay. Madrid, Spain, 2001-2002

Floors	No. of cases / No. residents and workers	Rate (%)	P (χ^2 test)
1st	19 / 60	31.7	
2nd	35 / 84	41.7	0.4179
3rd	26 / 76	34.2	
Modules			
1st Floor			
A	8 / 20	40	
B	4 /20	20	0.3674
C	7 /20	35	
2nd Floor			
D	7 / 20	35	
E	13 / 24	54.2	0.5131
F	8 / 20	40	
G	7 / 20	35	
3rd Floor			
H	4 / 20	20	
I	3 / 16	18.7	0.0543
J	8 / 20	40	
K	11 / 20	55	
Room/Bathroom			
(1:1)	5 / 24	20.8	
(2:1)	28 / 76	36.8	0.3965
(4:2)	35/ 88	39.8	
Double	12 / 32	37.5	

The temporary distribution of the outbreak reflected in the epidemic curve (Figure 1) completes the characteristics of a interpersonal transmission pattern, with several picks of incidence and with intervals without new cases. Nearly 70% of the cases were identified within a period of 30 days: from December 27 through January 25. An important decrease could be observed later on.

Figure - Epidemic Curve. Keratoconjunctivitis outbreak. Madrid, Spain, 2001-2002



The multivariate logistic regression model showed that the three factors that

The multivariate logistic regression model showed that the three factors that appeared as independent risk factors were urinary incontinence (OR= 3.5), autonomy (OR= 9.7) and use of shared bathroom (OR= 6.1) (Table 3).

Table 3 - Univariate and multivariate analysis of risk factors. Madrid, Spain, 2001-2002

Variable	OR (CI 95%)	Adjusted OR* (CI 95%)
Autonomy	3.93 (1.91 – 8.08)	9.69 (3.54 – 26.56)
Incontinence	1.84 (1.01 – 3.35)	3.51 (1.56 – 7.87)
Food dependence	0.83 (0.40 – 1.73)	
Toilet dependence	1.20 (0.68 – 2.13)	
Bathroom dependence	0.99 (0.46 – 2.14)	
Dress dependence	1.43 (0.80 – 2.54)	
Cognitive deterioration	1.38 (0.77 – 2.46)	
Shared bathroom	2.35 (0.83 – 6.71)	6.11 (1.49 – 25.05)

* Because of the fact that forward stepwise method was used only to reflect significant variables in the model.

In a total of 9 clinical samples from 26 different patients (34.6%) isolation of adenovirus was possible in Hep-2 cell cultures. DNA from clinical samples were extracted and amplified. Nucleotide sequences from amplified products were studied using the corresponding sequences available in the GenBank data sequence. All 9 samples presented 100% homology with adenovirus type 8. Analysing a phylogenetic tree built with nucleotide sequences from each serotype, an individual cluster was very strongly supported with bootstrap values of 100%.

Discussion

Adenovirus type 8 was detected and identified in this outbreak as the etiological agent. This virus is considered the main agent producing EKC and has acquired particular relevance as a causal agent of nosocomial infections. Its specific biological characteristics and the drop of the prevalence of protective antibodies found in the general population could be the direct cause related with the particular epidemiological pattern (13). This virus is also characterised to produce mainly ocular disease in adults, although it has also been identified especially as pathogen of the upper respiratory tract in children (14).
Although an exhaustive investigation was carried out on the first cases, it was not possible to identify the initial source of infection of this outbreak. The first case identified consulted the ophthalmologist several days after the onset of EKC symptoms with an antecedent of eye irritation due to spilling of eau de cologne. Perhaps in this case the real date of symptom onset of EKC was mistaken and occurred several days later. This patient's infection would be associated to the medical examination at the ophthalmologist. Nevertheless, the possible existence of EKC cases in patients attending the ophthalmology services in this area of Madrid during these dates was also investigated, and no identification of any similar cases was detected, even although ophthalmological clinics, contamination of devices, solutions and the hands of personnel have all been frequently implied in community EKC outbreaks (6-8, 11, 13, 15-18) .

Of the factors that could be investigated in connection with the presence of EKC in the resident population, the most strongly identified was the autonomy to wander through the building. Residents with this factor were over nine times more likely to develop the infection, compared with residents without autonomy. The autonomy to wander through the building increased the probability of contact, either with other residents who had developed the disease or were still asymptomatic and/or with different surfaces and objects. This factor may play a relevant role in the dissemination of this outbreak.
Residents who shared a bathroom were six times more likely to develop the disease than those with private bathrooms,. Using the same bathroom would increase the likelihood of sharing towels and other objects. Several authors have checked the inefficiency of some disinfectants against the adenovirus spread (15,16,19). A confirmed characteristic of adenovirus is its high capacity to conserve the infective potential and to resist and persist over long periods of time (over 28 days) on surfaces such as plastic and metal in unfavorable conditions (20).
As described in the literature (6,8, 13, 15) , a possible explanatory factor in the maintenance of viral transmission was the presence of an large number of workers affected throughout the epidemic period (especially personnel who were in direct contact with the residents). This is an important factor to take into account in order to prevent and interrupt the transmission chain, because these persons could be a possible viral reservoir and a constant source of exposure for residents. In our study, the attack rate inside the group of personnel with functions related to direct care (care staff) was 2.4 times great than that of the group composed of workers without direct contact with the ill residents, although this difference was not statistically significant. Another fact that supports this influence was the association between the illness and urinary

that supports this influence was the association between the illness and urinary incontinence. The risk of EKC in these patients was over 3 times greater than in other patients. In relation to this last factor, it may be worth noting that the care of those patients is closer and more intensive, due to more frequent physical contact and longer daily attention from personnel, which represents an increment of the risk for spreading the infection. Another possible aspect to consider was is the difficulty of establishing an exhaustive control on rigorous compliance with the established prevention and control regulations, given the high number of workers of the facility.

Both a high number of cases and a long period before the outbreak is resolved have been characteristic in other EKC outbreaks described in the literature reflecting the difficulty of controlling nosocomial transmission despite the establishment of rigorous prevention measures (21). These difficulties have led to the development of infection control policies and procedures (ICPPs) in some ophthalmological institutions (22), which have been demonstrated to be effect in reducing the number of outbreaks and cases. The control measures implemented in this outbreak were based on methods of personal hygiene health education targeting residents and workers, especially regarding the isolation of patients, handwashing, cleaning and disinfection of surfaces and instruments, use of treatments and administrative norms that favours the resolution of the outbreak (withdrawing affected workers, restricting access to common areas). An important aspect to highlight in the control of this outbreak was the observed effect when diluted bleach solutions replaced amoniacal compounds during the usual disinfection of surfaces. This change was effective on 29 January, and 79% of the cases had onset of symptoms before this date (Figure 1).

The adoption of an appropriate case definition was difficult in this investigation, because of the practical impossibility of taking samples from all the patients who developed symptoms during the outbreak. Therefore, case identification was essentially based on clinical and epidemiological approaches. Furthermore, in elderly patients, who have a high prevalence of eye disease, the assessment of certain signs and symptoms can be very unspecific. Other aspects in connection with our case definition is that it permitted the study of false positives. One example is the study of a patient who was an institutional worker and presented with clinical symptoms compatible with conjunctivitis a month after the end of the outbreak. When the clinical samples from this patient were studied, a different serotype of adenovirus was identified (data not shown). It was concluded that this patient was not part of the outbreak of adenovirus type 8. The specific diagnosis methods for the detection and identification of viruses can solve not only the aetiology of an outbreak but also the definition of sporadic cases associated with it.

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