in most cases. All cases in which it was not necessary to remove the foreign body, vancomycin was included as a part of the antibiotic regimen.

The case we report here reflects not only the expected features of an infection caused by *C. cellulans* but also the probable long-term asymptomatic colonization of the catheter for more than a year, and the subsequent recurrence. It seems unlikely that both episodes could be independently trigger from a peripheral focus. Certain features of the microorganism such as low pathogenicity and biofilm formation could be involved in that long-term colonization. The presence of biofilm implies not only the lower effectiveness of antibiotics but also a diminished host immune response.[4] Most cases of *C. cellulans* infections led to catheter's removal for the complete eradication of the pathogen, whereas some authors have reported fully recovery by using vancomycin therapy (alone or in combination) and conservative management of the catheter.[2,5-8] However, in the case we report, this strategy was discouraged. Persistence of these microorganisms despite the use of antibiotics with *in vitro* activity may be partially explained by biofilm formation into the catheter's lumen.[4,9] Opportunistic pathogens like *C. cellulans* could increasingly being encountered due to the extensive use of long-term medical devices and a high survival rate of immunocompromised patients.

Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Community acute respiratory infections caused by enterovirus in the paediatric population☆

Infecciones respiratorias agudas comunitarias causadas por enterovirus en la población pediátrica

Dear Editor,

Enteroviruses are a family of viruses that predominantly infect the paediatric population, with non-specific clinical manifestations occurring in many cases. Infections generally present as flare-ups during the summer months, or as sporadic cases throughout the year. The main clinical manifestations are meningitis, self-limited febrile syndromes, exanthema, diarrhoea and neuromuscular diseases,[1,2] although there are very few data on their involvement in acute respiratory infections (ARIs).

Some studies seem to indicate that they may be the leading viruses that cause these infections during the winter months.[3,4] As such, we conducted a prospective study on their detection in these diseases. During the period between July 2015 and March 2016, we performed a prospective study on the presence of enterovirus in respiratory samples from all paediatric patients (<15 years of age) admitted to the Emergency Department with a suspected ARI. Clinical diagnoses were made based on the patients' symptoms and chest X-rays,[3,4] while viral detection was performed using a commercially available real-time RT-PCR gene amplification technique (Allplex® Respiratory Full Panel Assay; Seegene, South Korea). This technique differentiates between enterovirus and rhinovirus, but cannot serotype different enteroviruses. The enterovirus-positive samples were sent to the National Microbiology Centre of Madrid, where the final serotyping was performed.

2827 samples were analysed over the course of the study, of which 1646 (58.2%) tested positive. Of these, 98 (5.9%) corresponded to enterovirus and only 80 strains could be serotyped (81.6%). These 80 cases amount to 4.8% of the positive samples and 2.8% of the total samples analysed.

Serotyping showed that 18.7% were *Echovirus*, 38.7% *Coxsackievirus A*, 10% *Coxsackievirus B* and 32.5% other enteroviruses (Table 1). The most commonly detected types were: *Coxsackievirus A6* (17.5%), enterovirus group B (15%) and EV-D68 (11.2%). Among the *Echoviruses*, type *E11* was most common (33.3%); of the group A and B *coxsackieviruses, A6* (19.3%) and *B4* (50%) were the most prevalent. Moreover, in 7 cases (8.7%), co-infections with other viruses were detected, predominantly rhinovirus.

The aforementioned 80 patients comprised 63 boys (78.7%) and 17 girls (21.3%), the mean age of whom was 2.2 years (range: 6 days to 9 years). The majority of cases were detected between the months of November and February, and the main related conditions were: cold symptoms (51.2%), bronchiolitis (16.2%), bronchitis (10%), pharyngitis (8.2%), pneumonia (7.5%) and bronchospasm (6.2%).

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Table 1
Main respiratory infections caused by different types of enterovirus.

	Cold symptoms	Bronchiolitis	Bronchitis	Pneumonia	Bronchospasm	Pharyngitis	Total
Echovirus							15
E6	1						1
E7		1					1
E11	4	1					5
E13		1					1
E18	1						1
E20		2					2
E21				1			1
E30	1		1				2
E33	1						1
Coxsackievirus A							31
CA2				1			1
CA4	2						2
CA5			1	1		1	3
CA6	8	1	1	1	1	2	14
CA9	1	1					2
CA10	2	2	1		1		6
CA14						2	2
CA16	1						1
Coxsackievirus B							8
CB3	1						1
CB4	4		1	1			6
CB5						1	1
Other enteroviruses						26	
E71	3						3
D68	2	2	1	1	3		9
Group A EV	2						2
Group B EV	7	2	2			1	12
	41	13	8	6	5	7	80

Among those with cold symptoms, *Coxsackievirus A* was detected in 34.1%, *Echovirus* in 19.5% and group B EV in 17%. In the patients with bronchiolitis, *Echovirus* and *Coxsackievirus A* accounted for 38.4% and 30.7%, respectively, while the main virus involved in the bronchitis cases was *Coxsackievirus A* (37.5%). Of the 6 pneumonia cases, 50% were triggered by *Coxsackievirus A*, while EV-D68 was the most common type amongst patients with bronchospasm (60%). As for pharyngitis, *Coxsackievirus A* was behind 71.4% of cases.

10 of the patients (12.5%) required hospitalisation, although none was admitted to the ICU. The main diseases endured by these patients were pneumonia (40%), bronchospasm (40%) and bronchiolitis (20%). No patients died as a result or complication of an enterovirus infection. A history of asthma was the main factor associated with this type of infection. Of the 8 cases (10%), 3 (37.5%) were associated with EV-D68.

The involvement of enteroviruses in ARIs seems to depend on the time of year under analysis and the socio-sanitary conditions of the country in question. Accordingly, annual rates of 4–15%[5–7] have been reported, which is very similar to the 4.8% found in our study.

As regards the type of enterovirus involved, the absence of a predominant type seems to have been demonstrated.[2,8,9] The most commonly involved forms were *Coxsackieviruses A9* and *A16*, *Coxsackieviruses B1-6* and *Echoviruses 2, 4, 6 and 11*.[8] In one study by Trallero et al.,[10] *Echoviruses 6* (17%) and *11* (10%) were proven to be the most common forms in ARIs. In our study, we detected 23 different types of enterovirus, thus confirming its heterogeneity.

Enterovirus-related ARIs predominantly affect children under 5 years of age[1,2,5] and particularly those younger than 12 months, with bronchiolitis symptoms occurring frequently.[5,7] Our patients had a mean age of 2.2 years and bronchiolitis was the second most-common disease, although non-specific cold symptoms were predominant. Some studies have also implicated enteroviruses as triggers of pneumonia (1–7%).[2,5] The 6 cases observed in this study represented 7.5% of the ARIs caused by enterovirus. No patients were found to have associated neurological symptoms.

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Synergistic activity and clinical efficacy of fosfomycin and ciprofloxacin combination treatment for soft tissue infection caused by carbapenemase-producing *Enterobacter cloacae*☆

Actividad sinérgica y eficacia clínica de la asociación fosfomicina-ciprofloxacino en el tratamiento de una infección de malla quirúrgica con absceso de partes blandas por Enterobacter cloacae *productor de carbapenemasa*

The development of resistances to numerous antimicrobial agents by different pathogens is a serious problem in public health, as they limit the treatment options in infections caused by these pathogens to a remarkable extent. Moreover, the scant contribution of new molecules capable of acting against these modified strains has resulted in the need to explore other pathways, such as the recovery of old antimicrobial agents and associations of others which may turn out to be active.[1,2] Along these lines, fosfomycin is an antibacterial agent which has been known for a number of decades; it is active against a wide range of microorganisms, including strains of multi-resistant gram-negative bacilli. Nonetheless, the principal limitation on the use of fosfomycin in the treatment of systemic infections is the development of resistance during therapy, associated with the high frequency of mutations observed in different *in vitro* studies,[3] although this limitation may be prevented by using the antibiotic in combination with other molecules, obtaining, at the same time, synergic antibacterial activity.[2,4] Although the data obtained *in vitro* are suggestive and seem to point in this direction, its translation into clinical practice is not very common. In this study we present a case of surgical mesh infection by a strain of carbapenemase-producing *Enterobacter cloacae*, refractory to different antimicrobial regimens, which was finally treated successfully with a combination of ciprofloxacin and fosfomycin that presented synergic activity to the microorganism that had previously been demonstrated in the laboratory.

The subject was a 75-year-old, hypertensive, asthmatic woman who had recently been admitted owing to flare-ups of her COPD. During one such flare-up, she developed intestinal incarceration from a prior supra-umbilical hernia. A surgical intervention was performed, with the placement of a mesh, which in the immediate post-operative period showed signs of infection with the formation of a fistula. A number of different microorganisms were isolated in the culture from the exudate of the fistula; these were treated with different antimicrobial regimens, but with no sustained clinical improvement. In the final exudate sample taken, a strain of VIM-type carbapenemase-producing *Enterobacter cloacae* was isolated, initially detected by phenotypic methods and subsequently confirmed by PCR, through the amplification of an internal fragment of the blaVIM gene (350 nt); the amplicon obtained was not sequenced, owing to which the specific enzymatic variant was not defined. The strain was only sensitive to tigecycline and aminoglycosides. An abdominal CT scan showed a fistula between the transverse colon and a mass of soft tissue adjacent to the surgical mesh, with antimicrobial treatment being started with amikacin (750 mg/day) and parenteral tigecycline (starting dose 100 mg, followed by 50 mg every 12 h). Two months later, the patient underwent further surgery, partially extracting the infected mesh and closing the fistula. The patient developed an episode of reversible acute renal failure and on post-operative day nine presented a fever spike, with VIM-producing *Enterobacter cloacae* once again being isolated in the exudate from the fistula, now resistant to tigecycline and only sensitive to amikacin. In light of the persistence of the infra-umbilical tissue mass, once again observed through a CT scan, a combination of parenteral ciprofloxacin (400 mg/8 h) and parenteral fosfomycin (1 g/8 h) was prescribed, since the association had been shown to be synergic for the microorganism, through both combined diffusion gradients (E-Test) and through the design of lethality curves with the aforesaid antimicrobial agents. At 24 h, the patient remained afebrile, with a clinical and analytical improvement being observed over the following days. One month later, upon discharge, the treatment was replaced with ciprofloxacin 500 mg/12 h and fosfomycin 500 mg/8 h, both taken orally. Treatment was suspended after one year, with the patient remaining asymptomatic since then.

The minimal inhibitory concentrations of the isolated strains were the same on both occasions, presenting a pattern of high resistance to the majority of the antimicrobial agents tested (Table 1). The phenotypic analyses of the isolations presented identical patterns, suggestive in both cases of a metalocarbapenemase-producing strain. The activity of fosfomycin and ciprofloxacin, both alone and in combination, was ascertained by means of a dynamic study of the lethality curves using an initial inoculum of 5×10^5 cfu/ml of the microorganism on the basis of the corresponding MICs of both compounds. The number of CFUs was determined at 2, 4, 6, 8 and 24 h, with a synergic affect being considered as a 100-times reduction in the number of cfu/ml with the combi-

Table 1
Sensitivity patterns for a strain of VIM-producing *Enterobacter cloacae* in the infection of a surgical mesh.

	MIC (mg/l) of the isolations[a]	
Antimicrobial	1st isolation	2nd isolation[b]
Ampicillin	≥32	≥32
Amoxicillin/clavulanate	≥32	≥32
Piperacillin/tazobactam	≥128	≥128
Cefuroxime	≥64	≥64
Cefotaxime	≥64	≥64
Cefepime	≥64	≥64
Ertapenem	≥8	≥8
Imipenem	≥16	8
Gentamicin	8	≥16
Amikacin	≤2	≤2
Ciprofloxacin	8	8
Fosfomycin	128	128
Tigecycline	1	≥8

[a] By means of automated microdilution (Vitek-2) and diffusion gradient.
[b] Fifty-eight days after the first isolation.

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