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Nosocomial Outbreak of *Corynebacterium striatum* Infection in Patients with Chronic Obstructive Pulmonary Disease▽

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We describe an unusual cluster of *Corynebacterium striatum* infections in 21 patients with chronic obstructive pulmonary disease (COPD) admitted to a medium-size respiratory unit. Eleven isolates from eight patients occurred simultaneously within a month. *C. striatum* is a potentially pathogenic microorganism with the ability to produce nosocomial infectious outbreaks and respiratory colonization in patients with advanced COPD.

Corynebacterium species are found as colonizers of the skin and other tissues and in the environment (23, 27, 30). In addition to *Corynebacterium diphtheriae*, other *Corynebacterium* spp. have been reported to be pathogenic with some frequency, including *C. amycolatum* (24), *C. jeikeium* (formerly group JK), and *C. urealyticum* (formerly group D2) (8). Although *C. striatum* is one of the most frequently isolated coryneforms identified, there is little evidence linking *C. striatum* with infections in most locations (16, 21, 22, 25, 29, 31). The role of *C. striatum* as a potential cause of respiratory infections is difficult to establish. The clinical relevance of the isolation of *Corynebacterium* species from respiratory samples must be balanced by obtaining their correct identification and studying their abundance, their isolation as a single microorganism or their predominance when they are found in association with other microorganisms, and the repetition of positivity (23). In our hospital environment, *C. striatum* is occasionally isolated from cultures of sputum. The unusual clustering of patients in our respiratory ward produced a sentinel signal that justified the study of a possible outbreak.

The Hospital Joan March in Bunyola, Mallorca, Spain, is a secondary health care center that hosts a convalescence and rehabilitation department and a ward with 26 beds aimed at delivering care to patients with severe, chronic respiratory disease referred from tertiary-care hospitals within our catchment area. The Microbiology Laboratory based at Hospital Son Llàtzer is responsible for processing of the samples.

All positive samples reported here were obtained from the microbiological study of spontaneous sputum specimens obtained on admission from patients with an infectious exacerbation of chronic obstructive pulmonary disease (COPD), defined according to the of criteria Anthonisen et al. (1); during the follow-up of a patient's respiratory infection; or after hospital admission from patients with a newly identified infection that needed to be studied. The quality of samples was assessed by use of the scoring system of Murray and Washington (18) and current international guidelines (17). Identification of the isolates as *C. striatum* was based on colony morphology and pigmentation, Gram staining, motility, the catalase reaction, and the results obtained with the RapID CB Plus system (Remel, Lenexa, KS), which offers results within 4 h. In all cases the identification was confirmed within 24 h by use of the API Coryne system (BioMèrieux, l'Etoile, France), with 100% agreement achieved between both methods (10, 12, 14).

Antibiotic susceptibility was tested by the disk diffusion method (Oxoid SA, Spain) in Mueller-Hinton agar supplemented with 5% blood for all antibiotics tested except penicillin and ampicillin, for which the Etest system (AB Biodisk, Solna, Sweden) was used. The antibiotics tested included penicillin (10 U), ampicillin (10 μg), tetracycline (30 μg), gentamicin (10 μg), cefazolin (30 μg), vancomycin (30 μg), erythromycin (15 μg), imipenem (10 μg), ciprofloxacin (5 μg), and rifampin (30 μg).

The susceptibility criteria of the CLSI (formerly the NCCLS) (19) for *Staphylococcus* spp. were used for all antibiotics tested except penicillin and ampicillin, for which thresholds for *Listeria* spp. were used.

Twenty-one patients were admitted to Hospital Joan March within a period of 18 months (January 2004 to June 2005) due to an infectious respiratory exacerbation. The demographic and clinical characteristics of the patients indicated that they all had severe COPD (5), 18 were males and 3 were females, the mean age was 72 years (age range, 57 to years 88), and the patients had significant tobacco exposure (mean, 55.6 pack-years of cigarette smoking, where pack-year values are calculated as the number of cigarettes smoked per day divided by 20 and multiplied by the number of years the person has smoked). COPD was labeled as predominantly emphysema in nine patients (42.9%) and not specified in the rest of the patients. The severities of the cases of COPD, according to the

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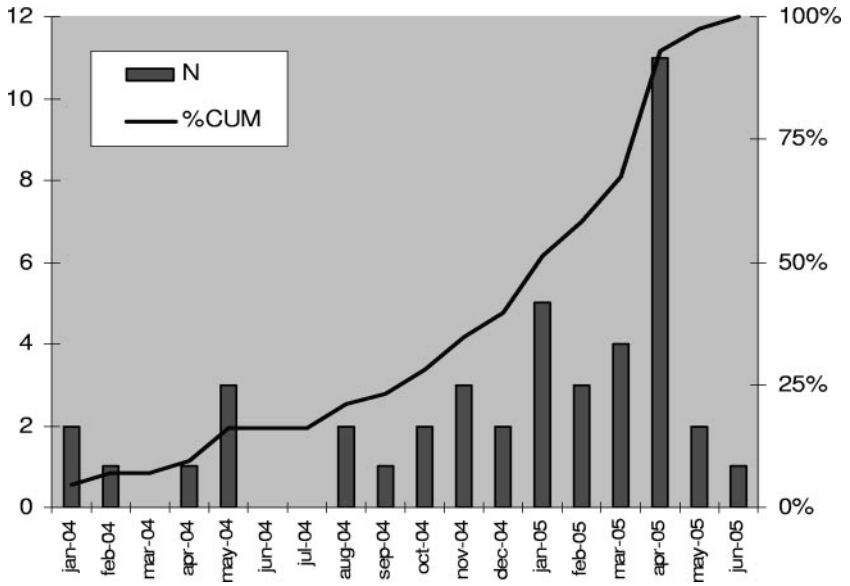

FIG. 1. Epidemic curve for *C. striatum* over time. N, number of isolates; %CUM, cumulative percent.

spirometry thresholds of the current ATS/ERS guidelines (5), were 0% mild, 35.7% moderate, 35.7% severe, and 28.6% very severe. Many of the patients required home care assisted technologies, including long-term oxygen therapy (47.6%) and aerosolized therapy (23.8%). The mean Charlson comorbidy index was 2.76, and the mean number of admissions due to COPD exacerbation in the previous year was 2.48 (range, 0 to 7 admissions).

During the study period of 18 months, the 21 patients had 49 admissions-readmissions in our hospital only, that is, a mean per patient of 2.33 (range 1 to 4), with a mean duration of admission of 44 days (range, 5 to 176 days).

Figure 1 shows the epidemic curve of the outbreak. The observed slow growth curve is suggestive of a nosocomial infection, with transmission from person to person. Table 1 shows the chronology of all 43 positive sputum samples and the respective patient room and bed, a record of the organisms isolated before the identification of *C. striatum*, the antibiotics that had been prescribed within the 10 days before the isolation of *C. striatum*, sputum sample quality, the associated microorganisms, and the clinical response after treatment according to the antibiogram.

To date, published reports identifying *C. striatum* isolates in respiratory samples as causal agents of disease are scarce. Until 1993 there were only three individual case reports of the confirmed pathogenicity of *C. striatum* (2, 3, 6). Since 1993, the isolation of *C. striatum* appears to have become more common (4, 7, 15, 20, 28). Initially, in two of these series (4, 15), a genotype study of the strains was conducted and confirmed patient-to-patient transmission. Brandenburg et al. (4) obtained samples from patients and from the hands of their caretakers and suggested that caretakers could have collaborated in the transmission. Recently, Otsuka et al. (20) reported 48 isolations of *C. striatum* from 1994 to 1998, with 75% of these samples being of respiratory origin and with all of them obtained from patients who had had long hospital admissions and who had received several courses of antibiotics. Genotyping identified 14 different patterns of *C. striatum*, with types A, D, and E associated with nosocomial outbreaks of respiratory origin and, in particular, with subtypes A1, A2, D2, and E associated with resistance to a broad range of antibiotics.

The outbreak reported here is unprecedented in the medical literature because it includes a large number of cases of *C. striatum* infection detected in sputum samples from patients with chronic respiratory disease in a hospital ward clustered in time and space; additionally, 11 cases were clustered in a single month (April 2005), and the outbreak affected one-third of the patients admitted to the ward. Several determinant factors may explain this outbreak of nosocomial infection, in which transmission was from patients and via caretakers: our hospital specializes in the care of patients with severe obstructive pulmonary disease who have many susceptibility factors (9, 13, 20, 26), high levels of use of health care resources (including multiple admissions), and repeated courses of antibiotic treatment; and the respiratory ward requires the generalized use of masks and glasses for oxygen delivery, inhalers, spacers, and nebulizers. Regrettably, without genotyping of the strains we cannot fully confirm this statement.

Most likely, factors that contributed to the end of this outbreak were the death of patient 5, who had 11 isolations until the time of his death in April 2005, and the reinforcement of implementation of universal preventative hygiene measures, both in the environment and by caretakers, after the identification of this outbreak. There were no further isolations of *C. striatum* in respiratory samples during the following 6 months.

Three of the six deaths during the study period occurred in patients from whom *C. striatum* was isolated in a pure culture and for whom no other independent cause of death was reported. Therefore, a causal link between death and *C. striatum* infection could be strongly hypothesized.

Previous authors (4, 11, 20, 31) noted that the rates of susceptibility of *C. striatum* to β-lactams and aminoglycosides are variable, with high levels of resistance to erythromycin, tetracycline, rifampin, and ciprofloxacin and with all strains sensitive to vancomycin. Our results on the antibiotic sensitiv-

TABLE 1. *C. striatum* outbreak in COPD patients

Patient no. (sample no.)[a]	Date (mo/day/yr)	Room and bed	Organism(s) previously isolated in sputum[b]	Antibiotic treatment 10 days earlier[c]	Sputum quality[d]	Associated organism(s) in sputum culture[e]	Follow-up posttreatment[f]
1 (1)	1/23/04	5a	AlcNi	TOB, Inh	G5	CStr	Improved
1 (2)	1/27/04	5a	AlcNi	TOB, Inh	G5	CStr	Improved
2 (1)	2/10/04	7a		LVX	G5	CStr	Improved
1 (3)	4/30/04	22a	CStr		G5	CStr, StM	Improved
3 (1)	5/17/04	33	MRSA, HIn, PsA	CAZ, TOB	LQ	CStr	Improved
3 (2)	5/17/04	33	MRSA, HIn, PsA	CAZ, TOB	LQ	CStr	Improved
1 (4)	5/17/04	11a	StM, CStr	CAZ, VAN	LQ	CStr	Improved
1 (5)	8/19/04	19a	StM, CStr	TZP, SXT, DOX, COL	G5	CStr, StM, AFu, Ca	Improved
1 (6)	8/27/04	19a	CSt, StM, AFu, Ca	ITC, SXT	G5	CStr, StM	Improved
4 (1)	9/8/04	19b	MRSA, PsA		LQ	CStr	Worsening
5 (1)	10/5/04	11a	StM, SrrM	CIP	G5	CStr, StM	Improved
1 (7)	10/11/04	19a	StM, CStr	SXT, MIN	LQ	CStr	Improved
5 (2)	11/3/04	11a	CStr, StM	IPM, SXT	G5	CStr	Improved
1 (8)	11/5/04	19a	StM, CStr		LQ	CStr	Improved
5 (3)	11/24/04	11a	CStr	IPM, CLR	G5	CStr	Transferred
6 (1)	12/14/04	9a		LVX	LQ	CStr	Improved
7 (1)	12/21/04	21	StM, AFu, HIn	LVX	LQ	CStr	Deceased
5 (4)	1/3/05	13b	AFu, CStr	ITC, CIP, SXT	G5	CStr	Same
1 (9)	1/14/05	5b	CStr, MoraxC	CIP, CAZ	G5	CStr, StM	Deceased
5 (5)	1/14/05	13b	CStr	ITC, CIP, AMX	LQ	CStr	Improved
5 (6)	1/27/05	13b	CStr	ITC, AMP	G5	CStr	Improved
8 (1)	1/28/05	1a	PsA, StM	SXT, MIN	LQ	CStr, PsA	Improved
9 (1)	2/8/05	9b		LVX, FEP, TOB	G5	CStr, MRSA	Improved
10 (1)	2/9/05	5b	AFlv		G5	CStr	Improved
11 (1)	2/25/05	5a	PsA	CAF, TOB	LQ	CStr	Deceased
5 (7)	3/3/05	23	CSt, Klp, StM, AFu	ITC, MIN	G5	CStr, StM	Same
5 (8)	3/14/05	23	StM, CStr	ITC, CIP, AMX	G5	CStr, StM, Klp	Improved
12 (1)	3/16/05	3b	PsA	LVX, TOB	G5	CStr	Improved
13 (1)	3/18/05	13b	AchXy, CoryJk	SXT	LQ	CStr	Improved
14 (1)	4/6/05	17b		ITC, IPM, LVX	G5	CStr	Deceased
15 (1)	4/7/05	19b	StM, StPn		LQ	CSt, MRSA	Deceased
16 (1)	4/13/05	11b		LVX	LQ	CStr	Improved
17 (1)	4/14/05	17a	MRSA, StM, AsFu	CAF, LVX, ITC	G5	CStr	Improved
5 (9)	4/16/05	23	Klp, StM, CStr	ITC, IPM	G5	CStr, StM	Improved
2 (2)	4/16/05	27	CStr, PsA, MRSA	SXT	G5	CStr, PsA	Improved
12 (2)	4/19/05	3b	CStr	AMC	LQ	CStr	Same
5 (10)	4/21/05	23	StM, CStr	ITC	G5	CStr, StM, Klp	Worsening
5 (11)	4/22/05	23	Klp, StM, CStr	ITC, AMC	G5	CStr, StM, Klp	Deceased
18 (1)	4/25/05	21b	PsA	FEP, TOB	G5	CStr, StM	Improved
17 (2)	4/28/05	17a	StM, AFu, CStr	ITC, CIP, AMX	LQ	CStr	Improved
19 (1)	5/23/05	5a		LVX	G5	CStr, PsA	Improved
20 (1)	5/25/05	21b		AMC	G4	CStr	Improved
21 (1)	6/28/05	13a	MRSA, StPn		G4	CStr, EAu	Improved

[a] Numbers of patients and numbers of samples positive for *C. striatum* by culture of sputum, in chronological order. Overall, there were 21 patients and 43 samples. Patient 1 had 9 positive samples; patient 5 had 11 positive samples; patients 2, 3, 12, and 17 had 2 positive samples; and the remaining 15 patients had only 1 positive sample each.

[b] History of isolation of microorganisms in sputum up to 1 year before the isolation of *C. striatum*. The abbreviations for the microorganisms are as follows: AlcNi, *Alcaligenes denitrificans*; CStr, *Corynebacterium striatum*; MRSA, methicillin-resistant *Staphylococcus aureus*; HIn, *Haemophilus influenzae*; PsA, *Pseudomonas aeruginosa*; StM, *Stenotrophomonas maltophilia*; Afu, *Aspergillus fumigatus*; Ca, *Candida albicans*; SrrM, *Serratia marcescens*; MoraxC, *Moraxella catarrhalis*; Aflv, *Aspergillus flavus*; Klp, *Klebsiella pneumoniae*; AchrXy, *Achromobacter xylosoxidans*; CoryJk, *Corynebacterium jeikeium*; EAu, *Staphylococcus aureus*.

[c] History of exposure to antibiotics and antifungals within the 10 days before the isolation of *C. striatum*. Abbreviations for antibiotics and antifungals: TOB, tobramycin; LVX, levofloxacin; CAZ, ceftazidime; VAN, vancomycin; TZP, piperacillin-tazobactam; SXT, trimethoprim-sulfamethoxazole; DOX, doxycycline; COL, colistin; ITC, itraconazole; CIP, ciprofloxacin; MIN, minocycline; IPM, imipenem; CLR, clarithromycin; AMX, amoxicillin; AMP, ampicillin; FEP, cefepime; AMC, amoxicillin-clavulanic acid.

[d] G5, <10 epithelial cells per field and >25 polymorphic nuclear leukocytes per field; G4, 10 to 25 epithelial cells per field and >25 polymorphic nuclear leukocytes per field; LQ, low quality (<10 epithelial cells per field and <10 polymorphic nuclear leukocytes per field).

[e] Microorganisms isolated in association with *C. striatum* in each of the positive samples. See footnote *b* for the definitions of the abbreviations.

[f] Clinical follow-up after the completion of treatment with antibiotics according to antibiogram. Overall, 6 patients died, 31 improved, 2 remained the same, 2 worsened, and 1 was transferred.

ities of the *C. striatum* strains from this outbreak mirror the ones from previous publications: vancomycin, 100%; imipenem, 93%; cefazolin, 74.4%; penicillin and ampicillin, 67.4%; tetracycline, 23.2%; erythromycin, 18.6%; gentamicin, 9.3%; and rifampin and ciprofloxacin, 0%. According to the sensitivity patterns obtained by Otsuka et al. (20), by which *C. striatum* is considered and emerging, multidrug-resistant, nosocomial pathogen, we have observed in our samples that the criterion of multidrug resistance (resistance to three or more antibiotics of different families) applies to 100% of the strains isolated in our nosocomial outbreak, 65% of which were resistant to four or five different antibiotic groups, 6.9% were sensitive only to imipenem and vancomycin, and 11% were sensitive only to vancomycin.

We conclude that *C. striatum* is an emerging multidrug-resistant, potentially pathogenic microorganism that is able to cause nosocomial infections and respiratory colonization in patients with advanced, severe COPD. It can be transmitted between patients, from person to person, and via caretakers; and *C. striatum* infections should be treated according to the results of the antibiogram. Once the organism is identified, universal hygiene measures should be observed to avoid further spread and outbreaks.

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