ORIGINAL ARTICLE

Clinical significance of *Corynebacterium striatum* isolated from human samples

L. Martínez-Martínez[1], A.I. Suárez[1], J. Rodríguez-Baño[2], K. Bernard[3] and M. A. Muniáin[2]

[1]Department of Microbiology and [2]Infectious Diseases Unit, Hospital Universitario Virgen Macarena, Seville, Spain; and [3]National Laboratory for Bacteriology and Enteric Pathogens, Laboratory Centre for Disease Control, Ottawa, Ontario, Canada

Objective: To evaluate the clinical significance of and describe factors associated with *Corynebacterium striatum* infection.

Methods: A retrospective chart review was performed of the *C. striatum* isolated in a university hospital from January 1991 to July 1995. *C. striatum* was identified using conventional methods, the API CORYNE system and cellular fatty acid profiles.

Results: In the study period, *C. striatum* was isolated from clinical samples in 127 patients. In 49 patients, data from clinical charts were considered insufficient for evaluation. In 26 cases, the microorganism was considered to be the etiologic agent of an infectious process. In the remaining 52 patients, the organism was considered to be a colonizer. Before the infection all the patients had been hospitalized for some underlying condition, and 22 (85%) of them had received antibiotics previously. Six patients died. In two of them, death was a consequence of their underlying disease and in the remaining four, death was related to the *C. striatum* infection.

Conclusions: *C. striatum*, a microorganism traditionally considered to be an avirulent member of the normal human nasopharyngeal and skin flora, may opportunistically cause infections in hospitalized patients with underlying diseases and previous antibiotic treatments.

Key words: *C. striatum*, coryneform bacteria, nosocomial infections

INTRODUCTION

Coryneform bacteria other than *Corynebacterium diphtheriae* have often been considered as colonizers or contaminants [1]. More recently, due in part to improved microbiological techniques, the survival of immunocompromised patients and increased use of medical devices, the clinical importance of these microorganisms has been recognized, particularly as a cause of opportunistic infection [1–3]. Recent changes in the taxonomy of coryneform bacteria make it difficult at this moment to evaluate the actual importance of particular species of the genus *Corynebacterium* as a cause of infections in humans [3]. Most of the reports refer to *C. jeikeium* [4–6] or *C. urealyticum* [7,8] and, to a lesser extent, to *C. amycolatum* [9], *C. pseudodiphtheriticum* [10,11], and *C. glucuronolyticum* [12]. The significance and prevalence of most other coryneform bacteria (including genera other than *Corynebacterium*) are not well known.

C. striatum has been isolated as part of the normal human nasopharyngeal flora and from the skin of the cheek, forehead and the upper part of the trunk [13]. Several case reports [14–26] and two series [27,28] comprising six and three cases respectively have been published. Person-to-person transmission of *C. striatum* in intensive care units has been reported, but with limited clinical information [29,30]. We have previously reported the microbiological identification of 31 *C. striatum* strains isolated from 24 patients in the

Corresponding author and reprint requests:

L. Martínez-Martínez, Department of Microbiology, Hospital Universitario Virgen Macarena, Apdo 914, 41080, Seville, Spain

Tel: +34 95 4552862 Fax: +34 95 4377413

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period January 1991 to October 1993 [31]. Unfortunately, clinical data concerning these 24 patients were incomplete in many cases. In this report we present the clinical data from patients (with complete clinical records available) from whom *C. striatum* was isolated in the period January 1991 to July 1995.

MATERIAL AND METHODS

Patients

We reviewed the clinical charts of patients from whom *C. striatum* was isolated during the period January 1991 to July 1995 at the Hospital Universitario Virgen Macarena (Seville, Spain), an 800-bed teaching hospital with a laboratory receiving samples from the hospital and outpatient clinics. Isolates of *C. striatum* obtained from sterile fluids, catheters (≥15 CFU by the rolling-plate method), urine culture (≤2 species, $>10^5$ CFU/mL) and pure or predominant culture from wound exudates and bronchial aspirates obtained with a bronchoscopic catheter were considered potentially significant.

The clinical charts of patients from whom potentially significant *C. striatum* strains were cultured were assessed according to CDC criteria [32] in order to define infection. In the case of surgical wounds and ulcers, diagnosis of infection by *C. striatum* required isolation of the organism from the depths of the wound/ulcer and the presence of at least three of the following: redness, swelling, heat, pain hypersensitivity and abscess formation. In addition to the CDC criteria, a further requirement was for the physician in charge of the patient to suspect an infectious process at the site from which *C. striatum* was isolated, and that, after isolation of the organism, a change in treatment should be effected: surgical debridement, antibiotic treatment with agent(s) to which the organism was susceptible in vitro, or catheter removal.

The data from clinical charts indicated in Table 1 were recorded for this study.

Microbiological studies

Clinical samples submitted to the microbiology laboratory were processed according to conventional methods, as previously described [31]. *C. striatum* strains isolated from January 1991 until October 1993 were identified using conventional tests, the API CORYNE system, and cellular fatty acid profiles, as previously described [31]. The remaining isolates were identified with the API CORYNE system and conventional tests. Strains identified by the API CORYNE system as maltose-negative *C. xerosis* (presumably *C. amycolatum* in view of the new available data [9]), that could be misidentified as *C. striatum*, were excluded on the basis of the morphology of the organism in Gram's stain, colonial morphology, time to ferment sugars, and hydrolysis of tyrosine [31].

RESULTS

In the study period, *C. striatum* was isolated from clinical samples from 127 patients. Only 26 patients (from whom 38 isolates were obtained) fulfilled the strict criteria established for the diagnosis of infection. The remaining 101 patients were excluded either because the clinical charts were incomplete for evaluation purposes (49 patients), or because the organism was considered a colonizer (52 patients) according to the CDC criteria for definition of infection.

C. striatum was isolated as single agent in 25 out of the 26 infected patients. In the remaining case (patient no. 22), *C. striatum* and *Fusobacterium nucleatum* were isolated from a skin abscess over an arteriovenous fistula, whilst *C. striatum* on its own was also recovered from blood cultures. In 16 (62%) patients, *C. striatum* was cultured from skin chronic ulcers or surgical wounds. The organism was also recovered from blood in one patient, as previously stated, from bronchial lavage in four (15%), from intravenous catheter in two (8%), and from pleural fluid, peritoneal fluid, urine and the exudate from a balanoprepucial inflammation in one (4%) patient each.

Clinical characteristics of the 26 patients are summarized in Table 1. There were 20 (77%) males and six (23%) females. The mean age was 58.5 years (range 22–84). Fever (≥38°C) was present in 21 (80%) patients and leukocytosis (≥10 000 cells/mL) in 16 patients (62%). All the patients were hospitalized and had an underlying systemic condition or had undergone surgery, or both. The mean previous hospital stay was 20.7 days (range 3–50). The associated conditions were surgery in 12 (45%) cases, neoplasia in six (22%), tuberculosis in three (11%), diabetes mellitus in five (19%), chronic obstructive lung disease in two (8%), and heart failure in two (8%). All patients were HIV negative.

All patients but one (a patient with intravenous catheter infection) presented local signs of inflammation, three of them with abscess formation. Twenty-two patients (85%) were receiving antibiotic therapy when *C. striatum* was isolated, and 15 of them (58%, including three patients on antituberculous drugs) were receiving more than one antimicrobial agent. Nine of these patients were receiving a β-lactam which could be considered active in vitro against the corresponding *C. striatum* isolate. The remaining 13 patients were receiving an antimicrobial agent to which *C. striatum* was resistant in vitro (data not shown).

Table 1 Summary of data

Patient	Age/ sex	Type of infection	Underlying condition	Source of isolate	Previous antibiotic	Previous hospital stay (days)	Antibiotic treatment	Outcome
1	72/F	Leg ulcer, sepsis	Diabetes, neuropathy	Ulcer aspirate	CIP, CC	3	CEF	Death
2	59/M	Surgical wound	Larynx neoplasia	Wound aspirate	CC, TB	9	VAN	Cure
3	64/F	Bronchopneumonia	COPD, tuberculosis	Bronchial aspirate	INH, PYZ, RIF	30	VAN	Death
4	74/M	IV catheter, phlebitis	Hip replacement	IV catheter	CRX, FOX	13	None	Cure
5	66/M	Surgical wound	Vertebral plasmocytoma	Wound aspirate	FIX	22	CIP	Lost to follow-up
6	28/F	Plantar ulcer	Diabetes, neuropathy	Ulcer aspirate	CIP, TB	3	AMX/ CLAV	Lost to follow-up
7	66/M	Surgical wound	Hip replacement, gastric perforation	Wound aspirate	CTX, FOX, MTD	45	AMP	Cure
8	52/M	Bronchopneumonia	Pneumectomy, lung cancer	Bronchial aspirate	CAZ, CIP	24	TEI	Death
9	27/M	Empyema	Cerebral hemorrhage	Pleural fluid	CTX, AZT, VAN	11	MTD	Death
10	64/M	Cystitis	Penis reconstruction	Urine	AMX/CLAV	20	None	Cure
11	24/M	Surgical wound	Multiple trauma	Wound aspirate	AZT, CTX	50	None	Cure
12	68/M	Spontaneous peritonitis	Metastatic neoplasia	Peritoneal fluid	None	40	None	Death
13	78/F	Leg ulcer	Diabetes, neuropathy	Ulcer aspirate	CIP	20	AMP	Cure
14	66/M	Surgical wound	Cavum neoplasia, tuberculosis	Wound aspirate	INH, PYZ, RIF	30	None	Cure
15	82/M	Balanitis	Diabetes. Pancreatitis	Exudate	AMX/CLAV	30	None	Cure
16	30/M	Decubitus ulcer	Spina bifida	Ulcer aspirate	FURAX	10	VAN	Cure
17	54/M	Bronchitis	Heart failure	Bronchial aspirate	AMX/CLAV	27	VAN	Cure
18	68/F	Surgical wound	Cholecystectomy	Wound aspirate	CIP	19	None	Cure
19	69/M	IV catheter	Heart failure	IV catheter	None	10	AZT, VAN	Death
20	22/M	Surgical wound	Teratocarcinoma	Wound aspirate	CC	41	AZT	Cure
21	59/M	Bronchitis	COPD, tuberculosis	Bronchial aspirate	INH, PYZ, RIF	25	VAN	Cure
22	50/F	AV fistula	Chronic renal failure	Blood, abscess aspirate	None	3	VAN, GEN	Cure
23	67/M	Surgical wound	Gastrectomy	Wound aspirate	CIP, CC	19	VAN	Cure
24	84/M	Leg ulcer	Varices	Ulcer aspirate	CLX	8	AMP	Cure
25	56/M	Leg ulcer	Cirrhosis	Ulcer aspirate	None	12	None	Cure
26	75/M	Leg ulcer	Diabetes	Ulcer aspirate	CIP, CC	16	VAN	Improve-ment

Note: CIP, ciprofloxacin;, CC, clindamicin; TB, tobramycin; INH, isoniazid; PYZ, pyrazinamide; RIF, rifampin; CRX, ceftriaxone; FOX, cefoxitin; FIX, cefixime; CTX, cefotaxime; MTD, metronidazole; CAZ, ceftazidime; AZT, aztreonam; VAN, vancomycin; AMX/CLAV, amoxicillin/clavulanate; FURAX, nitrofurantoin; CLX, cloxacillin; AMP, ampicillin; TEI, teicoplanin; CEF, cefazolin; GEN, gentamicin; COPD, chronic obstructive pulmonary disease; AV, arteriovenous; IV, intravenous.

The infection resolved in 17 (65%) patients: six were cured with surgical cleansing or catheter removal (but without antimicrobial therapy), six after surgical drainage plus antibiotic treatment, and five with antimicrobial treatment alone. Six patients died; five of them had received antimicrobial therapy, and one of them had not because of advanced metastatic disease. In two of them, death was clearly a consequence of the underlying condition (patients no. 12 and no. 20). In three patients (no. 1, no. 8 and no. 9), death was attributed to *C. striatum* infection. Patient no. 6 had long-standing chronic obstructive lung disease and tuberculosis of recent diagnosis. *C. striatum* infection may have contributed to the death of this patient. The remaining three (patients no. 5, no. 6, and no. 26) were lost to follow-up after an initial improvement.

ILLUSTRATIVE CASE REPORTS

The following cases are representative of the clinical characteristics of infection associated with *C. striatum*.

Case 9 has been previously reported [20].

Case 1

A 72-year-old female patient, who had diabetes, hypertension and heart failure, was admitted because of an infected ischemic ulcer in her right leg which had been unsuccessfully treated with oral ciprofloxacin (500 mg

PO b.i.d.) and clindamycin (300 mg PO q.i.d.). The ulcer presented clear signs of infection. The patient was afebrile. The leukocyte count was $20 \times 100/mm^3$, with 93% neutrophils. In a needle aspirate of the ulcer, Gram-positive rods were observed within neutrophils and extracellularly; *C. striatum* grew in pure culture from this sample and from a second sample obtained the next day. The patient was treated with cefazolin (2 g IV t.i.d.), but died of septic shock.

Case 2

A 59-year-old man presented with surgical wound infection after thyroidectomy for thyroid neoplasm. He was put on clindamycin (600 mg IV. q.i.d.) and tobramycin (100 mg IV b.i.d.) but the wound became purulent, with abscess formation. *C. striatum* was isolated in pure culture from a needle aspirate of the wound. The patient was treated with vancomycin (1 g IV b.i.d.). Two days later the organism was again cultured after surgical cleansing of the abscess. Vancomycin was continued for 10 days, with resolution of the infection.

Case 3

A 64-year-old woman with long-standing chronic obstructive lung disease was admitted to hospital because of pulmonary tuberculosis with severe respiratory insufficiency requiring orotracheal intubation. Treatment with isoniazid, rifampin and pyrazinamide was started. After a transitory improvement, the patient again presented fever (38.7°C) and a marked respiratory deterioration. Chest X-rays revealed new infiltrates. Two separate bronchial aspirates with a protected catheter yielded a pure culture of *C. striatum*. The patient was started on vancomycin (1 g IV b.i.d.) but her condition deteriorated and she died of respiratory failure 2 days later.

Case 4

A 74-year-old man admitted for total hip joint replacement and given intravenous cephalosporins for 10 days presented with fever (38°C) and signs of infection at the intravenous catheter insertion site. More than 15 colonies of *C. striatum* grew in culture of the tip of the catheter by the rolling-plate method. The infection resolved without further antibiotic treatment.

Case 22

A 52-year-old woman with chronic renal failure had presented 7 months previously with signs of infection at the surgical scar of the arteriovenous fistula and the appearance of a deep skin sinus. Five months later, *C. striatum* had been obtained in pure culture from the infection site, but was considered a contaminant, and the patient was not given antibiotic treatment. Fifteen days before the present admission an abscess appeared over the fistula. The patient presented fever (38°C). The abscess drained spontaneously. Three days later *C. striatum* was isolated from blood culture. Treatment was started with vancomycin (1 g IV b.i.d.) but the patient remained febrile. The arteriovenous device was removed. *C. striatum* and *Fusobacterium nucleatum* were obtained from the culture of the device. The patient was cured after 3 weeks of intravenous vancomycin treatment.

DISCUSSION

The first case of *C. striatum* infection was published in 1980 by Bowstead and Santiago in a patient with chronic lymphocytic leukemia who had a pleuropulmonary infection [15]. Since then, several case reports have been communicated, although not all cases present enough data to identify the organism: pulmonary infection in a patient with chronic obstructive airways disease [16] or in intubated patients [14,20], four cases of native valve endocarditis [18,22,25,26], one case of pacemaker-related endocarditis [23], two cases of bacteremia [17,19] and one case of meningitis [24]. Two series have been published, including three and six patients, respectively [27,28]. The isolated microorganisms were obtained from various sources (sputum, vaginal exudate, blood, intravenous catheter, peritoneal fluid, skin, conjunctiva and, in one patient, from uterus, placenta and urine). All patients from both series recovered after antibiotic treatment or surgery. Leonard et al [29] have reported the isolation of *C. striatum* in 11 patients. Some of these patients experienced improvement after antibiotic treatment, although the authors had no clearcut evidence that these isolates were acting as opportunistic pathogens.

Recognition of *C. striatum* as a human pathogen may have been hindered by the inability of the clinical laboratory to identify the organism because its colonies may be confused with those of coagulase-negative staphylococci [31]. Moreover, *C. striatum* may be misidentified as a species of coagulase-negative staphylococcus when some automated method of identification/susceptibility testing is used. For these reasons, a Gram stain is critical in order to identify *C. striatum*. Even if this is carried out, there may be problems in correctly identifying the bacterium, particularly when there is exclusive reliance on the API CORYNE system, since strains of *C. amycolatum* (previously *C. xerosis*) may be misidentified as *C. striatum* when using this system [3,31]. Colonial morphology, time to ferment sugars and hydrolysis of tyrosine help to differentiate the species [3,31].

C. striatum was isolated in some of our patients from sources (ulcers and surgical wounds) where the organism could be considered a contaminant or colonizer. However, we believe that our inclusion criteria minimize this possibility. In fact, such rigorous criteria may account for the high percentage of isolates considered as colonizers or contaminants, and it might be suggested that the actual incidence of human infections caused by *C. striatum* may be even higher than that presented in this report. A prospective study is in progress to evaluate this possibility.

From the published cases it seems that most but not all patients have been hospitalized and have had an underlying or associated disease. In this report the majority of our patients had been hospitalized for many days. The patients in our series presented heterogeneous underlying conditions, including neoplasia in six patients, diabetes in five and, surprisingly, tuberculosis in three. A case-control study should be performed to assess whether these and other factors are related to *C. striatum* infection.

Leonard et al have presented evidence of transmission of a single *C. striatum* strain in 11 hospitalized patients in an intensive care unit (ICU) [29]. More recently Brandenburg et al [30] have shown long-term persistence of *C. striatum* in a surgical ICU affecting 14 mechanically ventilated patients. The strains were proven to be the same by means of biotyping, antibiotyping, and random amplification of polymorphic DNA. Patient-to-patient transmission probably occurred via hands of personnel. In a third of our cases the organism was also obtained from patients in the ICU, although the epidemiological relationship of these isolates has not yet been established.

Corynebacteria in general have been most frequently isolated from the skin and mucosae of patients who have received broad-spectrum antibiotics [18], as was the case with most of our patients. Eight out of 11 (73%) patients in the series by Leonard et al [29] had received β-lactam antibiotics, primarily cephalosporins and penicillins, before the isolation of *C. striatum*. In our case (Table 1), 22 out of 26 (85%) patients were receiving antimicrobial agents (mainly beta-lactams, ciprofloxacin and/or clindamycin); three patients were being treated for tuberculosis with rifampin, isoniazid and pyrazinamide. Considering the NCCLS breakpoints for non-fastidious bacteria [33], the organism was resistant in vitro to the antimicrobial agent(s) used at the moment of the isolation in 13 of these 22 patients. Unfortunately, definition of susceptibility and resistance to antimicrobial agents in *C. striatum* (and other coryneform bacteria) is difficult because breakpoints are not yet available specifically for this group of organisms. Moreover, Tattevin et al [25] have shown high MBC values of amoxycillin and ceftriaxone (128 and 64 μg/mL, respectively) compared to MIC values (1 and 8 μg/mL, respectively), which makes it even more difficult to correlate in vitro susceptibility testing of *C. striatum* with in vivo results.

Seventeen patients were cured of their infection: six after surgical cleansing and/or catheter removal; five after antimicrobial therapy; and six after both surgical cleansing/catheter removal and antimicrobial therapy. Six patients died, one of them without receiving any treatment because of the severity of his underlying disease; an additional patient received antimicrobial therapy with an agent to which his isolate was resistant in vitro. Three patients died in spite of being treated with antimicrobial agents active in vitro. All six patients were previously severely debilitated. Additionally, antimicrobial therapy based on in vitro susceptibility data was often delayed because of the time (about 2–3 days after the sample was obtained) required for identification and susceptibility testing of *C. striatum*. It seems from this series that the underlying condition and the local measures taken are as important as the antimicrobial treatment in the prognosis of these patients.

With the improvement of microbiological techniques and the survival of patients with underlying disease and/or immunosuppression, *C. striatum* may be recognized as a cause of infection with different degrees of severity in hospitalized patients.

In conclusion, the results from this study show the role of *C. striatum* as a cause of human infection, particularly in hospitalized patients with underlying diseases, and previous antimicrobial agent treatments.

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