Journal of Microbiology, Immunology and Infection (2011) 44, 456–460

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ORIGINAL ARTICLE

Bacterial infection in association with snakebite: A 10-year experience in a northern Taiwan medical center

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Received 17 June 2010; received in revised form 25 July 2010; accepted 31 August 2010

KEYWORDS
Bacterial infection;
Cobra;
Snakebite

Background: Microbiological data of secondary wound infections following snakebites is rarely reported in Taiwan. The objective of this study was to assess the secondary wound infection after venomous snakebites.
Methods: We conducted a 10-year retrospective survey on patients admitted for venomous snakebites and microbiological data of wound cultures at a medical center in northern Taiwan.
Results: Between April 2001 and April 2010, 231 patients who experienced snakebites were included. Male predominated, accounting for 62.3% (144). The age range of patients was 4–95 years. Ninety-five (41.1%) people were bitten by *Trimeresurus mucrosquamatus*, followed by *Tstejnegeri*, and cobra. A total of 61 pathogens were obtained from 21 patients. Thirty-nine (63.9%) isolates were gram-negative bacteria, 14 (23%) gram-positive pathogens, and 8 (13.1%) anaerobic pathogens. There were 17 patients bitten by cobra in these 21 patients. *Morganella morganii* and Enterococcus species were the most common pathogens identified in the wound cultures.
Conclusion: Cobra bite causes more severe bacterial infection than other kinds of snakebites. Oral amoxicillin/clavulanate plus ciprofloxacin or parenteral piperacillin/tazobactam alone can be the choices for empirical or definitive treatment, and surgical intervention should be considered for established invasive soft tissue infections.

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doi:10.1016/j.jmii.2011.04.011

Introduction

There are many kinds of snakes in Taiwan, including venomous and nonvenomous snakes. Six common venomous snakes include *Trimeresurus mucrosquamatus*, *T stejnegeri*, cobra, *Bungarus multicinctus*, *Deinagkistrodon acutus*, and *Daboia russelii siamensis*.[1–3] Snakebite is a common emergent condition. About 300–1,000 people are bitten by snakes every year. With antivenom therapy, the mortality rate has decreased from 6.6% to 1.5% since 1904.[4–6] The cause of death following snakebite is often because of a toxic hemorrhagic effect or a neurotoxic effect with secondary bacterial infection. However, bacteriological data on wound cultures following snakebite is rare in Taiwan. Hence, we surveyed the patients admitted for snakebites at our medical center in northern Taiwan in the past 10 years.

Materials and methods

Our hospital is a tertiary medical center with 3,000 beds serving for a population of 2,600,000 inhabitants in Taipei, Taiwan. We initiated our study by searching for the patient list by the ICD-9 coding, 989.5, of who experienced venomous snakebites during the period of April 2001 to April 2010. Their medical charts were reviewed.

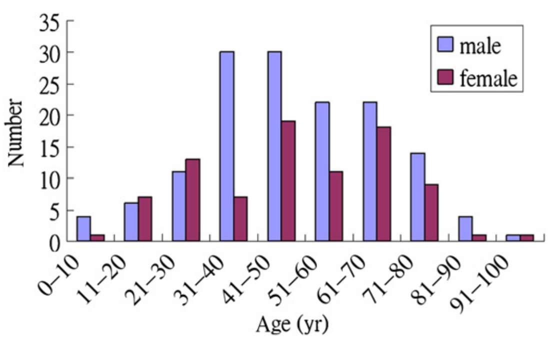

Figure 1. Age distribution of 231 patients experiencing snakebite between April 2001 and April 2010.

The data on patient age, gender, time of attack and locality, body parts bitten, the snake species, and recovery conditions were collected. The snake species involved was confirmed primarily on the basis of the snake that was brought to the hospital by the patient or the family or witnessed by the patient. If the snake species could not be identified, we categorized it as a snake of unknown species.

Wound cultures were performed for patients who experienced severe wound infection during their hospital stay following the snakebite. Bacterial identification was performed using the automated system VITEK 2 (BioMérieux, Inc., Durham, NC, USA). The antimicrobial susceptibility was determined by the disc-diffusion method.

Results

In this 10-year survey, 231 patients were admitted for snakebites. Of them, 144 (62.3%) were men (Fig. 1). The age range of patients was 4–95 years. Ninety-five (41.1%) people were bitten by *T mucrosquamatus*, 50 (21.6%) by *T stejnegeri*, 25 (10.8%) by cobra, 10 (4.3%) by *B multicinctus*, and 50 (21.6%) by unknown species (Table 1).

From April to October (Spring to Summer) in northern Taiwan, 170 snakebites (73.6%) occurred (Fig. 2). Seventy-one patients received snakebites while working in a farm or field (Table 2). The other places where injury occurred were the outdoor yards (63 cases), bushes or forests (45), and inside the homes (34). About 76.5% of bites that occurred inside the houses were bitten by cobra and *T mucrosquamatus*. Most *B multicinctus* (70%) bites occurred in the field and forest areas. A total of 117 patients were bitten on the lower extremities and 114 patients were bitten on the upper extremities.

All 231 cases were admitted with pain and swelling in the wounds after snakebites. After admission, 59/231 (25.5%) patients experienced cellulitis. Among them, 26/59 (44%) patients evolved into worsening wound infections and needed surgical intervention. Six needed wound incision and pus drainage, and 20 needed debridement and fascitomy for necrotizing fasciitis or compartment syndrome. The percentages of patients requiring surgery of total

Table 1 Epidemiological studies of snakebite in Taiwan since 1966

Area & Sort	Case number (mortality rate, %)								References
	Total cases	TM	TS	Cobra	BM	DA	DRS	Unknown and nontoxic	
Whole island	891 (13)	393 (6)	165	100	152 (6)	37	4	66 (1)	Sawai and Tseng[5]
Kaohsiung	150 (4)	72	58	3	5 (2)	4 (2)	0	8	Sawai et al.[17]
Pintung	335 (17)	115 (2)	97	24 (2)	26 (5)	34 (6)	20 (2)	19	Sawai et al.[18]
South Taiwan	63 (4)	23 (1)	16	13	6 (3)	4	1	0	Kuo and Wu[19]
Some hospitals	189	66	54	17	6	2	1	43	Miao et al.[20]
Whole island PCC	541 (13)	121	121	54	40 (9)	16	15 (2)	174 (2)	Wu et al.[6]
North Taiwan	131	31	68	0	0	0	0	31	Chen et al.[1]
South Taiwan	46 (1)	6 (1)	20	6	5	1	1	7	Liao et al.[21]
Central Taiwan	282 (1)	38	37	102 (1)	25	4	1	75	Hung[7]
Our study	231 (1)	96	50	25 (1)	10	0	0	50	

BM = *Bungarus multicinctus*; DA = *Deinagkistrodon acutus*; DRS = *Daboia russelii siamensis*; PCC = Poison Consultation Center; TM = *Trimeresurus mucrosquamatus*; TS = *Trimeresurus stejnegeri*.

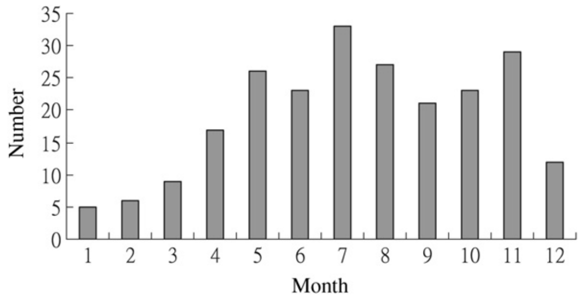

Figure 2. Seasonal distribution of 231 patients experiencing snakebite between April 2001 and April 2010.

patients with snakebite by cobra, *T mucrosquamatus*, and *T stejnegeri* were 60% (15/25), 1% (1/96), and 0% (0/50), respectively ($p < 0.001$).

In Table 3, a total of 61 bacterial pathogens were obtained from 21 patients with soft tissue infections, including 5 of 23 patients without surgery and 16 of 26 requiring surgery. Among 21 patients with microbiologically documented infections, 16 needed surgical interventions, 15 bitten by cobra and 1 by *T mucrosquamatus*. Four patients, two with cobra bite and two with snakebite by unknown snake species, did not have surgery. All but one of 21 patients survived, and the only fatal patient refused surgery and was discharged against advice. Of 210 patients in whom cultures were not performed, only a 23-year-old woman with breast cancer died of cobra bite.

Thirty-nine (63.9%) pathogens were gram-negative bacteria, followed by 14 (23%) that were gram-positive bacteria, and 8 (13.1%) that were anaerobic pathogens. Among gram-negative bacteria, *Morganella morganii* was the most common pathogen. Other important gram-negative pathogens included *Pseudomonas aeruginosa* and *Proteus vulgaris*. Enterococcus species was the most common gram-positive isolate. *Bacteroides fragilis* groups were the most common anaerobic pathogens. Of 21 patients with microbiologically documented pathogens, 17 patients had cobra bite, 1 was bitten by *T mucrosquamatus*, 1 by to *T stejnegeri*, and 2 by unknown species.

All gram-negative bacteria were susceptible to amikacin, ceftazidime, ciprofloxacin, and piperacillin/tazobactam (Table 4). All Enterococcus isolates were susceptible to vancomycin and 90% susceptible to ampicillin, and all *B fragilis* strains were susceptible to metronidazole, clindamycin and chloramphenicol.

Table 3 Bacterial isolates identified from snakebite wounds

Organisms	*n*
Aerobic gram-positive bacteria	14
Enterococcus species	12
Coagulase-negative staphylococcus species	1
Bacillus species	1
Aerobic gram-negative bacteria	39
Citrobacter amalonaticus	1
Citrobacter freundii	3
Escherichia coli	2
Klebsiella pneumoniae	1
Morganella morganii	14
Proteus mirabilis	1
Proteus vulgaris	4
Providencia rettgeri	3
Pseudomonas aeruginosa	5
Serratia liquefaciens	1
Serratia marcescens	1
Shewanella putrefaciens	3
Anaerobic bacteria	8
Bacteroides fragilis group	6
Peptostreptococcus species	2

Discussion

In our study, snakebite injury was more common in men. The reason may be that males had more outdoor time to work or field activity than females or because of more likely to attack or catch snakes. Such movements disturb snakes and make them more agitated causing them to attack people. A study of the seasonal distribution of snakebites indicated that snakebites occurred mainly in summer and early autumn and had a similar pattern to that described in a previous local epidemiological study on snakebites.[7,8]

A comparison of our survey with nine other studies undertaken in Taiwan since 1966 revealed that *T mucrosquamatus*, *T stejnegeri*, and cobra were the three most common snakes to attack people (Table 1). We observed that there are more hemorrhagic snakebite cases (including *T mucrosquamatus* and *T stejnegeri*) than neurotoxic-type cases in Taiwan. *T mucrosquamatus* bites are the most common in north Taiwan. Cobra bites may be more common in central Taiwan. Sometimes, *D acutus* and *D russelii siamensis* bites have been reported in south Taiwan.[7]

Table 2 Snake types and place of snakebites in north Taiwan

Snake types	Home	Yard	Field	Forest/bush	Waterside	Others	Total
TM	14	27	26	22	3	4	96
TS	1	12	22	10	3	2	50
Cobra	12	5	2	4	1	1	25
BM	1	1	4	3	1	0	10
Unknown	6	18	17	6	2	1	50
Total	34	63	71	45	10	8	231

BM = *Bungarus multicinctus*; TM = *Trimeresurus mucrosquamatus*; TS = *Trimeresurus stejnegeri*.

Table 4 Susceptibility of gram-negative bacteria isolated from wound of snakebites to common antibiotics

Susceptible strains, *n* (%)	AK	Amp	Cft	Caz	Cef	GM	Flo	Cip	P/T	A/S	TMP-SMX	Imi
Morganella morganii (14)	14 (100)	2 (14)	14 (100)	14 (100)	9 (64)	14 (100)	14 (100)	14 (100)	14 (100)	14 (100)	14 (100)	14 (100)
Pseudomonas aeruginosa (5)	4 (80)	0 (0)	0 (0)	5 (100)	0 (0)	5 (100)	1 (20)	5 (100)	5 (100)	2 (40)	1 (20)	5 (100)
Proteus species (5)	4 (80)	0 (0)	5 (100)	5 (100)	0 (0)	5 (100)	5 (100)	5 (100)	5 (100)	5 (100)	4 (80)	5 (100)
Citrobacter species (4)	3 (75)	3 (75)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)	4 (100)
Shewanella putrefaciens (3)	3 (100)	1 (33)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	1 (33)
Providencia rettgeri (3)	3 (100)	0 (0)	3 (100)	3 (100)	2 (67)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)
Escherichia coli (2)	2 (100)	1 (50)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)
Serratia species (2)	2 (100)	0 (0)	2 (100)	2 (100)	1 (50)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)
Klebsiella pneumoniae (1)	1 (100)	0 (0)	1 (100)	1 (100)	1 (100)	0 (0)	1 (100)	1 (100)	1 (100)	1 (100)	0 (0)	1 (100)

A/S = ampicillin/sublactam; AK = amikacin; Amp = ampicillin; Caz = ceftazidime; Cef = cefuroxime; Cft = cefotaxime; Cip = ciprofloxacin; Flo = flomoxef; GM = gentamicin; Imi = imipenem; P/T = piperacillin/tazobactam; TMP-SMX = trimethoprim-sulfamethoxazole.

According to our survey, cobra bites resulted in more severe complications, such as necrotizing fasciitis, compartment syndrome or rhabdomyolysis, and higher mortality rate than snakebites by other species. Fifteen of 25 people bitten by cobras needed incision, debridement, and even fasciotomy for necrotizing fasciitis and compartment syndrome. The cobra venom causes extensive local tissue destruction, mainly because of the effect of cytotoxins and myotoxic phospholipase A2. Phospholipase A2 in cobra venom was shown to have additional neuromuscular blocking activity *in vitro*.[9] The symptoms of neurotoxicity include ptosis, ophthalmoplegia, dysphagia, flaccid paralysis, respiratory paralysis, and coma.[10] A previous study showed that *Naja atra* bites induced neurotoxicity with muscle weakness in 15% (4/27) of the patients.[11] However, in our study, only one patient (1/50) experienced dizziness and vomiting after a cobra bite. The venom of cobra also showed significant hemolytic activity in animal studies. This may be because of the synergistic effect of cardiotoxin and phospholipase A2.[12,13]

Mixed bacterial infections were commonly observed in wound cultures with a combination of gram-positive, gram-negative, and anaerobic microorganisms. *M morganii* and Enterococcus species were the most common pathogens, especially in the cobra oral cavities,[8,14] as noted in the present study. Among aerobic gram-negative bacteria identified, *M morganii* was reported to be the main pathogenic organism in many bacteriological studies involving cases of snakebite wound abscesses.[15,16] More than three-quarters (76%, 13/17) of the wounds caused by cobras bites were colonized or infected by this pathogen, which was susceptible to amikacin, ceftazidime, ciprofloxacin, and piperacillin/tazobactam.

After snakebite, early use of antivenom showed a trend toward a better local outcome within 12 hours. Prophylactic use of antibiotics was still controversial.[16] In our study, cobra bite-related injuries were more severe than other species. Some studies suggested empirical antibiotic treatment for wound infections by cobra.[8,14] For minor wound infections, oral amoxicillin/clavulanate plus ciprofloxacin may be considered and for severe wound infections, parenteral piperacillin/tazobactam may be the choice for polymicrobial infections caused by snakebites. In summary, snakebites, especially cobra snakebite, may cause serious local complications. Oral amoxicillin/clavulanate plus ciprofloxacin or parenteral piperacillin/tazobactam alone can be the choices for empirical or definitive treatment, and surgical intervention should be considered for established invasive soft tissue infections.

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