

# *Aeromonas hydrophila* soft-tissue infection as a complication of snake bite: report of three cases

BY M. T. JORGE, S. DE A. NISHIOKA\*, R. B. DE OLIVEIRA, L. A. RIBEIRO AND P. V. P. SILVEIRA

*Centro de Ciências Biomédicas, Universidade Federal de Uberlândia, Uberlândia, MG, Brazil*

Received 25 September 1997, Revised 30 October 1997

*Aeromonas hydrophila* soft-tissue infection has been associated with fish and reptile bites. There have been three recent cases from Brazil of abscesses complicating snake bites in which *A. hydrophila* was isolated from the purulent exudates. One of the snakes responsible for the bites was a specimen of *Bothrops moojeni*, and the others were most probably also lance-headed vipers. These snakes have a local necrotizing, myotoxic, oedema-inducing venom that must have favoured the multiplication in the injured tissue of *A. hydrophila* strains, which were probably present in the mouth, fangs or venom of the snakes. The use of a tourniquet by two of the patients probably worsened the local envenoming, and contributed to the occurrence of soft-tissue infection. The patients had a good outcome after the abscesses were incised and drained, and after being treated with chloramphenicol. Chloramphenicol appears to be a good alternative for the empirical treatment of soft-tissue infection complicating snake bite in Brazil, because: it is active against the majority of the anaerobic and aerobic bacteria found in these abscesses, including *A. hydrophila*; it can be administered by the oral route; and it is inexpensive. Suitable alternatives are cotrimoxazole or fluoroquinolones, to which aeromonads are usually susceptible *in vitro*, associated with antibiotics, such as clindamycin and metronidazole, with an anti-anaerobic spectrum.

*Aeromonas* species are facultatively anaerobic, Gram-negative rods found as normal flora in non-faecal sewage, freshwater, and brackish water. These bacteria cause disease in fish, reptiles and amphibians. In humans, aeromonads can be isolated from the faeces of asymptomatic individuals, and have been associated with soft-tissue infections, acute gastrointestinal disease, sepsis (particularly in immunocompromised hosts), and, more rarely, with pneumonia, meningitis, endocarditis, osteomyelitis and septic arthritis (Gold and Salit, 1993; McGowan and Steinberg, 1995).

*Aeromonas hydrophila* is the species most commonly recovered from skin and soft-tissue

infections caused by aeromonads, which are usually associated with exposure to contaminated water and water-related injuries (Gold and Salit, 1993; McGowan and Steinberg, 1995). Although cases of soft-tissue infection by *A. hydrophila* complicating bites of other reptiles have been reported (Raynor *et al.*, 1983; Flandry *et al.*, 1989; Mekisic and Wardill, 1992), there appear to be only two reported cases associated with snake bite (Thisyakorn and Thisyakorn, 1988; Nishioka and Silveira, 1992b).

As part of an ongoing, prospective study on venomous snake bite in Uberlândia, south-eastern Brazil, three cases of abscesses caused by *A. hydrophila* complicating bites of snakes, probably all of them lance-headed vipers (genus *Bothrops*), were observed within 2 years in a single university hospital. These cases are reported below.

\* Author to whom correspondence should be addressed. Address for correspondence: Av. Teresina 1415, 38405-384 Uberlândia, MG, Brazil. E-mail: snishioka@hc.ufu.br; fax: 55 34 232 8620.

## CASE REPORTS

**Case 1**

A 34-year-old male was bitten on his right ankle, through his boot and sock, by a specimen of *Bothrops moojeni*. Before going to the hospital, he applied a tourniquet in the proximal segment of his right thigh for about 30 min, and put powdered tobacco on the wound. Physical examination performed at the Emergency Department revealed a single fang mark at the site of the bite, local ecchymosis, and swelling extending up to the knee. The patient complained of severe local pain. He was treated with 12 ampoules of polyvalent *Bothrops* antivenom [manufactured by Fundação Ezequiel Dias (FUNED), Belo Horizonte, Brazil] administered intravenously, and intravenous (i.v.) chloramphenicol (1 g four times daily) was started prophylactically on the orders of the attending physician. Twenty-four hours after the bite the patient had fever, the oedema had extended to his thigh, and the whole limb was hot and red. The patient developed an abscess which was incised and drained. Gram-negative rods were found by direct examination of the pus, which was cultivated in aerobic and anaerobic media. *Aeromonas hydrophila*, which was susceptible *in vitro* to chloramphenicol, gentamicin, amikacin, cefoxitin, ceftriaxone, cotrimoxazole, ciprofloxacin, pefloxacin and imipenem, and resistant to ampicillin and first-generation cephalosporins, was isolated in three different samples. Two blood cultures were negative. The patient was discharged from the hospital much improved after having received i.v. chloramphenicol for 6 days. He was supposed to continue to take oral chloramphenicol (500 mg four times daily for 8 more days), but it is unknown whether he complied with this schedule as he did not return for a follow-up visit.

**Case 2**

While working in a farm, a 15-year-old male was bitten on his right hand by a lance-headed viper which was not captured or killed for identification. He applied a tourniquet in the middle segment of his right forearm, and

within a few hours the swelling extended up to the forearm, and he had severe local pain and profuse sweating. Several bite marks were noticed on his right hand. The patient was given eight ampoules of polyvalent *Bothrops* antivenom (FUNED), and within the next 24 h his pain improved but the oedema extended up to the whole limb, local inflammatory signs became evident and he had fever. A right hand abscess was drained on the fifth day; an *A. hydrophila* strain which was sensitive to cefoxitin, ceftriaxone, gentamicin, amikacin, cotrimoxazole, ciprofloxacin, pefloxacin, and imipenem, and resistant to ampicillin and first-generation cephalosporins, was isolated from the pus. Therapy with i.v. chloramphenicol (4 g) was instituted on the day after the drainage, and the patient was discharged taking oral chloramphenicol (2 g/day) for 13 more days. When last seen, 25 days later, he was asymptomatic.

**Case 3**

A 48-year-old male was bitten on his left ankle by a snake described by him as a lance-headed viper. He was initially seen at a local hospital, where he was given antivenom (five ampoules of polyvalent *Bothrops* antivenom, presumably manufactured by FUNED), and on the following day he was referred to the hospital in Uberlândia because he was oliguric. Examination of the bitten extremity revealed the presence of several scratches at the site of the bite, and of inflammatory signs involving his left lower limb up to the knee. He had mild hyperazotaemia but, after intravenous hydration, mannitol, and alkalination of the urine with sodium bicarbonate, his creatinine and blood-urea nitrogen levels normalised. He also had several episodes of vomiting, and a single one of haematemesis which was attributed to an erosive oesophagitis; he had no clotting abnormalities at the time. Another complication was an abscess on his left leg, which was drained on the fourth day after the bite. The *A. hydrophila* isolated from the pus was sensitive *in vitro* to chloramphenicol, cefoxitin, ceftriaxone, gentamicin, amikacin, ciprofloxacin, pefloxacin, imipenem and meropenem, and resistant to cotrimoxazole,

ampicillin, and first-generation cephalosporin. After the drainage and treatment with chloramphenicol (4 g/day, i.v., for 8 days, and then 2 g/day for 6 days) the patient had progressive improvement of the inflammatory signs, and the fever disappeared. He was well when discharged on the 10th day after the bite.

## DISCUSSION

Snake-bite-associated soft-tissue infections in Brazil have only been reported as a complication of lance-headed viper bite (Andrade *et al.*, 1989; Jorge *et al.*, 1990, 1994; Nishioka and Silveira, 1992b). *Morganella morganii* and other Gram-negative bacilli (and to a lesser extent anaerobes and enterococci) have been isolated from these abscesses. The same micro-organisms have been cultivated from swabs of the mouth and fangs of lance-headed vipers, which are believed to be the source of the bacteria (Jorge *et al.*, 1990). Aerobic Gram-negative rods and anaerobes, including *Clostridium* species, have also been isolated from the venom and oropharyngeal swabs of other snakes around the world which have soft-tissue infection as a complication of their bite, such as North American rattlesnakes and Malayan pit vipers (*Calloselasma rhodostoma*) (Goldstein *et al.*, 1979; Theakston *et al.*, 1990). Interestingly, Enterobacteriaceae, *Pseudomonas aeruginosa* and Gram-positive cocci are part of the mouth flora of South American rattlesnakes (*Crotalus durissus terrificus*) (Garcia-Lima and Laure, 1987), but abscesses complicating their bite have not been reported. Snakes of the genus *Bothrops* have proteolytic, necrotizing, myotoxic and oedema-inducing actions (Ferreira *et al.*, 1992) which probably create a favourable local environment for the multiplication of bacteria (Jorge *et al.*, 1994). The use of a tourniquet worsens the local envenoming, and is possibly a risk factor for the occurrence of soft-tissue infection.

*Aeromonas hydrophila* has been isolated from infections related to the use of medicinal leeches (Lineweaver, 1991) and to bites of catfish (Murphy *et al.*, 1992), piranha (Revord

*et al.*, 1988) and sharks (Royle *et al.*, 1997). It has also been isolated from the mouth of a marsupial: the American opossum (*Didelphis virginiana*) (Howell and Dalsey, 1990). Among reptiles, *A. hydrophila* infection has been associated with alligator and crocodile bites (Raynor *et al.*, 1983; Flandry *et al.*, 1989; Mekisic and Wardill, 1992). In the case of bites by fish and reptiles other than snakes there is no local envenoming, but the trauma is considerably more severe than in snake bites, and the injuries are usually water-related, which increases the likelihood of contamination by *Aeromonas* (Gold and Salit, 1993).

Infection of soft tissue with *A. hydrophila* following snake bite only appears to have been reported twice before, once in Thailand (Thisyakorn and Thisyakorn, 1988) and once in Brazil (Nishioka and Silveira, 1992b), the latter infection complicating a lance-headed viper bite. Although the snake was captured in only one of the present cases, it is likely that all three patients were bitten by lance-headed vipers, because of the presence of local envenoming, which is highly indicative of bites by these snakes in the area of Brazil where the cases were bitten (Nishioka and Silveira, 1992a). Although the observation of several teeth marks and of scratch-like marks at the site of the bites on cases 2 and 3, respectively, indicate that the bites were of colubrid snakes (Nishioka *et al.*, 1995), *Philodryas olfersii*, the local colubrid whose bite is mostly associated with local envenoming (Nickerson and Henderson, 1976), is a green snake, and should be easily differentiated from a lance-headed viper if seen by the victim or witness. None of the cases reported here were associated with exposure to water. It is unlikely that the abscesses were acquired after the admission of the patients to the hospital, although nosocomial soft-tissue infections with *A. hydrophila* have been reported (Goings, 1979).

Aeromonads are susceptible *in vitro* to chloramphenicol, aminoglycosides, tetracycline, cotrimoxazole, fluoroquinolones, and extended-spectrum cephalosporins, whereas they are usually resistant to ampicillin and first-generation cephalosporins, and the activity of amoxicillin/clavulanate against them

has been inconsistent (Burgos *et al.*, 1990; Koehler and Ashdown, 1993; Jones and Wilcox, 1995). There might be some geographical variation of the susceptibility of *Aeromonas* species to antibiotics, as isolates of these bacteria in Taiwan have been shown to be more resistant to cotrimoxazole and some aminoglycosides and extended-spectrum cephalosporins than strains from the U.S.A. and Australia (Ko *et al.*, 1996).

Based on the present cases and the little information already available, the prognosis of soft-tissue infections by *A. hydrophila* complicating snake bite appears to be good. Surgical incision and drainage of abscesses are probably the most important procedures and may be effective even in the absence of other therapeutic measures (Gold and Salit, 1993). Chloramphenicol has been recommended in Brazil as the first-choice antibiotic for the empirical treatment of abscesses complicating snake bites (Anon., 1993). This recommendation is based on the fact that all types of aerobic bacteria isolated from abscesses and from the mouth and venom of snakes have consistently been susceptible *in vitro* to this antibiotic (Andrade *et al.*, 1989; Jorge *et al.*, 1990, 1994; Nishioka and Silveira, 1992b), and the fact that chloramphenicol also has a strong action against anaerobes (Standiford, 1995). Chloramphenicol also appears to be suitable for the empirical treatment of these abscesses because of its low cost, an important advantage

given that poor peasants and rural workers constitute most of the population at risk of snake bite. When administered by the oral route, moreover, this antibiotic achieves serum concentrations comparable with those seen when it is administered intravenously, and it has good penetration in all tissues (Standiford, 1995). The only argument against the use of chloramphenicol is its bone-marrow toxicity, a (fortunately rare) life-threatening side-effect which can be irreversible.

Fluoroquinolones and, to a lesser extent, cotrimoxazole are possible alternatives to chloramphenicol for the treatment of soft-tissue infections by *A. hydrophila*, given that they can also be administered by the oral route and in a more convenient schedule (twice a day compared with four times a day for chloramphenicol). As many soft-tissue infections involving aeromonads (probably including those following snake bite) are polymicrobial and may involve anaerobes (Gold and Salit, 1993), an antibiotic with an anti-anaerobic spectrum, such as metronidazole or clindamycin (both available for oral administration), should also be given if chloramphenicol is not used. When *Aeromonas* bacteraemia complicates soft-tissue infection, a rare event in immunocompetent individuals, initial therapy should be with intravenous antibiotics such as aminoglycosides, third-generation cephalosporins or fluoroquinolones.

## REFERENCES

- ANDRADE, J. G., PINTO, R. N. L., ANDRADE, A. L. S. S., MARTELLI, C. M. T. & ZICKER, F. (1989). Estudo bacteriológico de abscessos causados por picada de serpentes do gênero *Bothrops*. *Revista do Instituto de Medicina Tropical de São Paulo*, **31**, 363–367.
- ANON. (1993). *Manual de Vigilância Epidemiológica; Acidentes por Animais Peçonhentos; Identificação, Diagnóstico e Tratamento*. São Paulo: Centro de Vigilância Epidemiológica 'Professor Alexandre Vranjac'.
- BURGOS, A., QUINADOS, G., MARTINEZ, R., ROJO, P. & CISTERNA, R. (1990). In vitro susceptibility of *Aeromonas caviae*, *Aeromonas hydrophila* and *Aeromonas sobria* to fifteen antibacterial agents. *European Journal of Clinical Microbiology and Infectious Diseases*, **9**, 413–417.
- FERREIRA, M. L., MOURA-DA-SILVA, A. M., FRANÇA, F. O., CARDOSO, J. L. & MOTA, I. (1992). Toxic activities of venoms from nine *Bothrops* species and their correlation with lethality and necrosis. *Toxicon*, **30**, 1603–1608.
- FLANDRY, F., LISECKI, E. J., DOMINGUE, G. J., NICHOLS, R. L., GREER, D. L. & HADDAD JR, R. J. (1989). Initial antibiotic therapy for alligator bites: characterization of the oral flora of *Alligator mississippiensis*. *Southern Medical Journal*, **82**, 262–266.

- GARCIA-LIMA, E. & LAURE, C. J. (1987). A study of bacterial contamination of rattlesnake venom. *Revista da Sociedade Brasileira de Medicina Tropical*, **20**, 19–21.
- GOINGS, S. A. J. (1979). Surgeon a clue in puzzle of unusual outbreak. *Hospital Infection Control*, **6**, 57–59.
- GOLD, W. L. & SALIT, I. E. (1993). *Aeromonas hydrophila* infections of skin and soft tissue: report of 11 cases and review. *Clinical Infectious Diseases*, **16**, 69–74.
- GOLDSTEIN, E. J. C., CITRON, D. M., GONZALEZ, H., RUSSELL, F. E. & FINEGOLD, S. M. (1979) Bacteriology of rattlesnake venom and implications for therapy. *Journal of Infectious Diseases*, **140**, 818–821.
- HOWELL, J. M. & DALSEY, W. C. (1990). Aerobic bacteria cultured from the mouth of the American opossum (*Didelphis virginiana*) with reference to bacteria associated with bite infections. *Journal of Clinical Microbiology*, **28**, 2360–2361.
- JONES, B. L. & WILCOX, M. H. (1995). *Aeromonas* infections and their treatment. *Journal of Antimicrobial Chemotherapy*, **35**, 453–461.
- JORGE, M. T., MENDONÇA, J. S., RIBEIRO, L. A., SILVA, M. L. R., KUSANO, E. J. U. & CORDEIRO, C. L. S. (1990). Flora bacteriana da cavidade oral, presas e veneno de *Bothrops jararaca*: possível fonte de infecção no local da picada. *Revista do Instituto de Medicina Tropical de São Paulo*, **32**, 6–10.
- JORGE, M. T., RIBEIRO, L. A., SILVA, M. L. R., KUSANO, E. J. U. & MENDONÇA, J. S. (1994). Bacteriology of abscesses complicating *Bothrops* snake bite in humans: a prospective study. *Toxicon*, **32**, 743–748.
- KO, W. C., YU, K. W., LIU, C. Y., HUNG, C. T., LEU, H. S. & CHUANG, Y. C. (1996). Increasing antibiotic resistance in clinical isolates of *Aeromonas* in Taiwan. *Antimicrobial Agents and Chemotherapy*, **40**, 1260–1262.
- KOEHLE, J. M. & ASHDOWN, L. R. (1993). In vitro susceptibilities of tropical strains of *Aeromonas* species from Queensland, Australia, to 22 antimicrobial agents. *Antimicrobial Agents and Chemotherapy*, **37**, 905–907.
- LINEWEAVER, W. C. (1991). *Aeromonas hydrophila* infections following clinical use of medicinal leeches: a review of published cases. *Blood Coagulation and Fibrinolysis*, **2**, 201–203.
- MCGOWAN JR, J. E. & STEINBERG, J. P. (1995). Other Gram-negative bacilli. In *Principles and Practice of Infectious Diseases*, 4th Edn, eds Mandell, G. L., Bennett, J. E. & Dolin, R. pp. 2106–2116. New York: Churchill Livingstone.
- MEKISIC, A. P. & WARDILL, J. R. (1992). Crocodile attacks in the Northern Territory of Australia. *Medical Journal of Australia*, **157**, 751–754.
- MURPHY, D. K., SEPTIMUS, E. J., WAAGNER, D. C. (1992). Catfish-related injury and infection: report of two cases and review of the literature. *Clinical Infectious Diseases*, **14**, 689–693.
- NICKERSON, M. A. & HENDERSON, R. W. (1976). A case of envenomation by the South American colubrid, *Philodryas olfersii*. *Herpetologica*, **32**, 197–198.
- NISHIOKA, S. A. & SILVEIRA, P. V. P. (1992a). A clinical and epidemiologic study of 292 cases of lance-headed viper bite in a Brazilian teaching hospital. *American Journal of Tropical Medicine and Hygiene*, **47**, 805–810.
- NISHIOKA, S. A. & SILVEIRA, P. V. P. (1992b). Bacteriology of abscesses complicating bites of lance-headed vipers. *Annals of Tropical Medicine and Parasitology*, **86**, 89–91.
- NISHIOKA, S. A., SILVEIRA, P. V. P. & BAUAB, F. A. (1995). Bite marks are useful for the differential diagnosis of snakebite in Brazil. *Wilderness and Environmental Medicine*, **6**, 183–188.
- RAYNOR, A. C., BINGHAM, H. G., CAFFEE, H. H. & DELL, P. (1983). Alligator bites and related infections. *Journal of the Florida Medical Association*, **70**, 107–110.
- REVORD, M. E., GOLDFARB, J. & SHURIN, S. B. (1988). *Aeromonas hydrophila* infection in a patient with cyclic neutropenia following a piranha bite. *Pediatric Infectious Disease Journal*, **7**, 70–71.
- ROYLE, J. A., ISAACS, D., EAGLES, G., CASS, D., GILROY, N., CHEN, S., MALOUF, D. & GRIFFITHS, C. (1997). Infections after shark attacks in Australia. *Pediatric Infectious Disease Journal*, **16**, 531–532.
- STANDIFORD, H. C. (1995). Tetracyclines and chloramphenicol. In *Principles and Practice of Infectious Diseases*, 4th Edn, eds Mandell, G. L., Bennett, J. E. & Dolin, R. pp. 306–317. New York: Churchill Livingstone.
- THEAKSTON, R. D. G., PHILLIPS, R. E., LOOAREESUWAN, S., ECHEVERRIA, P., MAKIN, T. & WARRELL, D. A. (1990). Bacteriological studies of the venom and mouth cavities of wild Malayan pit vipers (*Calloselasma rhodostoma*) in southern Thailand. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **84**, 875–879.
- THISYAKORN, U. & THISYAKORN, C. (1988). *Aeromonas* infection following a snake bite: a case report. *Southeast Asian Journal of Tropical Medicine and Public Health*, **19**, 307–308.