Local skin reaction to intramuscular administration of enrofloxacin in pythons

Josip Miljković and Dražen Đuričić*

Abstract

Two cases of local skin reactions to intramuscular application of enrofloxacin in a reticulated python (*Malayopython reticulatus*) (6 years, 5.5 kg) and a Burmese python (*Python bivitatus*) (3 years, 25 kg) are presented. The reticulated python was treated for a swelling of the upper jaw, while the Burmese python had respiratory symptoms. The first python was treated with meloxicam for 7 days, but since the swelling did not go down, the local veterinarian consulted a reptile expert. Instead of the recommended marbofloxacin, the animal received an intramuscular injection of enrofloxacin, and swelling and a sterile abscess appeared at the injection site, with local pinkish skin discolouration. After marbofloxacin therapy was continued, the swelling disappeared. The white spotpatch at the site of the single application of enrofloxacin is still present after 3 months. The Burmese python received enrofloxacin and bromhexine hydrochloride intramuscularly for 14 days. Sterile abscesses and skin discolouration occurred at 3-4 sites of enrofloxacin application. Initially, the scales around the site of enrofloxacin application became pale and matte, later appearing as though the scales had melted or fused. Even 5 years later, a slight spherical bulge with a hard-elastic consistency can be felt. The treatment was carried out in another local clinic. Intramuscular application of enrofloxacin in pythons can lead to the formation of a sterile abscess at the injection site and long-term discolouration of the skin above that site, although some prescriptions warn of possible skin discoloration, but only after subcutaneous administration of enrofloxacin.

Key words: *Burmese python, discoloration, enrofloxacin, intramuscular administration, reticulated python, skin reaction*

Introduction

The non-venomous snakes of the genera *Python* and *Malayopython* belong to the family Pythonidae (with other nine genera) and live in Africa and Asia. They feed by wrapping themselves around the prey, which then dies from suffocation, internal bleeding and cardiac arrest.

The Burmese python (*Python bivittatus*, Kuhl, 1820) is an endangered species (classified as vulnerable on the IUCN Red List) native to Southeast Asia, while in Florida, USA it is considered an invasive species following its release into the wild by owners unable to care for their pets (Stuart et al., 2019). Females are longer (3.5-4.5 m) and heavier (30-40 kg) than males. Dwarf forms are found on the islands of Java, Bali and Sulawesi, with an average length of

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2-2.5 metres. Burmese pythons are mainly nocturnal rainforest dwellers.

The reticulated python (*Malayopython reticulatus*, Schneider, 1801) is a species of python and the longest snake in the world, native to South and Southeast Asia. They grow to between 2.5 and 6.5 metres in length and weigh up to 75 kg (Barker et al., 2015). Of the three subspecies, two are dwarf subspecies (*M. r. jampeanus* and *M. r. saputrai*) that originate from different islands of the Sulawesi archipelago (Auliya et al., 2002).

The Burmese python and the reticulated python, together with the ball python, are very popular in the pet trade, and numerous mutations (morphs) with different colours and patterns have been bred through selection. In captivity, snakes are often kept in inappropriate conditions, which can lead to chronic stress and various diseases (Martínez-Silvestre, 2014; Van Waeyenberge et al., 2018; Warwick et al., 2021). Diseases and other health problems in captive reptiles are usually the result of poor breeding management and are often caused by changes in environmental conditions (overcrowding, inappropriate temperature, humidity, light, nutrition and poor hygiene), but also by interactions with newly acquired animals. Potential pathogens of diseases in reptiles can be microorganisms (viruses, bacteria, fungi, etc.) and parasites, physical or chemical (cold, heat, toxins, etc.), mechanical (injuries, etc.) agents, and nutritional deficiencies (Mader, 1996; O'Rourke and Lertpiriyapong, 2015). Bacterial diseases in reptiles are successfully treated with antimicrobial preparations. Unfortunately, bacteria isolated from reptiles show varying degrees of resistance to most antimicrobial agents, including cephalosporins, penicillins, macrolides, lincosamides, tetracyclines, etc., while resistance to quinolones, chloramphenicol, and sulfonamides is less common (Cristina et al., 2022). Quinolones, especially marbofloxacin and enrofloxacin are commonly the drugs of choice once antimicrobial resistance has been identified.

Enrofloxacin is used in veterinary medicine as an antibacterial agent against numerous Gram-positive and Gram-negative bacteria, mainly due to the inhibition of bacterial gyrase and topoisomerase IV, enzymes that facilitate the processes of DNA replication, recombination and gene expression (Grabowski et al., 2022). Ciprofloxacin is the main active metabolite of enrofloxacin conversion, which likely occurs only in the liver (Waxman et al., 2014; Agius et al., 2020; Foster et al., 2023). Side effects or adverse effects of enrofloxacin use have been reported in numerous animal species, manifested as an inflammatory reaction at the injection site and changes in the skeleton (e.g. arthropathies, destruction and degeneration of articular cartilage, damage to tendons, etc.), reproductive system (e.g. reduced mobility and sperm production, increased mortality of embryos, reduced number of oocytes, etc.), nervous system, and immune system, but most often depending on the dose and the frequency of antibiotic use (Sarkozy, 2001; Bidell and Lodise, 2016; Hruba et al., 2019; Khusro et al., 2021; Grabowski et al., 2022). Enrofloxacin is also used to control bacterial infections in exotic animals (Mitchell, 2006), as it is rapidly resorbed after intramuscular, subcutaneous or oral administration in most reptile species and has a high bioavailability (Helmick et al., 2004).

Materials and methods

Two pythons, a purple albino reticulated python (*Malayopython reticulatus*), 6 years old and weighing 5.5 kg, and a granite het albino Burmese python (*Python bivitatus*), 3 years old and weighing 25 kg, are

shown in these cases. The owner of these snakes is located in Split, Croatia. In both cases, the animals were clinically examined and treated in various local veterinary clinics, so data on possible sampling or additional tests (e.g., blood tests, biochemical indicators, x-rays, ultrasound, etc.) was not accessible.

Presentation of cases

Case report 1:

After the owner noticed a swelling on the head (upper jaw) of the reticulated python (Figure 1), professional help was requested. The swelling most likely occurred as a result of repeatedly hitting the head against the terrarium glass. Treatment with the non-steroidal anti-inflammatory drug meloxicam (Metacam, Boehringer Ingelheim Animal Health, Lyon, France) for 7 days was initiated immediately. Since the swelling did not subside, the local veterinarian sought the advice of a reptile expert from the Faculty of Veterinary Medicine, University of Zagreb, who recommended antibiotic therapy with marbofloxacin at the recommended dosage. However, this drug was not available to the veterinarian, so the animal was given an intramuscular injection of enrofloxacin (Enroxyl, Krka, Novo Mesto, Slovenia) instead of marbofloxacin. The next day after enrofloxacin therapy,

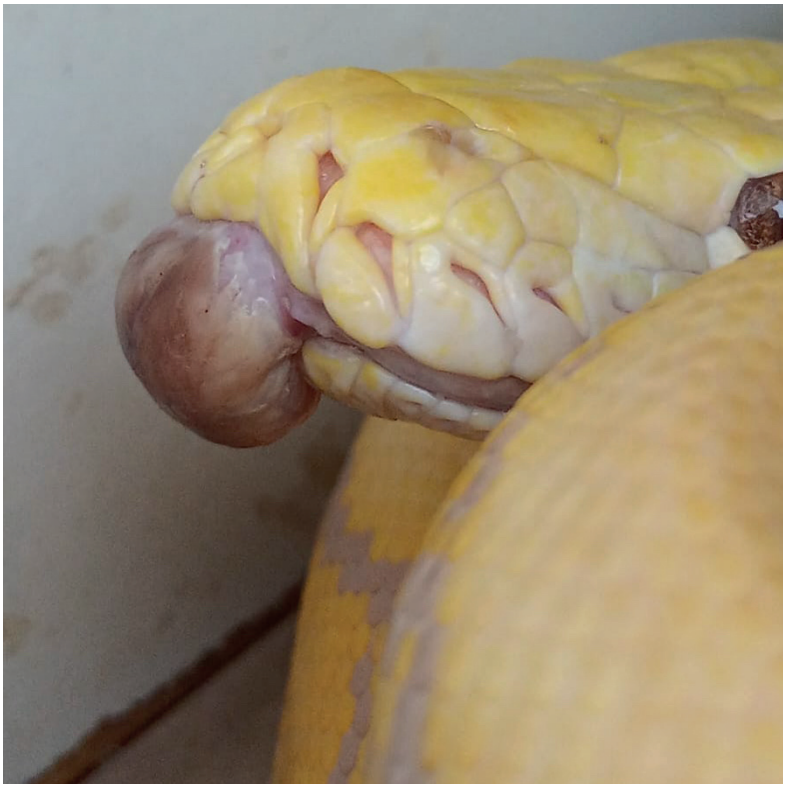

Figure 1. Swelling of the upper jaw of the reticulated pyton (*Malayopython reticulatus*) (June 29, 2024)

Figure 2. Skin reaction (July 4, 2024) 24 h after IM administration of enrofloxacin (pink patch)

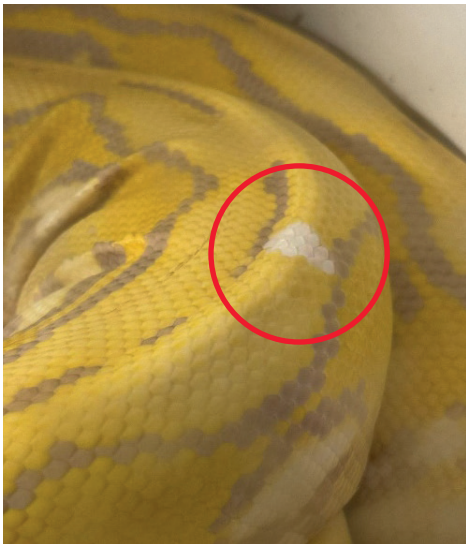

Figure 3. Skin discoloration (white patch) at the site of the single application of enrofloxacin after 3 months (October 8, 2024))

a sterile abscess (Figure 2), swelling and a change in skin colour (pink patch), appeared and persisted for 2 months. After the first dose, Enroxyl was discontinued, and treatment with Marbocyl was continued for 7 days. Thereafter, the swelling on the jaw disappeared, but the discoloration (white patch) at the site of the single application of enrofloxacin is still present even after 3 months (Figure 3).

Case report 2:

In 2019, a 3-year-old Burmese python had respiratory symptoms (heavy breathing with open mouth), after which it received enrofloxacin (Baytril, Bayer Animal Health, Leverkusen, Germany) and bromhexine hydrochloride (Bisolvon, Boehringer Ingelheim, Ingelheim am Rhein, Germany) intramuscularly for 14 days. Sterile abscesses and skin discolouration occurred at 3-4 sites of enrofloxacin application. Initially, the scales around the site of enrofloxacin application became paler and matte (Figure 4). At these sites, it appeared as though the scales had melted, and a slight spherical bulge with a hard-elastic consistency could still be palpated even five years after administration (Figure 5). The treatment was carried out at another local clinic.

Discussion

Almost all veterinary medical preparations used to treat reptiles are not registered for that group of animals (i.e., they are mostly used off-label). Due to the specific anatomical, physiological and behavioural differences between species, it is more difficult to select a suitable antimicrobial agent for reptiles than for mammals. Relatively few pharmacokinetic and pharmacodynamic studies have been conducted on the use of antimicrobial agents in reptiles, and in only a small number of species, so doses are usually empirically derived or prescribed from a different species or groups of reptiles (Jacobson, 1999; Gibbons, 2014). Agius et

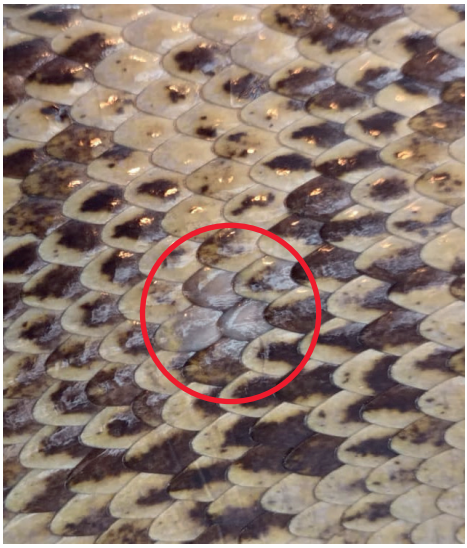

Figure 4. Paler (and matte) scales around the site of enrofloxacin application

Figure 5. Scales that appear as though melted (five years after administration)

al. (2020) used enrofloxacin for the treatment of systemic infections in Asian house geckos, while Pees et al. (2008) found that enrofloxacin can be successfully used to treat lung disease in sea turtles and Indian pythons. In our case, pneumonia in a Burmese python was also successfully treated with enrofloxacin, after which the animal made a full recovery. According to Lewbart (2001), the quinolone compound enrofloxacin (Baytril, Bayer Animal Health, Germany) appears to be safe and effective in reptiles and can be administered intramuscularly (IM), subcutaneously (SC) or orally (PO) at a dose of 5–10 mg/kg/day for 7–21 days, and can be diluted with sterile physiological solution. Similar to Young et al. (1997), enrofloxacin can be administered to treat *Pseudomonas* spp. infection in young Burmese pythons at a dose of 10 mg/kg IM, followed by 5 mg/kg every 48 hours (Young et al., 1997), while the Merck Veterinary Manual recommends administering a PO dose of 5–10 mg/kg/day after the first IM application, as the injection causes necrosis at the injection site (Aiello and Moses, 2016). In the Carpenters' Exotic Animal Formulary (Carpenter, 2018) enrofloxacin is prescribed for most reptile species at a dose of 5–10 mg/kg every 24 hours PO, SC, IM or intracelomic (Ice), but IM administration is painful and can cause skin discolouration or tissue necrosis when administered subcutaneously. In our cases, discolouration occurred even though enrofloxacin was administered intramuscularly and not subcutaneously, as stated in the previous indications. When enrofloxacin is administered SC, it is recommended to dilute it with sterile saline solution. For *Pseudomonas* infections in reticulated pythons, intramuscular administration of enrofloxacin is recommended at a dose of 6.6 mg/kg IM every 24 hours or 11 mg/kg IM every 48 hours (Carpenter, 2018), while for Burmese pythons, rattlesnakes and pit pythons, a dose of 10 mg/kg is recommended every 48 hours (Carpenter, 2018; 2023).

Conclusion

Intramuscular application of enrofloxacin in the Burmese python and the reticulated python may result in the formation of a sterile abscess at the injection site and long-term discolouration of the skin at this site. Some prescriptions warn of possible skin discolouration, but only after subcutaneous administration of enrofloxacin, although this is not supported by the literature reference for snakes but for other groups of reptiles.

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Lokalna kožna reakcija na intramuskularnu primjenu enrofloksacina u pitona

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Prikazana su dva slučaja lokalne kožne reakcije na intramuskularnu primjenu enrofloksacina u mrežastog pitona (*Malayopython reticulatus*) (6 godina, 5,5 kg) i burmanskog pitona (*Python bivitatus*) (3 godine, 25 kg). Mrežastom pitonu liječena je oteklina na gornjoj čeljusti, dok je burmanski piton imao respiratorne simptome. Prvog pitona liječili su 7 dana meloksikamom, budući da oteklina nije nestala lokalni je veterinar zatražio savjet stručnjaka za gmazove s Veterinarskog fakulteta Sveučilišta u Zagrebu. Umjesto preporučenog marbocilina, životinja je liječena intramuskularnu injekciju enrofloksacina, nakon čega se pojavio otok i sterilni apsces s ružičastom lokaliziranom diskoloracijom kože. Nakon nastavka terapije marbofloksacinom otok je nestao. Bijela mrlja na mjestu jednokratne primjene enrofloksacina bila je i dalje prisutna nakon tri mjeseca. Burmanski piton primao je enrofloksacin i bromheksin hidroklorid intramuskularno 14 dana. Na 3-4 mjesta primjene enrofloksacina pojavili su se sterilni apscesi i promjena boje kože. Prvo su ljuskice oko mjesta aplikacije enrofloksacina poblijedjele i bez sjaja, a kasnije je izgledalo kao da su se ljuskice otopile ili spojile. I danas, 5 godina poslije, može se napipati blago kuglasto ispupčenje tvrdo-elastične konzistencije. Liječenje je provedeno u drugoj lokalnoj klinici. Intramuskularna primjena enrofloksacina u pitona može prouzročiti stvaranje sterilnog apscesa na mjestu uboda kao i dugotrajnu promjenu boje kože iznad toga mjesta. Neke upute upozoravaju na moguću promjenu boje kože, ali tek nakon subkutane primjene enrofloksacina.

Ključne riječi: *burmanski piton, diskoloracija, enrofloksacin, intramuskularna primjena, kožna reakcija, mrežasti piton*