FUNGAL INFECTIONS IN REPTILES—AN EMERGING PROBLEM

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Abstract

Dermatomycoses as well as disseminated systemic mycoses are caused by emerging obligate pathogenic fungi of the families *Onygenaceae* and *Clavicipitaceae* in captive as well as in free-living reptiles. Isolation and differentiation of fungal agents and evaluation of their pathogenicity in diseased reptiles using histopathological examination are necessary to determine the pathogenicity of a fungal isolate in the disease process. Fungi formerly known as *Chrysosporium* anamorph of *Nannizziopsis vriesii* have recently been reassigned to the family *Onygenaceae*, order Onygenales (Eurotiomycetidae, Eurotiomycetes, and Ascomycota), based on phylogenetic studies. To date, 9 different reptile pathogenic species are known from this family, grouped in 3 phylogenetic lineages. The most relevant are *Nannizziopsis guarroi* affecting inland bearded dragons (*Pogona viticeps*) and green iguanas (*Iguana iguana*), as well as *Ophidiomyces ophiodiicola* in free-living snakes, which cause deep fungal dermatitis. Treatment with voriconazole is possible in bearded dragons and girdled lizards (*Cordylus giganteus*). Other obligate pathogenic fungi belong to the family *Clavicipitaceae*, which causes granulomatous glossitis, pharyngitis, and dermatitis, as well as disseminated visceral mycosis, in various lizards, tortoises, turtles, and crocodilians. No reports exist about successful treatments against fungal pathogens in the family *Clavicipitaceae*. Also, voriconoazole should be used carefully in chameleons, as it does not seem to be well tolerated in these species.

Key words: *Nannizziopsis guarroi; Chamaeleomyces granulomatis; Chamaeleomyces viridis; Metarhizium anisopliae; Purpureocillium lilacinum*

Historically, reptile fungal infections have often been described as opportunistic pathogens. This may be partly true for yeast infections of the gastrointestinal tract as well as for mold infections of wounds and the cloaca. Conversely, dermatomycoses, as well as disseminated systemic mycoses, are caused by emerging obligate pathogenic fungi of different orders in captive as well as free-living reptiles.[1] Isolation and differentiation of fungal agents and evaluation of their pathogenicity in diseased reptiles using histopathological examination are necessary to determine a fungal isolate as pathogenic in a disease process. The knowledge of a fungal organism's pathogenicity is especially important for clinicians who have to interpret mycological results. However, mycological findings should be based on culture results as well as differentiation of the isolates with molecular biological methods or matrix-assisted laser desorption ionization-time-of-flight mass spectrometry (MALDI-TOF MS). The latter diagnostic technique does not appear available for the differentiation of reptile-associated fungi, as no reports exist. Obligate reptile pathogenic fungi from the families *Onygenaceae* and *Clavicipitaceae* as well as nonhuman pathogenic environmental fungi are not included in the commercially available MALDI-TOF MS database.[2,3] However, MALDI-TOF MS is a rapid and reliable alternative to multilocus sequencing for the differentiation of facultative reptile pathogenic yeasts and molds and it is most likely that future databases would be expanded to cover reptile isolates in the near future.[4,5] To date, the gold standard of fungal differentiation for fungal organisms that infect reptile species is multilocus sequencing of the large

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or small subunit and the internal transcribed spacer region of the nuclear ribosomal gene. Many reports exist that do not include species differentiation or associated histopathological findings, so that the pathogenic role of the fungi remains unclear. However, some reports exist from recent years that demonstrate the pathogenicity of obligate pathogenic fungi from the families *Onygenaceae* and *Clavicipitaceae*.

CHRYSOSPORIUM ANAMORPH OF *NANNIZZIOPSIS VRIESII*-COMPLEX

Fungi formerly known as *Chrysosporium* anamorph of *Nannizziopsis vriesii* (CANV) have recently been reassigned to the family *Onygenaceae*, order Onygenales (Eurotiomycetidae, Eurotiomycetes, and Ascomycota) based on phylogenetic studies.[6] To date, 9 different reptile pathogenic species are known, clustered in 3 phylogenetic lineages: *Nannizziopsis* with *Nannizziopsis vriesii*, *Nannizziopsis dermatitidis*, *Nannizziopsis crocodile*, *Nannizziopsis barbata*, and *Nannizziopsis guarroi*; *Paranannizziopsis* with *Paranannizziopsis australasiensis*, *Paranannizziopsis californensis*, and *Paranannizziopsis crustacea*; and *Ophidiomyces* with *Ophidiomyces ophiodiicola*.[6] Fungal infection of the skin caused by members of the CANV-complex has been reported in various reptile species. *Nannizziopsis* spp. are pathogenic in lizards like *Ophidiomyces* spp. are in snakes. The most important fungal organism for commonly kept lizards is *N. guarroi*, which causes dermatitis in inland bearded dragons (*Pogona viticeps*)[7,8] and green iguanas (*Iguana iguana*)[9,10] in Europe and the USA. In the USA, Europe, and Australia, *O. ophiodiicola* causes fungal dermatitis in free-living as well as captive snakes.[11–13]

FIGURE 1. Head of a bearded dragon (*Pogona vitticeps*) with a yellow to brown crusty extensive skin lesion caused by *Nannizziopsis guarroi* infection.

Clinical Signs, Pathological Findings, and Affected Species

Typical clinical presentations of dermatomycosis in reptiles are yellow to brown crusty lesions of single scales, which may expand to involve extensive skin areas. Reptiles maintained as single animals, collections, and free-range reptiles can be affected. In bearded dragons, lesions are commonly called "yellow fungus disease" and are caused by the obligate fungal pathogen *N. guarroi* (Fig. 1).[6] The same disease appearance has been described in green iguanas,[6,9,14] leopard geckos (*Eublepharis macularis*),[15] different species of chameleons,[16,17] European green lizard (*Lacerta viridis*),[9] girdled lizard (*Cordylus giganteus*),[18] tuatara (*Sphenodon punctatus*),[6] brown tree snakes (*Boiga irregularis*),[12] garter snake (*Thamnophis* sp.),[19] green anaconda (*Eunectes murinus* murinus),[6] broad-headed snake (*Haplocephalus bungaroides*),[6] timber rattlesnakes (*Crotalus horridus*),[13] and saltwater crocodiles (*Crocodylus prosus*)[6,20] from North America, Europe, Asia, and Australia. Other than the previously described skin lesions, rare cases of systemic infection exist in the form of fungal granulomas involving the liver, which have been described in bearded dragons with *N. guarroi* infection.[21]

Diagnostic Procedures and Differentials

Lizards and snakes with brown crusty lesions should be carefully examined. Fungal dermatitis is a main differential disease diagnosis in cases when multiple individuals from one collection suffer from such lesions. Cytological and histopathological examination of the skin and underlying tissue biopsy samples are recommended to diagnose deep fungal dermatitis. Inflammatory cells consisting of heterophils, macrophages, and lymphocytes, as well as fungal conidia (aleurioconidia and arthroconidia), with budding and short solitary undulate, occasionally septate, and hyphae are often detected via cytological examination from dermal samples collected from infected individuals. Histopathological examination reveals granulomas in the epidermis as well as underlying tissues.