

Ophidian Serpentoviruses (Nidoviruses): What We Know, What We Don't Know, and What We are Figuring Out

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Abstract: Ophidian serpentoviruses, previously referred to as nidoviruses, are increasingly being identified as important agents of clinical disease in captive snake populations. Serpentovirus infections can cause severe and sometimes fatal upper respiratory and upper alimentary disease that can result in significant losses to private and zoological collections. The objective of this presentation is to introduce the audience to the history of the viruses in snakes (and other reptiles), and detail comparative clinical, gross, and histopathologic findings in various snake species naturally infected with ophidian nidoviruses from both published and unpublished data. The current diversity of serpentoviruses known of reptiles will be presented, including which species are more commonly found to be clinically affected, and what that means for large and mixed snake collections. A review of diagnostic options and developing tests and future research directions will also be presented. The intent of this talk is to present the information known about these viruses to clinicians in a way that focuses on features of clinical and management significance.

Introduction

Since the first reports of serpentovirus infections in snakes (previously referred to as nidoviruses) in 2014,¹⁻³ much has been learned about these important pathogens. Serpentoviruses are most commonly associated with disease in pythons,¹⁻⁵ but can also infect other species of boids.⁶ Rarely, they can also be detected by molecular screening in colubrids (R.O., oral communication, April 2019). They are known to infect captive snakes in North America²⁻³ and Europe,^{1,4,6-7} though both wild reservoirs of related viruses in native and feral, free-ranging boid species are suspected. Serpentoviruses can be an important cause of morbidity and mortality in captive collections, and as such represent an important emerging snake pathogen that reptile veterinarians should be familiar with. An overview of the clinical presentation, postmortem findings, diagnostic testing options, and biosecurity recommendations will follow in this brief review of ophidian serpentovirus infections.

Clinical Signs of Serpentovirus Infection

Serpentovirus infections manifest as oral and upper respiratory disease in pythons. Early signs of infection include reddening of the oral mucosa,⁵ excess oral mucus production,⁵ and may be associated with audible clicks and wheezes on respiration. The production of oral and nasal mucus can be copious, and may be evident on the sides of enclosures. The presence of excessive mucus is an important diagnostic feature, as it is something not commonly associated with other common viral respiratory infections in snakes, such as paramyxoviruses and reoviruses. Advanced serpentovirus infection is commonly associated with severe stomatitis and pneumonia with secondary Gram-negative bacterial infections.²⁻⁴ While antimicrobial therapy may be palliative in the short term, signs often recur. Evidence of severe respiratory distress, including abnormal posturing, open-mouth breathing, and continued excessive mucus production, are commonly observed in advanced cases (R.O., oral communication, April 2019).

Postmortem Findings

On gross necropsy, serpentovirus lesions are present in the oral and nasal cavities, the trachea, and, variably the orad (proximal) esophagus, and lungs.²⁻⁵ Necrotizing stomatitis and nasopharyngitis (choanal) with associated plaques of necrotic and exudative material are often the result of concurrent viral and bacterial infections.²⁻³ Abundant mucus or mucoid exudate is often present in the oral cavity, choanal, glottis/trachea, and esophagus. The lungs are often thick, edematous, and dark red, and may have the accumulation of mucus and/or exudate within the central lumen or faveoli that can extend back to the membranous portion of the caudal lung. Histologically, serpentovirus infections are characterized by proliferative and necrotizing inflammation of the oral, nasal, pharyngeal, proximal esophageal, sinus, and tracheal mucosa as well as proliferative pneumonia with prominent lymphocytic inflammation.²⁻⁵ Complicating secondary bacterial infections will add components of granulocytic inflammation and exudate accumulation in the aforementioned lesions.^{2,3} The documentation of proliferative inflammation of the proximal esophagus is an important diagnostic feature of serpentovirus infections not seen in paramyxovirus or reovirus infections. Viral inclusion bodies are not a reported feature of serpentovirus infections, and while viral inclusion-like structures can sometimes be seen in some cases, they are not a reliable diagnostic feature (R.O., oral communication, April 2019). As lung involvement may not be striking in early serpentovirus cases (particularly if animals are sacrificed for diagnostic screening), histologic examination of the glottis, trachea, oral mucosa, tongue, and proximal esophagus in addition to the lung are all recommended for serpentovirus diagnosis, and can easily be examined in a single sagittal section of the ventral oral cavity.

Diagnostic Testing Options

Antemortem diagnosis of serpentovirus infection is readily attainable of degenerate reverse-transcription polymerase chain reaction (RT-PCR testing) of a variety of samples. Swabs of the choanal and proximal esophagus using a polyester/rayon tipped, plastic shaft swab are preferred. Other samples, such as general swabs of the oral cavity, and tracheal washes are also good samples, though bacterial contamination (oral swabs) and dilution effects (tracheal washes) may decrease assay sensitivity (R.O., oral communication, April 2019). For postmortem sampling, frozen lung, trachea, and proximal esophagus are recommended. A number of private diagnostic and academic diagnostic laboratories offer RT-PCR testing. The most important thing to be aware of is the diversity of serpentoviruses identified to date. Labs offering specific RT-PCR or quantitative (real time) PCR tests may be able to detect specific viruses (such as ball python or green tree python serpentoviruses), but may miss other viruses. Since single hosts (such as ball pythons and green tree pythons) can be infected with a variety of serpentoviruses, broadly reactive degenerate RT-PCR is the preferred method for initial diagnostics. If candidate viruses are identified, then collection screening and surveillance by real time PCR becomes more useful.

Biosecurity Recommendations

One of the most commonly encountered questions regarding serpentovirus infections in snake collections is what measures can be taken to control the spread of the virus, which has strong potential for causing high morbidity and mortality within collections.³ Unfortunately, much of the background experimentation needed to accurately answer this question has not yet been performed; however, with the successful isolation and culture of this virus on susceptible cell lines,³ active research projects to establish assays to determine viral infectious titers and how those titers change in response to environmental conditions and susceptibility to common disinfectants are ongoing. In situ hybridization (ISH) visualization of viral nucleic acids in diseased snakes with multiple ophidian serpentoviruses documents the presence of abundant virus within the oral and respiratory mucoid secretions

(R.O., oral communication, April 2019), suggesting a strong potential for droplet transmission. Moreover, swallowed mucoid discharge and the detection of virus within the lumen of the gastrointestinal tract also suggests the potential for fecal viral transmission (R.O., oral communication, April 2019). As such, collection owners should be advised of the broad susceptibility of pythons (and some boids) to these viruses, and the potential for spread between different host species. Practices to minimize movement of material between enclosures/tubs (especially uneaten food items) and proper disinfection protocols should be encouraged. Antemortem screening and isolation of RT-PCR positive animals may also mitigate the effects of these pathogens in large collections. Appropriate quarantine protocols for new acquisitions with successive rounds of antemortem diagnostic screening are recommended before introduction of new animals into established groups.

Summary

Ophidian serpentoviruses (nidoviruses) are an important group of respiratory pathogens for which there is rapid evolution of veterinary medicine's understanding of their significance to captive snake collections. While there are limited treatment options for affected snakes, the diagnostic features of serpentovirus infections are distinguishable from other snake viral pathogens. With proper biosecurity and quarantine protocols, veterinarians and hobbyists/owners can work together to limit the potential effect of these viruses on captive animals.

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