

CASE REPORT

Vernal-like conjunctivitis in a western lowland gorilla (*Gorilla gorilla gorilla*)

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Abstract

Case description A 17-year-old female western lowland gorilla presented with bilateral ocular discharge, conjunctivitis, and rhinitis that was investigated and treated over a 34-month period. Clinical findings, diagnostic results, treatment, and follow-up are described.

Clinical finding A mild intermittent mucoid ocular discharge was initially noted. 10 months later, conjunctival hyperemia and thickening developed and progressed rapidly to a mass-like lesion covering the right eye. Hematology revealed eosinophilia. Conjunctival cytology revealed eosinophils and neutrophils, and histopathology revealed a chronic proliferative eosinophilic conjunctivitis. 21 months after, the ocular lesions were investigated the gorilla developed masses within both external nares. Histopathology of the nasal lesions revealed chronic-active eosinophilic rhinitis.

Treatment and outcome Treatment of the gorilla was based on protocols recommended for human patients. Protocols for mild, moderate, and finally severe disease were used, involving topical and oral combinations of treatments. The gorilla eventually responded to systemic immunosuppressant therapy recommended for severe refractory disease.

Clinical significance To the authors' knowledge, this is the first reported case of vernal-like conjunctivitis in a western lowland gorilla.

Key Words: conjunctivitis, cyclosporine, eye(s), gorilla, vernal

INTRODUCTION

Vernal conjunctivitis ('spring catarrh'), also known as vernal keratoconjunctivitis (VKC), is one of several forms of allergic conjunctivitis described in humans. It is an uncommon chronic ocular disease characterized by allergic inflammation of the ocular surface.^{1,2} Despite its name, occurrence is not limited to the spring—initial seasonal episodes become perennial after a few years.¹ VKC was traditionally considered a type I hypersensitivity reaction,³ but more recent studies have suggested a complex non-IgE-dependent mechanism.^{1,3,4}

This report describes a case of vernal-like conjunctivitis in a western lowland gorilla (*Gorilla gorilla gorilla*). The western lowland gorilla is native to Central Africa and is listed as critically endangered by the International Union for the Conservation of Nature's red list of threatened

species. Normal ocular anatomy of the western lowland gorilla has been previously reported.^{5,6} Reported ophthalmic disease includes cataract,⁷ hypertensive retinopathy,⁸ macular degeneration,⁹ and keratitis caused by *Onchocerca volvulus*.¹⁰ To the best of the authors' knowledge, this is the first report of vernal-like conjunctivitis in a western lowland gorilla.

CASE REPORT

History and signalment

A 17-year-old female western lowland gorilla (weight 85.7 kg; *Gorilla gorilla gorilla*) developed bilateral ocular discharge, conjunctivitis, and rhinitis that was investigated and treated over a 34-month period. The only prior medical history was a single episode of mastitis after giving birth 3 years previously.

The gorilla remained otherwise well throughout the entire period, and no other gorillas in the family group of 11 members were affected.

The initial clinical sign, noted by the keepers, was a mild and intermittent mucoid ocular discharge (Fig. 1a) that was unresponsive to oral NSAID therapy with meloxicam (Metacam 15 mg/mL oral suspension for horses; Boehringer Ingelheim Ltd., Berkshire, Bracknell, UK) 0.1 mg/kg PO q24 h $\times$ 3 days on three occasions over 10 months (Fig. 1a). No signs of apparent discomfort were noted. Conjunctival hyperemia and thickening developed 10 months after onset and was unresponsive to amoxicillin clavulanic acid (Clavaseptin 500 mg palatable tablets; Vetoquinol UK Ltd., Buckinghamshire, Penrith, UK) 15 mg/kg PO q12 h for 14 days and then 4 weeks later enrofloxacin (Baytril flavor tablets 150 mg; Bayer plc, Berkshire) 5 mg/kg PO q12 h $\times$ 14 days. The conjunctival signs progressed rapidly over a further 5 months. In the right eye, an extensive mass-like lesion obscured the eye (Figs 1b and 2a). Ocular irritation was manifested by frequent rubbing of the eyes.

Clinical examination

Examination under general anesthesia was performed at this stage (15 months from the onset). The gorilla was immobilized with 0.03 mg/kg medetomidine (Zalopine; Orion Pharma, Espoo, Finland) and 4 mg/kg ketamine (Narketan; Vetoquinol UK Ltd., Buckinghamshire) administered intramuscularly by remote injection. Induction was smooth, and the gorilla was intubated and maintained on oxygen/isoflurane.

Ocular examination revealed severe generalized hypertrophy and papillary proliferation of the palpebral and bulbar conjunctivae (Fig. 2b). In the left eye, this was most marked on the medial aspect of the globe. In the right eye, the proliferation was most marked on the dorsal palpebral conjunctiva and resulted in the formation of the extensive, mass-like lesion which completely covered the eye itself (Figs 1b and 2a). Organic debris (from bedding materials) adhered to the surface of the lesion. The conjunctival lesions extended to the eyelid margins in both eyes and obliterated the normal anatomy of the upper eyelid margin in the right eye. There were two focal swellings

within the upper eyelid margin of the left eye, consistent with chalazia. The conjunctivae of both eyes had a distinct 'cobblestone' appearance. The surface was friable and bled when touched with instruments. In both eyes, the bulbar conjunctivae immediately adjacent to the limbus were pigmented (normal for this species) and slightly thickened. There was no evidence of corneal pathology with slit-lamp biomicroscopy and the cornea was fluorescein negative in both eyes. Indirect ophthalmoscopy was not performed. The skin of both eyelids appeared relatively normal. Tear production was > 25 mm/minute in the left eye. Tear production was not assessed in the right eye because of the mass. The IOP was 9 mmHg in the left eye and 6 mmHg in the right eye (12.0 ± 4.3 mmHg [6]) (assessed by applanation tonometry, TonoPen (Mentor, Santa Barbara, CA, USA)). Examination of the oral cavity, throat, and external nares revealed no abnormalities. All superficial lymph nodes appeared normal. The rest of the clinical examination was unremarkable.

The abnormal conjunctiva was debulked by sharp surgical excision in both eyes. Although the excision was extensive in the right eye, not all abnormal conjunctivae were removed. Hemorrhage was minimal (cautery was not required, and no sutures were placed).

Diagnostic tests and results

Multiple diagnostic samples were obtained. These are summarized together with the respective results. Routine hematology and biochemistry were unremarkable apart from an eosinophilia of $0.5 \times 10^9/L$ ($0.00\text{--}0.38 \times 10^9/L$).¹¹ Serology for six infectious pathogens was negative (*Treponema pallidum*, simian T-lymphotropic virus, simian immunodeficiency virus, hepatitis A, hepatitis B, and hepatitis C). Conjunctival bacteriology (aerobic and anaerobic) revealed *Staphylococcus* species (coagulase negative) in both eyes, and nonhemolytic *E.coli* (right eye only). Fungal culture of the conjunctiva was negative. Conjunctival polymerase chain reaction (PCR) for four pathogens was negative (herpes simplex virus, *Treponema pallidum*, *Chlamydia trachomatis*, and *Haemophilus ducreyi*). Conjunctival cytology revealed eosinophils and neutrophils interspersed with scattered mast cells (Fig. 3a). Conjunctival histopathology (examined by a veterinary pathologist and reviewed by two



Figure 1. (a) Bilateral mucoid ocular discharge. (b) Red mass-like conjunctival lesion covering the right eye.

Figure 2. (a) Red mass-like conjunctival lesion covering the right eye. (b) Hypertrophy and papillary proliferation of palpebral and bulbar conjunctivae of the left eye.

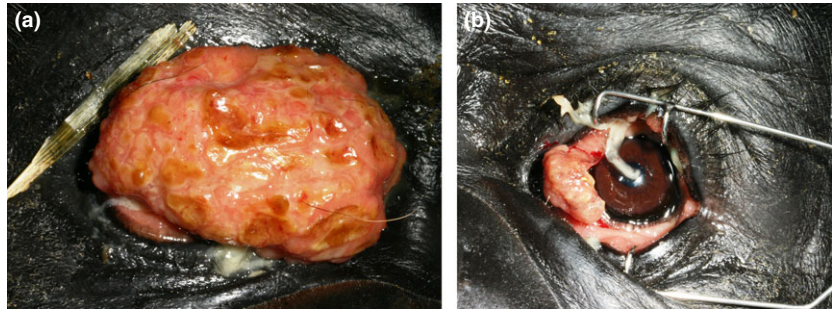
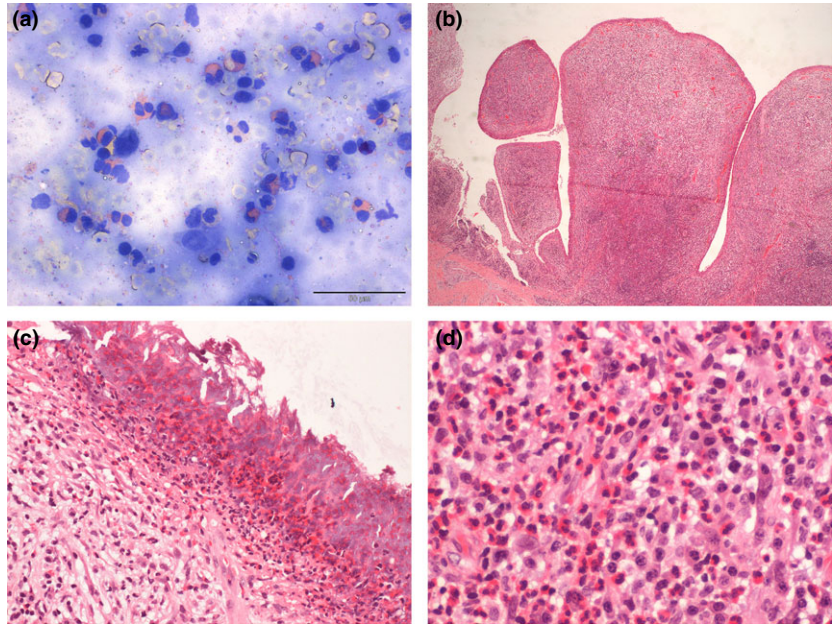


Figure 3. (a) Conjunctival cytology. An impression smear reveals mixed eosinophilic and neutrophilic inflammation (formalin artifact is present). (Modified Wright-Giemsa stain $\times 400$). (b) Conjunctival histopathology. Papilliform proliferation of conjunctiva corresponding to the cobblestone appearance seen clinically. (H&E $\times 20$). (c) Conjunctival histopathology. Ulceration associated with an eosinophilic exudate. (H&E $\times 200$). (d) Conjunctival histopathology. The conjunctival stroma is infiltrated and expanded by mixed eosinophil-rich inflammation. (H&E $\times 400$).



independent colleagues specializing in human ophthalmic pathology) revealed a chronic proliferative eosinophilic conjunctivitis associated with erosion (partial loss of the surface epithelium) and ulceration (complete loss of the surface epithelium down to the basement membrane) (Fig. 3b–d). No infectious agents including parasites were identified.

Diagnosis

The clinical and histopathologic findings were indicative of a hypersensitive etiology. The ophthalmic and histologic features of this case namely marked proliferative conjunctivitis associated with fibrovascular tissue formation, heavy eosinophilic infiltrate, and the formation of large papillae resembling cobblestones were consistent with vernal conjunctivitis in humans ('spring catarrh' or 'vernal catarrh'). More specifically, the diagnosis was a mixed-type vernal-like conjunctivitis (comprising the palpebral and limbal forms).

Follow-up

Up to 5 months Immediate postoperative treatment comprised meloxicam (Metacam 15 mg/mL oral suspension

for horses; Boehringer Ingelheim Ltd.) 0.1 mg/kg PO q24 h $\times$ 14 days, amoxicillin clavulanic acid (Clavaseptin 500 mg palatable tablets; Vetoquinol UK Ltd.) 15 mg/kg PO q12 h for 14 days, and azithromycin (Zithromax 250 mg capsules; Pfizer Ltd, Sandwich, Kent, UK) 750 mg PO q 24 h $\times$ 3 days).

The conjunctival thickening started to recur within 10 days of the surgery. The gorilla was immobilized again (using the same protocol; weight 86.0 kg) for subconjunctival methylprednisolone treatment (methylprednisolone acetate (Depomedrone V; Pfizer Ltd) 200 mg injected subconjunctivally into both upper eyelids) once the absence of corneal pathology had been reaffirmed. Oral antihistamine treatment was prescribed (fexofenadine, Telfast; Sanofi, Dagenham, UK, 180 mg PO q24 h $\times$ 5 months) in parallel with a training program for topical ophthalmic therapy.

The conjunctival thickening showed signs of regression within 1 week.

Five to 21 months After 5 months of positive reinforcement training, the gorilla started to accept saline eye drops (0.9% saline eye drops (Sodium chloride eye drops 0.9%, Martindale Pharma, Essex). The drops were applied

twice daily to both eyes for 4 weeks and then substituted with prednisolone eye drops (1% prednisolone acetate eye drops (Predforte eye drops, Allergan, Buckinghamshire) three times daily to both eyes. The VKC signs were controlled with the prednisolone eye drops for 5 months. Recurrence of conjunctival thickening and proliferation was managed by the addition of 0.5% cyclosporine A eye drops (intravenous cyclosporine A, Sandimmun, Novartis Pharma AG, Switzerland diluted with preservative-free artificial tears, Refresh tears, Allergan, Irvine, USA[10]) three times daily to both eyes in conjunction with the prednisolone acetate drops (also three times daily both eyes). The concentration of CsA was increased from 0.5 to 2% over 12 months. The combined topical steroid–cyclosporine therapy was ineffective, and the lesions continued to progress. Oral cyclosporine A (cyclosporine A 425 mg (Atopica; Novartis Animal Health UK Ltd., Surrey, Camberley, UK) PO q24 h ongoing) was prescribed 13 months after the initial sedation in addition to topical therapy with prednisolone and cyclosporine. For 16 months, the combination of oral and topical therapy was successful in preventing further deterioration of the ocular lesions although the existing lesions did not regress.

At 21 months despite the ocular lesions being well controlled, nonocular lesions were noted for the first time—smooth, pink masses within both external nares. There was no nasal discharge or apparent discomfort; there was mild upper respiratory noise but no evidence of dyspnoea. All the other gorillas in the group continued to appear normal and to be in good health. A third general anesthetic was performed (using the same protocol used on the first two occasions; 93.0 kg). Examination of the entrance to both nostrils revealed multiple small (1–10 mm diameter) smooth pink lesions from the nasal mucosa (Fig. 4). Multiple biopsies were submitted for histopathology. A repeat ocular examination revealed conjunctival lesions (as previously described) and no evidence of corneal pathology. A general examination was again otherwise unremarkable (including the oral cavity, throat,



Figure 4. Multiple pink lesions arising from the nasal mucosa.

and superficial lymph nodes). The subconjunctival injection of methylprednisolone was repeated in both upper eyelids (200 mg methylprednisolone acetate [Depomedrone V; Pfizer Ltd]).

Histopathology of the nasal lesions revealed chronic-active polypoid eosinophilic rhinitis, consistent with an allergic etiology.

Husbandry: The bedding substrate was changed at 21 months. The gorilla and her group had been kept in a house with straw bedding and an outside enclosure that used a deep litter straw system. The gorilla group's bedding was changed to wood wool (Heumuller Holzwooler, Germany), and the outside substrate was changed to sweet chestnut bark chippings (made on site). These changes did not lead to an improvement in the gorilla's symptoms over the next 5 months.

29 months 29 months after the initial sedation, the conjunctival masses started growing rapidly despite ongoing therapy with oral and topical cyclosporine and topical prednisolone.

At this point, the gorilla was prescribed oral prednisolone 1 mg/kg PO sid (Prednicare 5 mg tablets; Animalcare, York, UK). This treatment appeared to be very effective, and no side effects were noted. Within 1 month, the signs of ocular irritation and ocular discharge resolved, the nasal lesions were not visible and the conjunctival thickening was much reduced. Within 3 months, the conjunctival lesions were barely visible. At the time of writing, 6 months after oral prednisolone was initiated, the clinical signs remain in remission.

DISCUSSION

Vernal keratoconjunctivitis (VKC) in humans is a form of chronic allergic bilateral conjunctivitis characterized by eosinophilic inflammation of the tarsal conjunctiva (palpebral form), the bulbar conjunctiva (limbal form) or the cornea (keratitis), or a combination (mixed-type VKC).

Predisposing factors for VKC are male gender, young age, and a familial history of allergies. Although over 40% of patients have a family history of allergy,¹² no genetic predisposing factor has been identified for VKC. However, VKC is known to be more prevalent in some populations.¹ The gorilla in this case developed symptoms of VKC at the young age of 16 years (life span in captivity 40–50 years). She was born in captivity in France and transferred to a zoological park in the UK aged eight years. None of the gorilla's relatives in France, or her offspring in the UK, appear to suffer from allergic disease. In humans, VKC is primarily a disease affecting young individuals and it generally resolves after puberty.^{1,13} However, cases can be diagnosed at an older age,³ as is the case with this gorilla.

The most common presenting symptoms are itching (96.4%) and hyperemia (90.3%). Tearing and a sticky

mucous discharge are also typical.^{1,3,4} The inflammation and subsequent tissue remodeling in the conjunctiva result in the formation of papillae, which can become large enough to cause a 'cobblestone' appearance. In this case, the gorilla showed all of these clinical signs and developed large cobblestone papillae.

Diagnosis of VKC in humans is usually based on the characteristic clinical signs^{1,3} as there are no standardized diagnostic criteria.¹ In difficult cases, conjunctival cytology and histopathology can be used to demonstrate the presence of eosinophils.^{3,4} A case series of VKC in humans found that eosinophils were present in conjunctival scrapings in 85.1% of cases.³ Histopathology shows features of chronic inflammation with eosinophilic infiltrate at all stages of the disease.¹ Eosinophils were a prominent feature on both cytology (conjunctival) and histopathology (conjunctival and nasal) in this case. Total and specific IgE determination, as well as allergy skin prick tests are sometimes used to diagnose VKC in humans.^{3,4} However, they are not considered reliable⁴ as over 50% of patients with VKC test negative. They were not used in this case.

The association of VKC with allergic rhinitis is not characterized in detail,¹² but studies have showed that signs of allergic rhinitis occurred in 37%.^{12,14} In human, those with mixed-type VKC and eosinophilia have higher rates of rhinitis.¹² The gorilla was in accordance with this, having mixed-type VKC, allergic rhinitis, and a circulating eosinophilia.

The diagnosis was made from the characteristic clinical signs (pruritus, hyperemia, mucoid ocular discharge, conjunctivitis, and allergic rhinitis) and the cytology and histopathology (eosinophilic conjunctivitis and rhinitis).

The mainstay of VKC treatment is symptomatic treatment with topical therapy,^{3,4,15} although treatment should be tailored according to the severity of disease.¹³ In humans, a 'stepladder' pattern of treatment has been suggested.¹⁶ In this case, the 'stepladder' was followed as far as possible given the limitations of treating a gorilla in captivity. The gorilla's treatments went through those recommended in humans for mild, moderate, and severe disease, and she eventually responded to the systemic immunosuppressants recommended for severe refractory disease. Training the gorilla to reliably accept eye drops took 5 months, and the maximum frequency accepted was three times daily, which is a low frequency when compared to what is prescribed in humans which is typically up to five times daily. There was therefore a strong reliance on oral medication (antihistamines, cyclosporine A, and corticosteroids) alone and in conjunction with topical therapy in this case.

Antihistamines are commonly used in the treatment of VKC.^{1,2,4} They are used topically rather than systemically in humans but were used orally whilst the gorilla received training for topical therapy. They were ineffective. Topical steroid therapy in humans can cause cataract and glaucoma.^{1,3,4,17} This was a concern as immobilization

would be necessary for accurate monitoring by means of tonometry and intraocular examination. Subconjunctival corticosteroid injections were effective for 3 months on two occasions. This has been shown to be useful in cases of VKC refractory to conventional treatment in humans.^{18–21} Topical corticosteroids eye drops were initially effective but only for 6 months. The combination of topical and oral prednisolone was very effective in reducing the size of the conjunctival lesions and the symptoms such as itching, hyperemia, and mucous discharge.²²

In severe forms of VKC that require chronic medication, alternatives to corticosteroids are recommended.² Topical formulations of cyclosporine A have been shown to be successful and safe alternatives in such cases.^{1,2,4,10,23,24} In this case topical cyclosporine was introduced to reduce the dose of steroid eye drops and to try to achieve better control. This was ineffective. Oral cyclosporine has been used in humans in severe vision-threatening VKC.¹⁶ Oral cyclosporine did not affect regression of the conjunctival lesions but stopped progression for 9 months. Furthermore, nasal lesions developed during the oral cyclosporine phase. In summary, oral therapy was much more effective than topical therapy and oral prednisolone was much more effective than cyclosporine A.

In humans VKC environmental triggering factors have been identified, such as sun, wind, and salt water.¹ No specific factors were identified in this case. Although its name suggests that VKC is a seasonal disease, 23% of cases continue throughout the year without remission,³ as in this case. It has been suggested to avoid contact with commonly known allergens like plants and flowers as part of VKC management.¹ Common allergens associated with allergic eye disease are grass pollens.¹² A change of bedding from straw to sweet chestnut bark chippings and wood wool was ineffective. The bedding was not changed earlier because of cost (GPB £8000) and disruption to the gorilla group.

To the authors' knowledge, this is the first reported case of vernal-like conjunctivitis in a gorilla. The presenting signs were very similar to those seen in humans, and the diagnostic test results were also comparable. As in some cases of VKC in humans, allergic rhinitis was present. Treatment was limited by the fact that it took 5 months to train the gorilla to comply with topical ophthalmic medication. However, even then topical treatment was only partially effective. A modified stepladder approach to treatment was followed.

VKC is a chronic condition that can only be managed rather than cured. It is difficult to predict the course of the disease. This gorilla will likely need intensive lifelong medication to control the symptoms and provide an acceptable quality of life.

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