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Authors: Tamborini, Alice, Robertson, Elise, Talbot, Jessica J, and Barrs, Vanessa R

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# Sinonasal aspergillosis in a British Shorthair cat in the UK

Alice Tamborini<sup>1</sup>, Elise Robertson<sup>1</sup>, Jessica J Talbot<sup>2</sup>  
and Vanessa R Barrs<sup>2</sup>

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## Abstract

**Case summary** A 13-year-old, castrated male, British Shorthair cat presented for investigation of chronic, intermittent, bilateral epistaxis and stertor. CT revealed severe asymmetric bilateral intranasal involvement with extensive turbinate lysis, increased soft tissue attenuation and lysis of the sphenopalatine bone and cribriform plate. On retroflexed pharyngoscopy, a plaque-like mass occluded the choanae. Rostral rhinoscopic examination revealed extensive loss of nasal turbinates, necrotic tissue and mucosal fungal plaques in the left nasal cavity. The right nasal cavity was less severely affected. The nasal cavities were debrided extensively of plaques and necrotic tissue. *Aspergillus fumigatus* was isolated on fungal culture, and species identity was confirmed using comparative sequence analysis of the partial  $\beta$ -tubulin gene. On histopathology of nasal biopsies, there was ulcerative lymphoplasmacytic and neutrophilic rhinitis, and fungal hyphae were identified on nasal mucosa, consistent with a non-invasive mycosis. The cat was treated with oral itraconazole after endoscopic debridement, but signs relapsed 4.5 months from diagnosis. Residual left nasal fungal plaques were again debrided endoscopically and oral posaconazole was administered for 6 months. Fourteen months from diagnosis, the cat remains clinically well with mild intermittent left nasal discharge secondary to atrophic rhinitis.

**Relevance and novel information** This is the first case of rhinoscopically confirmed sinonasal aspergillosis to be diagnosed in a cat in the UK. Endoscopic confirmation of resolution of infection is useful in cases where mild nasal discharge persists after treatment.

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## Introduction

Aspergillosis is a mycotic disease affecting a diverse range of human and animal hosts, including mammals and birds.<sup>1–7</sup> In cats, two forms of aspergillosis affect the upper respiratory tract: sinonasal aspergillosis (SNA) and sino-orbital aspergillosis (SOA). In dogs, SNA accounts for >99% of reported cases and is considered non-invasive. This is in contrast to feline aspergillosis, where SOA is reported to be the most common form (65% of reported cases) and is invasive.<sup>1–7</sup>

## Case description

A 13-year-old, castrated male, British Shorthair cat presented for investigation of chronic, intermittent, bilateral mucopurulent nasal discharge, epistaxis, stertor and anorexia. The cat had been diagnosed with lymphoplasmacytic rhinitis elsewhere, 5 years previously. On physical examination, no abnormalities were found and vital

parameters were normal. Results of a complete blood count, coagulation profile and biochemistry were within normal limits. CT of the skull revealed extensive abnormalities affecting both nasal cavities, including bilateral obliteration of the air spaces of the nasal meati extending from the nares rostrally, to the ethmoid ethmoid turbinates caudally. Turbinate detail was obscured by soft tissue/fluid attenuating material, with extension of

<sup>1</sup>VRCC, Laindon, UK

<sup>2</sup>Faculty of Veterinary Science, School of Life and Environmental Sciences, University of Sydney, Sydney, NSW 2006 Australia

### Corresponding author:

Vanessa Barrs BVSc, PhD, MVetClinStud, FANZCVS,  
Faculty of Veterinary Science, University of Sydney,  
Sydney, NSW 2006, Australia  
Email: vanessa.barrs@sydney.edu.au



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similarly attenuating material into the nasopharynx. There was destruction of the sphenopalatine bone on the left side. A focal area of increased attenuation of the right nasal turbinates was also evident at the level of the rostral orbit, but there was no mass effect or erosion/displacement of the vomer bone. The cribriform plate was not intact. No changes were detected in the orbital, frontal and nasal bones.

A 4.0 mm × 60 cm bronchoscope was used for retroflexed pharyngoscopy under general anaesthesia. A large 3 cm × 2 cm plaque was visualised occluding the caudal nasopharynx. A bilateral infraorbital splash nerve block was administered (bupivacaine HCl BP 2.64 mg/ml equivalent to bupivacaine HCl anhydrous 2.5 mg/ml, 0.5 mg/kg total) prior to performing rostral rhinoscopy. The caudal oropharynx was packed with swabs to protect the lower airways. Rostral lavage of the nasal cavity was performed using 10 ml aliquots of sterile saline but failed to dislodge material for diagnostic sampling.

Nasal cavity examination was performed using a 1.9 mm × 30 degree oblique integrated telescope (Karl Storz 67030BA) with continuous saline irrigation. There was extensive turbinate bone destruction in both nasal cavities, mainly involving the middle nasal meati to the level of the ethmoid turbinates, and the ventrocaudal meatus. Fungal plaques were observed adherent to nasal mucosa and surrounded by polypoid tissue (Figure 1). The left nasal cavity was more severely affected than the right. Both nasal cavities were aggressively debrided of fungal plaques using 3 mm cupped biopsy forceps (Karl Storz 69133) at premeasured depths following confirmation of plaque locations on rhinoscopic evaluation (Figure 1). Fresh oropharyngeal swabs were pre-placed and 10 ml aliquots of saline were injected via the rhinoscope egress port for rostrocaudal evacuation of plaques. Post-debridement rostral rhinoscopic examination was performed to confirm complete removal of all visible fungal plaques. The oropharynx was actively suctioned throughout the procedure and on recovery to prevent aspiration. A 0.1% ephedrine nasal solution was applied topically into the nasal cavities using cotton swabs inserted into the nostrils, to stem postoperative haemorrhage. An oesophageal feeding tube was placed.

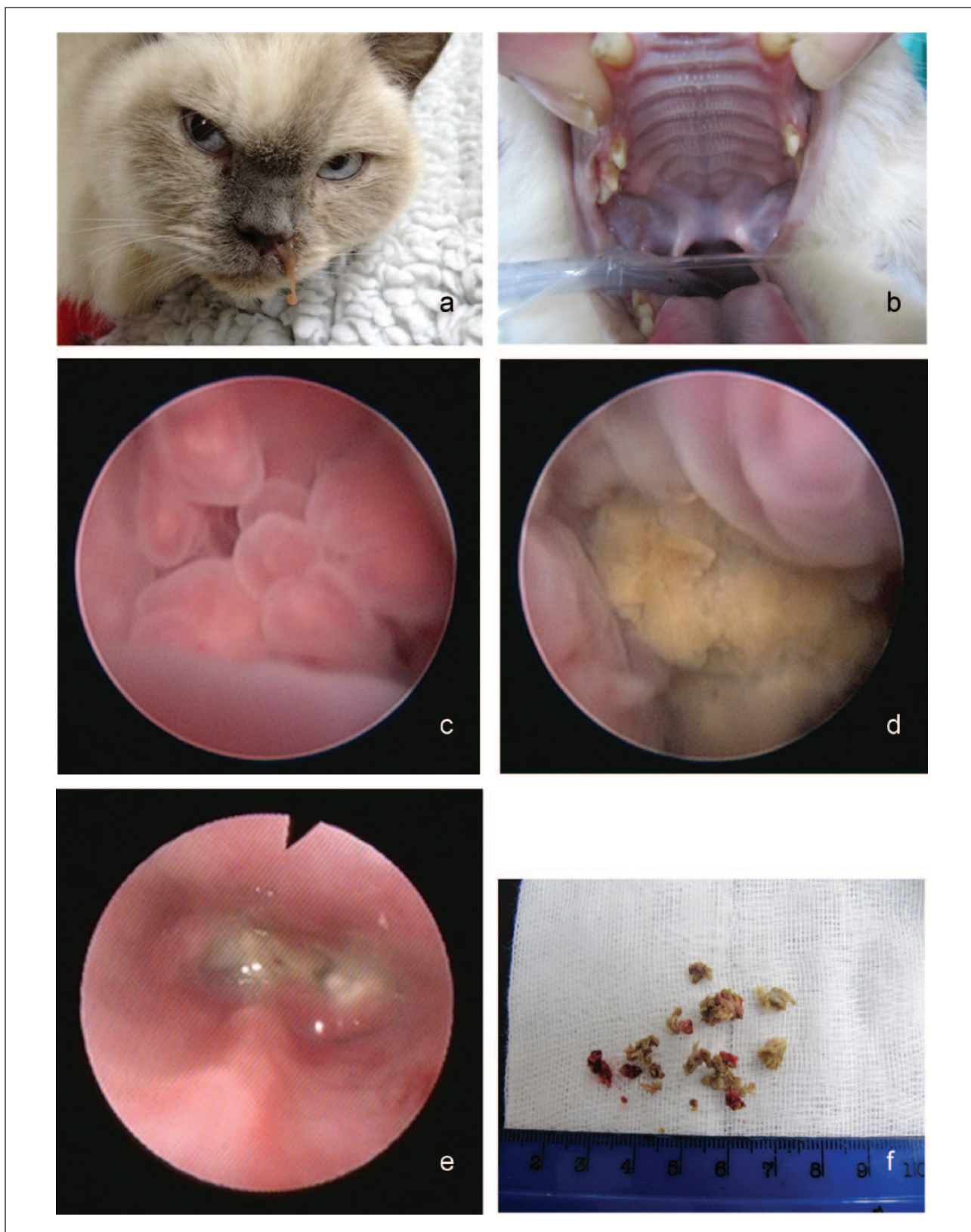
On histopathology of the nasal biopsies there was moderate-to-marked ulcerative lymphoplasmacytic and neutrophilic rhinitis, and fungal hyphae were identified. There was no evidence of invasion of the submucosa by fungal hyphae, with the organisms accumulating on the mucosal surface. Histology of the polypoid tissue observed on rhinoscopy showed hyperplastic, reactive tissue. *Aspergillus fumigatus* was isolated from culture of plaque material, and definitively identified on comparative sequence analysis of the internal transcribed spacer (ITS) region and partial  $\beta$ -tubulin genes and alignment with reference sequences of *A. fumigatus* (100% identity).

Other supportive therapy included intravenous fluid therapy (Hartmann's solution 2 ml/kg/h; Aquapharm, Animalcare UK) at 2 ml/kg/h, buprenorphine (Buprecare 0.015 mg/kg q6–8h IM; Animalcare UK), pradofloxacin (Veraflox 25 mg/ml oral suspension 7.5 mg/kg q24h PO; Bayer US), meloxicam (Metacam 0.05 mg/kg q24h PO; Boehringer Ingelheim Vetmedica US) and itraconazole (Itrafungol 10 mg/ml oral solution, 1.5 mg/kg q24h PO; Elanco UK). The oesophageal feeding tube was removed at recheck examination 2 weeks after discharge from hospital due to marked clinical improvement including return of appetite. Renal parameters and liver enzyme activities were within reference intervals (RIs) on serum biochemistry. Meloxicam was stopped after 5 weeks.

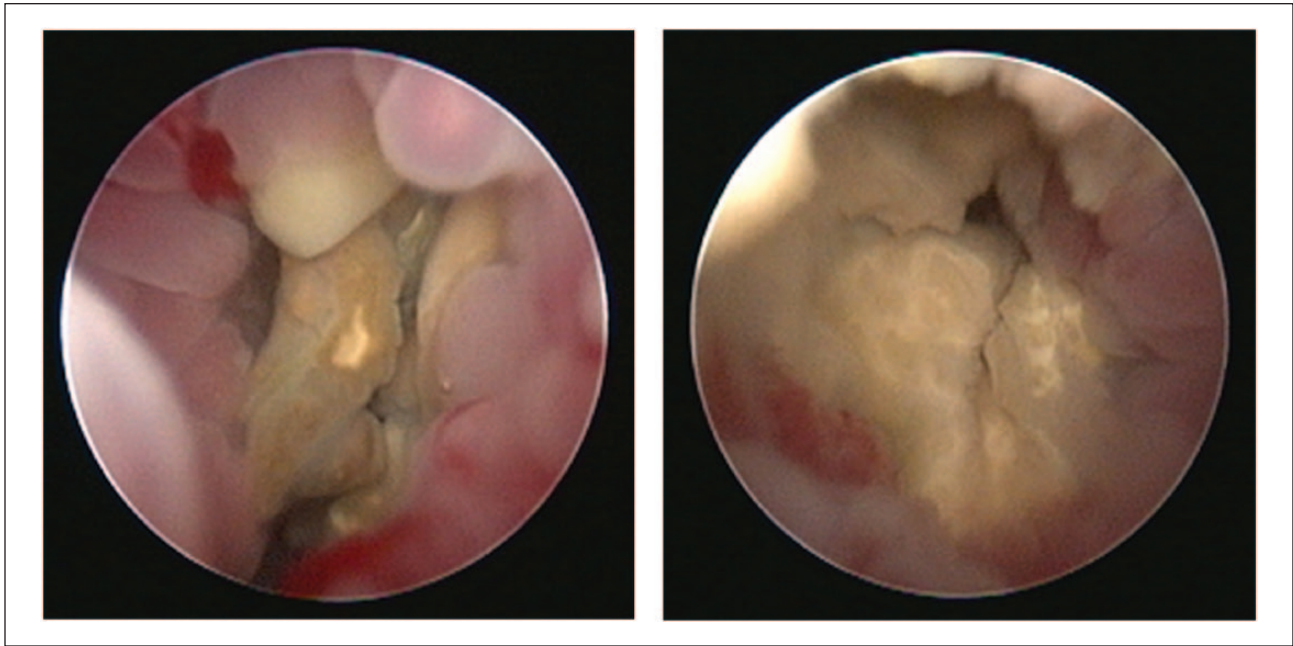
Three months after starting itraconazole treatment, a marked increase in alanine aminotransferase (ALT) concentration (1460 U/l; RI 12–130 U/l) was detected on routine monitoring at a re-check examination and itraconazole was withdrawn. Pradofloxacin was continued and a combination of S-adenosylmethionine (SAME; 20 mg/kg q24h PO) and silybin (Zentonil Advanced 5 mg/kg q24h PO; Vetoquinol France) was prescribed for 2 weeks. Two weeks later, the cat re-presented for recurrence of clinical signs (mucoïd nasal discharge, epistaxis and stertor). ALT concentration (176 U/l) was mildly increased. Itraconazole oral suspension was restarted at a lower dose (1 mg/kg q 24h PO). Pradofloxacin and a combination of SAME and silybin were continued.

Despite itraconazole therapy, the nasal discharge progressively worsened, ALT concentration again increased (301 U/l) and the cat became inappetent. Six months after initial diagnosis, a repeated bilateral rostral rhinoscopic evaluation was performed. Fungal plaques were identified in the left nasal cavity at the level of the ethmoid turbinates in the middle nasal meatus (Figure 2). Aggressive rhinoscopic debridement was performed, as previously described. After the procedure, posaconazole (Noxafil 40 mg/ml oral suspension; Merck Sharp & Dohme) commenced at 2.5 mg/kg q12h PO with food, for 6 months. Pradofloxacin, SAME and silybin were stopped once clinical improvement and normal ALT concentration were obtained, respectively. Clinical signs resolved and liver enzymes remained normal during therapy.

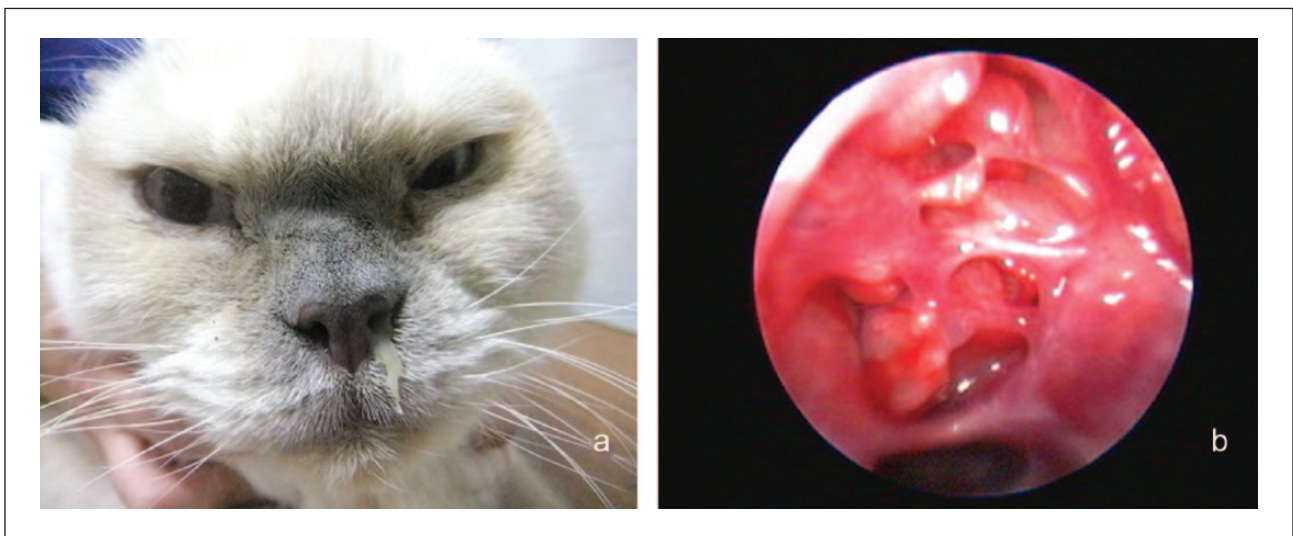
Four weeks after stopping posaconazole, the cat re-presented with mild nasal discharge. Rhinoscopic evaluation was performed to rule out possible clinical relapse. There was extensive turbinate atrophy on the left side allowing direct visualisation into the left frontal sinus. Areas of polypoid tissue involving the dorsal and middle meati were also seen (Figure 3). The right nasal cavity was similarly but less severely affected. No fungal plaques were observed. The nasal discharge was considered likely secondary to the atrophic rhinitis, although biopsy was not performed. The cat was discharged with no medications and an improvement of the nasal



**Figure 1** British Shorthair cat with sinonasal aspergillosis at presentation: (a) haemopurulent nasal discharge; (b) oral examination, note the absence of a mass or ulceration in the pterygopalatine fossa commonly seen in sino-orbital aspergillosis; (c) anterograde rhinoscopy left nasal meatus, polypoid and hyperplastic appearance of nasal mucosa in the left nasal meatus; (d) anterograde rhinoscopy left nasal meatus, fungal plaques adherent to nasal mucosa; (e) retroflexed pharyngoscopy, fungal plaques visualised in the choanae; (f) fungal plaques removed with active debridement



**Figure 2** Anterograde rhinoscopy. Left nasal meatus 6 months after diagnosis: fungal plaques and polypoid appearance of nasal mucosa, confirming relapse of infection



**Figure 3** Twelve months after diagnosis: (a) mucopurulent nasal discharge; (b) anterograde rhinoscopy showing atrophic rhinitis and sinus exposure

discharge was seen. Thirteen months from initial diagnosis, the cat remains clinically well.

### Discussion

Feline upper respiratory tract aspergillosis (URTA) has been rarely reported in Europe.<sup>1-7</sup> To our knowledge, only eight other cases of URTA have been described in cats from Belgium, Italy, Switzerland and the UK.<sup>1-7</sup> SNA and SOA are the most common forms of aspergillosis in European dogs and cats, respectively.<sup>1-17</sup> The breed of cat

in this report reflects the previously reported predisposition of pure-bred brachycephalic cats of Persian lineage to develop URTA.<sup>6</sup> No sex predilection is apparent and pure-bred brachycephalic cats account for more than a third of all cases. The median age at diagnosis is reported to be 6.5 years (range 16 months–13 years).<sup>1-17</sup>

The exact pathogenesis of SNA remains unclear. However, sinonasal mucosal colonisation associated with reduced mucociliary clearance, decreased number and/or function of phagocytic cells, or impaired sinus

eration and drainage has been described in humans.<sup>18–22</sup> In general, cats with SNA and SOA are systemically immunocompetent. Whether the predisposition for aspergillosis in brachycephalic pure-bred cats, as in this case, is due to conformational abnormalities of the skull, affecting nasolacrimal drainage or an inherited defect in fungal immunity.<sup>2,6,11</sup> Nasal polyposis is a risk factor for fungal rhinosinusitis in humans, but the polypoid changes observed in the nasal mucosa of this cat were considered most likely to be a reactive change to fungal infection.<sup>22</sup>

Clinical signs of SNA in cats are similar to those reported for chronic rhinosinusitis, including sneezing, nasal discharge and epistaxis.<sup>1,3–12,16,17</sup> In the present case, despite evidence of cribriform plate lysis on the CT images, no neurological signs were observed. This reflects our experience, in which cribriform plate destruction is reasonably common in canine and feline SNA, but fungal invasion into the central nervous system (CNS) is rare. This is in contrast to feline SOA, where CNS involvement is more common, especially in chronic infections.<sup>6</sup>

Definitive diagnosis in this case was based on identification of fungal plaques during rhinoscopy, and fungal hyphae on histopathology of nasal biopsies, along with positive fungal culture.<sup>1,6,15</sup> Comparative sequence analysis of the ITS and partial  $\beta$ -tubulin genes confirmed the molecular identity of the infecting isolate in this cat as *A fumigatus*, the most commonly reported cause of SNA in cats.<sup>6,7</sup> Where molecular identification facilities are not readily available, *A fumigatus* can be differentiated from other species in *Aspergillus* section *fumigati* by its ability to grow at 50°C.<sup>6</sup>

Treatment of SNA includes debridement of fungal lesions along with systemic antifungal therapy or topical intranasal azole infusion (clotrimazole or enilconazole), or a combination of all three.<sup>1,2,11,15,23</sup> Debridement of fungal plaques is key to successful resolution of canine and feline SNA. In this case, the cat was treated with aggressive rhinoscopic debridement followed by oral itraconazole. Intranasal clotrimazole infusion was not performed due to the breach in the cribriform plate. Intranasal azole infusion is generally contraindicated in this situation as fatal meningoencephalitis can occur if clotrimazole contacts the brain.<sup>5,24,25</sup> In this case it was considered that treatment benefits were negated by potential significant adverse effects. Unfortunately, when systemic itraconazole treatment was suspended because of hepatotoxicity, relapse of infection occurred. Based on clinical outcome in previous cases of SNA and reported adverse neurological effects to voriconazole, we decided to use posaconazole as a second-line antifungal treatment.<sup>4,11,16,26–28</sup> Posaconazole is well tolerated after oral administration and is infrequently associated with hepatotoxicity.<sup>11,16,26</sup> Given the good initial response

of the case here to itraconazole, the lack of success after restarting itraconazole at the time of clinical relapse may have been due to the lack of fungal plaque debridement prior to re-starting the treatment. Posaconazole offers a good second-line monotherapy treatment and has a low risk of hepatotoxicity. In the light of the emergence of azole-resistant isolates of *A fumigatus* in the environment and among clinical strains in people and dogs, antifungal susceptibility testing, which was not performed in this case, is recommended.

## Conclusions

To our knowledge, this is the first case of rhinoscopically confirmed SNA diagnosed in a cat living in the UK. Endoscopic debridement of fungal plaques was an important treatment modality. Topical intranasal infusion of clotrimazole was not performed because of a breach in the cribriform plate. Posaconazole monotherapy was useful for long-term management after hepatotoxicity occurred with itraconazole monotherapy.

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