CANINE SINO-NASAL ASPERGILLOSIS: PARALLELS WITH HUMAN DISEASE

Michael J. Day

School of Clinical Veterinary Science
University of Bristol
CANINE ASPERGILLOSIS

SINO-NASAL DISSEMINATED
HUMAN ASPERGILLUS SINUSITIS

<table>
<thead>
<tr>
<th>INVASIVE</th>
<th>NON-INVASIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acute necrotizing</td>
<td>• Fungal ball</td>
</tr>
<tr>
<td>• Chronic</td>
<td>• Allergic</td>
</tr>
<tr>
<td>• Granulomatous</td>
<td>• Chronic-erosive</td>
</tr>
</tbody>
</table>

IMMUNO-COMPROMISED

IMMUNO-COMPETENT
Canine sino-nasal aspergillosis most closely approximates human chronic-erosive, non-invasive, fungal sinusitis
CANINE SINO-NASAL ASPERGILLOSIS
SIGNALMENT

• Medium to large breed
• Dolichocephalic or mestaticcephalic
• Young to middle-aged
• Not immuno-compromised
• No underlying disease
AETIOLOGY

A. fumigatus

RARELY
Penicillium
A. niger
A. nidulans
A. flavus
CLINICAL

- Relatively uncommon

- Chronic, serous to mucopurulent or sanguinopurulent nasal discharge

- Unilateral becoming bilateral

- Episodic epistaxis

- Regional pain
CLINICAL

• Stertor, stridor or open-mouth breathing

• Depigmentation, ulceration or hyperkeratosis of nasal planum

• Facial deformity

• Ocular involvement/epiphora
DIAGNOSIS REQUIRES A COMBINATION OF METHODS
DIAGNOSIS

IMAGING

• Radiology
• CT
• MRI
DIAGNOSIS

RHINOSCOPY

• Visualize fungal plaque

• Assess tissue damage
DIAGNOSIS

NASAL CYTOLOGY

• Lavage
• Brush
• Squash of biopsy
DIAGNOSIS

BIOPSY

Culture from biopsy
DIAGNOSIS

SEROLOGY

• AGD
• CIEP
• ELISA
• Serum galactomannan
DIAGNOSTIC CRITERIA

1. Characteristic imaging changes
2. Serum antibody
3. Positive culture
THERAPY

SYSTEMIC MEDICAL

• Rarely used
• Ketoconazole
• Itraconazole
• Fluconazole

• Success rate up to 70%
THERAPY

INDWELLING CATHETER

• Repeated enilconazole

• Prolonged single clotrimazole
THERAPY

Follow-up with clotrimazole cream instilled via trephine holes to frontal sinus
OUTCOME

Successful cure in 90%

10% may recur

May develop secondary bacterial rhinitis
IMMUNOPATHOGENESIS
DETECTION OF FUNGAL DNA IN TISSUE BY REAL-TIME PCR
METHODOLOGY

• Rhinoscopy 'gold standard'

• Tissue biopsy from standard site and EDTA blood

• Enzymatic and mechanical disruption

• Ribosomal RNA gene

• Taqman probes

• Normalized to G3PDH
## DETECTION OF FUNGAL DNA IN TISSUE BY REAL-TIME PCR

<table>
<thead>
<tr>
<th>Pen-Asp</th>
<th>SNA (n=14)</th>
<th>LPR (n=7)</th>
<th>Neoplasia (n=13)</th>
<th>Normal (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. fumigatus</td>
<td>7</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>A. terreus</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A. flavus</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A. niger</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

All dogs positive but > copy number in dogs with SNA
Biopsies

- Sensitivity 1.00
- Specificity 0.06

Blood

- Sensitivity 0.71
- Specificity 0.24

PEN-ASP
A. fumigatus

Sensitivity 0.50  Sensitivity 0.21
Specificity 0.97  Specificity 0.45
HISTOPATHOLOGY

Superficial plaque
No invasion of deeper tissue

• Ulceration
• Necrosis
• Haemorrhage
• Chronic-active inflammation
• Granulation
• Bony destruction
CD4+ & CD8+ T cells (either dominates) TCRαβ > TCRγδ

IgG+ > IgA+ PC

CD1+ MHCIIB+ dendritic cells

MHCIIB+ macrophages

MAC387+ macrophages & neutrophils
IMMUNE FUNCTION

Real-time, RT-PCR normalized to multiple housekeeper genes for determination of expression of key cytokine and chemokine mRNA
MAIN FEATURES

• Th1 profile in SNA vs Th2-like in LPR

• IL-12 and IL-23 in SNA vs IL-23 in LPR; suggests role for Th17 cells in both

• IL-10 & TGFβ expression suggests Treg [or Th1 differentiation] element and may explain chronicity of infection
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