Canine nasal tumors: prolonging survival and improving quality of life

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Overview
- Review of nasal tumors and staging tests
- “Standard” therapies
- Symptomatic therapy, “salvage” procedures
- Novel ideas to improve survival and quality of life
  - Receptor inhibitors: Palladia
  - Improving RT techniques: IMRT/IGRT, SRT
  - Reirradiation of recurrent nasal tumors

Canine intranasal cancer
- Carcinomas (70% of nasal cancers in dogs)
  - Adenocarcinoma
  - Squamous cell carcinoma (SCC)
  - Non-keratinizing SCC/transitional carcinoma
- Sarcomas
  - Chondrosarcoma
  - Osteosarcoma
- Lymphoma, mast cell tumor, melanoma, plasma cell tumors
Why do dogs get nasal cancer?

- **Environmental causes?**
  - Humans: Carpenters, cigarette smoking
  - Dogs:
    - Dolichocephalic breeds in smoking households have 2-2.5 x risk of developing nasal cancer
    - Owner use of indoor coal or kerosene heaters increased risk by 2-4 x
  - Breed predispositions
    - Increasing nasal length
  

Canine intranasal cancer

- Locally invasive
  - Sneezing, epistaxis, facial deformity, nasal stertor
  - Seizures, exophthalmos
- Uncommonly metastatic at time of diagnosis
  - Regional lymph nodes, lungs
  - Rarely to bones, other sites

- **Physical exam**
  - Skull
  - Oral cavity
  - Eyes
  - Mandibular lymph nodes
Staging tests for nasal cancer

- CBC/chem/UA/coag
- Thoracic radiographs
- Abdominal imaging as part of staging
- Nasal cavity imaging
- Biopsy and histopathology
- LN aspirates

CT scan for RT planning

CT scans for RT planning
Positioning and set up for RT

CT scan reconstruction

Use of CT scans in RT planning
Treatment options for nasal tumors in dogs

“What happens if I do nothing?”
- 139 dogs with untreated nasal carcinomas
  - Median ST 95 days (range, 7–1114 days)
  - Addition of NSAIDs did not prolong survival
  - Dogs with epistaxis had shorter ST
    - MST 88 days versus 224 days if no epistaxis

Rassnick KM, JAVMA Aug 1 2006: 401-6

Chemotherapy for nasal cancer
- Not widely studied due to likely poor perfusion of chemotherapy into bulky nasal tumors
- May be used as a radiation sensitizer
- Chemotherapy study
  - Carboplatin, doxorubicin, piroxicam: 75% objective response rate in 8 dogs (CT follow up)

Langova V, Aust Vet J Nov 2004: 676
Surgery for nasal cancer in dogs

- Surgery alone: outcomes similar to no therapy
- Surgery after RT:
  - If residual disease seen on CT scan post-RT
  - MST 48 months (n=13) versus 20 months for RT alone (n=40)
  - 5/13 dogs that had surgery had severe long-term complications


Radiation therapy for nasal cancer

- External beam RT
  - Clinical signs improve in >70% of dogs
  - Median survival times approximately 12 months
    *50% 1-year, 20% 2-year survival

RT protocols

- “Definitive”
  - 16-20 daily fractions
  - Goal: achieve long-term tumor control (>1 year)
- “Palliative”
  - 4-5 weekly fractions
  - Goal: improve QOL
Radiation therapy for nasal cancer

- Normal tissue side effects limit radiation doses
  - Acute: mucositis, dermatitis/desquamation, alopecia, keratitis, conjunctivitis

Late side effects of RT

- Cataracts
- Fibrosis/stricture
- Secondary tumor formation

Ocular and skin side effects

- Acute
- Late
“Other” therapies for nasal cancer

- "Salvage" procedures:
  - Hydropulsion of the tumor/nasal cavity
  - Cryoablation of nasal tumors
  - Carotid artery ligation
- Palliative: NSAIDs, antibiotics, antihistamines, steroids
  - Subjective responses to these drugs in most dogs
  - Not documented to improve survival times

Outcome of treatment for nasal cancer in dogs to date...

- Treatment usually improves clinical signs and QOL, but long-term tumor control or "cure" is uncommon due to persistent tumor in the nasal cavity
- Ultimately, most dogs are euthanized due to recurrence of clinical signs which indicates tumor progression

Negative prognostic indicators in dogs with nasal cancer

- Age >10 years
- Higher stage
- Histopathology- SCC worse than adenoCA
- Presence of distant metastasis at diagnosis
- Lack of resolution of clinical signs after therapy
- Facial deformity
"How can we prolong survival and improve QOL for dogs with nasal cancer?"

- Novel strategies
  - Use of growth factor receptor inhibitors (Palladia®)
  - Improved radiation treatment planning and delivery techniques that allow dose escalation to tumor and decreased normal tissue side effects
  - Reirradiation of recurrent nasal tumors

Tyrosine Kinase Receptor Inhibitors

- Inhibit VEGF receptors, which are present on >90% canine nasal carcinomas (Shiomitsu Vet Comp Oncol June 2009)
- Radiation sensitizers
- Antiangiogenic properties
- 7 dogs with nasal carcinomas
  - 5/7 had clinical benefit from Palladia for a median of 18 weeks

London, Vet Comp Oncol June 2011

Results after Palladia treatment
**New RT technology @ NCSU**

- IGRT: image-guided radiation therapy
- IMRT: Intensity-modulated radiation therapy
- SRT: stereotactic radiotherapy

**IMRT (intensity-modulated radiation therapy)**

- Computer-aided optimization treatment planning process with the goal of conformal avoidance of critical normal structures
- Allows for homogenous dose throughout tumor volume with sharp dose fall off at the boundary of normal tissue
Comparison of side effects

First day of IMRT

Last day of IMRT

Ocular sparing in dogs with sinonasal tumors treated with IMRT

- Compared to historical controls
- Results: significant decrease in both acute & late ocular toxicity in IMRT group
- Survival times between groups were not different; MST 411 and 420 days
- Proof of lower toxicity in IMRT patients “paves the way” for dose escalation to tumors and hopefully improved tumor control

SRT (stereotactic radiotherapy)

- “Stereotactic”: use of a precise 3D mapping technique to guide a procedure
- SRT is a high-dose, image-guided course of RT delivered in 1-5 treatments
- Precise positioning results in minimal normal tissue dose and allows dose escalation

Lawrence et al., VRUS 2010(5): 561-70.
SRT

- Fewer anesthetic episodes (1-5) due to high dose/treatment
- Radiation biology of SRT impacts tumor control
- Acute side effects uncommon, late side effects not widely documented
- SRT used to treat some nasal tumors, similar survival times expected to traditional courses of RT

Reirradiation of recurrent tumors

- Often not considered due to concerns about side effects
- Few published studies have confirmed efficacy and lack of severe side effects
- If nasal tumor recurrence is suspected, repeat imaging and consultation with a radiation oncologist to discuss options is indicated

Future directions in nasal cancer: potential studies

- Evaluation of repeat CT imaging post-RT
- Outcomes for patients treated with SRT: efficacy, survival and side effects
- Interactions between receptor inhibitors or novel chemotherapy agents and RT