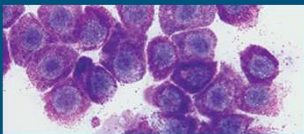


Canine Mast Cell Tumors: a clinical approach and updates on medical management

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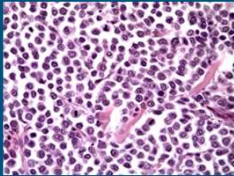
Overview

- Grading
 - Different grading schemes
 - Prognostic panels?
- Post-operative treatments
 - Radiation, electrochemotherapy, chemotherapy
- Inoperable MCTs
- New and newish therapies
 - Stelfonta
 - Gilvetmab
 - Autologous vaccines?



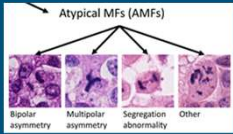
Mast cell tumor grading

- Cutaneous tumors*
- Best predictor of biologic behavior
 - BUT NOT PERFECT!
- Patnaik grading system
 - Grades 1-3
 - Cytoplasmic boundaries, mitoses, granularity, nuclear/cellular shape
 - Grade 2 (intermediate grade) tumors?
 - Inter-pathologist disagreement




Mast cell tumor grading

- Kiupel grading
 - Low vs. high grade
 - High grade criteria
 - ≥ 7 mitoses/10 hpf
 - ≥ 3 bizarre nuclei/ 10 hpf
 - ≥ 3 multinucleated cells/ 10 hpf
 - karyomegaly
- More accurately predicts biologic behavior!
- Both grades on biopsy reports



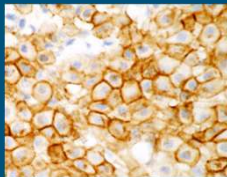
Mast cell tumor grading

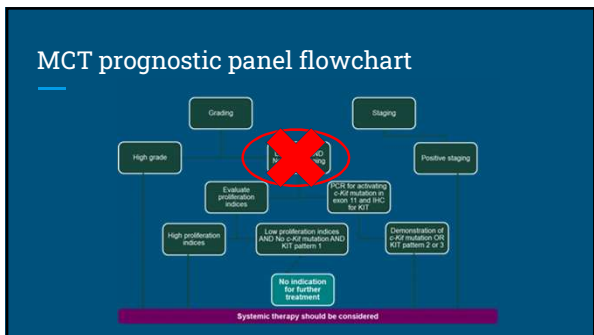
- Clinical application
 - What is provided on a biopsy report?
 - Margins
 - Patnaik grade
 - Kiupel grade
 - Mitotic count
 - Location of tumor
 - Call your local oncologist*



Mast cell tumor grading

- Prognostic panel
 - Ki67
 - Argyrophilic nucleolar organizer regions (AgNORs)
 - Proliferating cell nuclear antigen (PCNA)
 - Kit immunostaining
 - c-Kit mutation status
- Clinical use and interpretation?





Post-operative treatments

- To treat or not to treat?
- Treating for **LOCAL RECURRENCE** for incompletely excised tumors
 - Recurrence rate - between 10-30%
 - Scar revision surgery?
 - Radiation therapy
 - Electrochemotherapy
 - Chemotherapy?

Post-operative treatments

- Treating for **LOCAL RECURRENCE** for incompletely excised tumors
- Radiation therapy (RT)
 - Definitive protocols
 - Expected local cure for low to intermediate grade tumors
 - Effective long term control in high grade setting
 - Acute side effects
 - Coarsely fractionated protocols?



Post-operative treatments

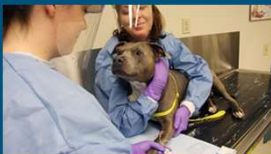
- Treating for **LOCAL RECURRENCE** for incompletely excised tumors
- Electrochemotherapy (ECT)
 - What is ECT?
 - ~2-4 weeks following surgery with 1-2 sessions
 - Bleomycin IV, Cisplatin intralesionally
 - 7-15 % recurrence rates post ECT
 - Median time to recurrence = 53 months in one study
 - Well-tolerated, cutaneous "burns"
 - Limited by scar size

Post-operative treatments

- Treating for **LOCAL RECURRENCE** for incompletely excised tumors
- Medical therapy/Chemotherapy?
 - Not typically considered

Post-operative treatments

- High grade mast cell tumors
 - Consider local therapy if incomplete excision
 - 50-95% metastatic rate
 - Systemic therapy is warranted*
 - Vinblastine
 - Lomustine
 - Palladia



Post-operative treatments

- High grade mast cell tumors
 - Vinblastine (VBL)
 - Gold standard
 - Once every week x 4, then every other week x 4
 - Post-operative tx - MST = 3.8 yrs
 - 70% 1- and 2-year disease free intervals
 - Current national backorder



Post-operative treatments

- High grade mast cell tumors
 - Lomustine (CCNU)
 - Second line
 - Myelosuppressive, hepatotoxic
 - Hosoya et al. 2009 → 100% and 77% 1- and 2- year disease free intervals
 - Hay and Larson, 2019 → MST = ~2.5 yr



Post operative treatments

- High grade mast cell tumors
 - Palladia (toceranib phosphate)?
 - Receptor tyrosine kinase inhibitor
 - Use in microscopic disease?
 - Adverse events



Inoperable MCTs

- Radiation therapy
 - Hypofractionated protocols
 - Typically once weekly x 4
 - 76%- 85% overall response rate
 - Combine with Palladia*
 - Treatment of the local lymph node
 - Degranulation




Inoperable MCTs

- Chemotherapy
 - Downstage disease
 - Vinblastine - 78% partial response rate
 - Lomustine
 - Chlorambucil
 - Palladia*
 - Practical for chronic use
 - Prednisone



Inoperable MCTs

- Chemotherapy
 - Palladia***
 - My treatment of choice for inoperable MCTs
 - Receptor tyrosine kinase inhibitor
 - Higher response rates in c-Kit mutated tumors
 - Do not follow label dose!
 - ~45% remission rate with 60% clinical benefit
 - Median response time → ~4.5 months
 - Adverse events



New therapies

- Stelfonta®
 - Tigilanol tiglate
 - Non-metastatic cutaneous and SQ tumors*
 - > 1 cm in diameter, < 10 cm³
 - Dose = 0.5 ml per cm³
 - Retreat in 28 d if resolution not achieved
 - Steroid and antihistamine pre-treatment!
 - Care with handling and injecting!



New therapies

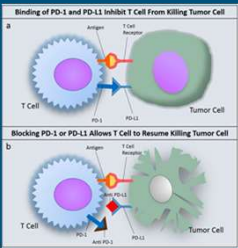
- Stelfonta
 - De Ridder et al., JVIM, 2021.
 - 75% complete response (CR) at 28 d
 - No recurrence in 93% at 84 d
 - Additional dose achieved CR in 8 dogs
 - Wound formation associated with efficacy
 - Off label use in horses




FIGURE 2 Photo series showing examples of the typical progression of clinical response after treatment of a single MCT with tigilanol tiglate, MCTx, mast cell tumors.


New therapies

- Gilvetmab
 - Monoclonal antibody
 - Binds PD-L1
 - Conditionally licensed for melanomas and MCTs
 - Limited data
 - Limited availability
 - Very expensive



New therapies

- Autologous vaccines
 - Review of technology
 - Torigen
 - Safe!
 - Efficacy?
- Personalized medicine?



Multiple MCTs

- Common!
- Brachycephalic breeds, Pit Bulls, Labradors
- Typically low grade
- Staging for repeat offenders?
- Surgery 🐾
- Systemic therapy?



Histamine blocking therapies

- H1 blockers - anti-anaphylactic
- H2 blockers - GI protective
- Active ulceration?
 - Sucralfate, misoprostol
- Use for gross disease!
- Unknown benefit in microscopic disease setting
- **NOT** thought to be anti-neoplastic



References

- Available upon request!



Questions

