Mast Cell Tumors on a Case-by-Case basis

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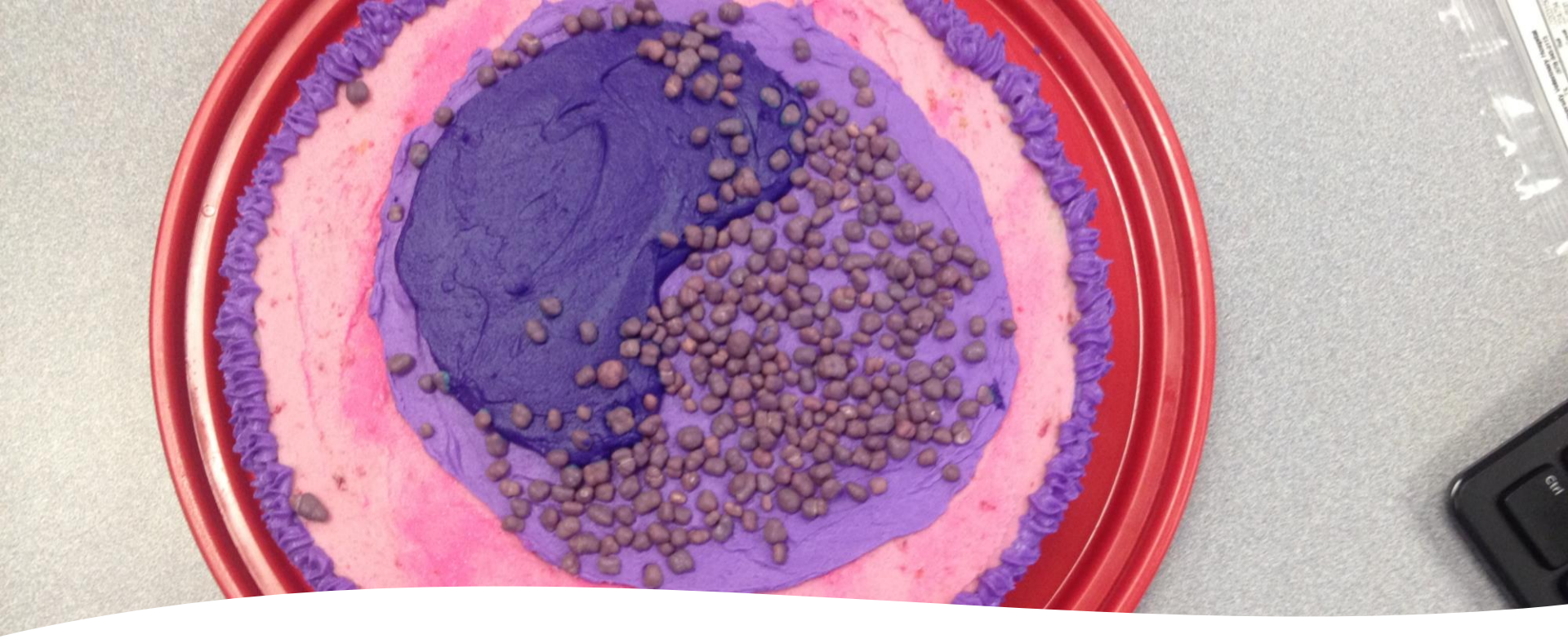
Leading Specialty Healthcare for Pets



Talking points

- Review of mast cell disease.
- Individual cases.
- Questions/discussion.

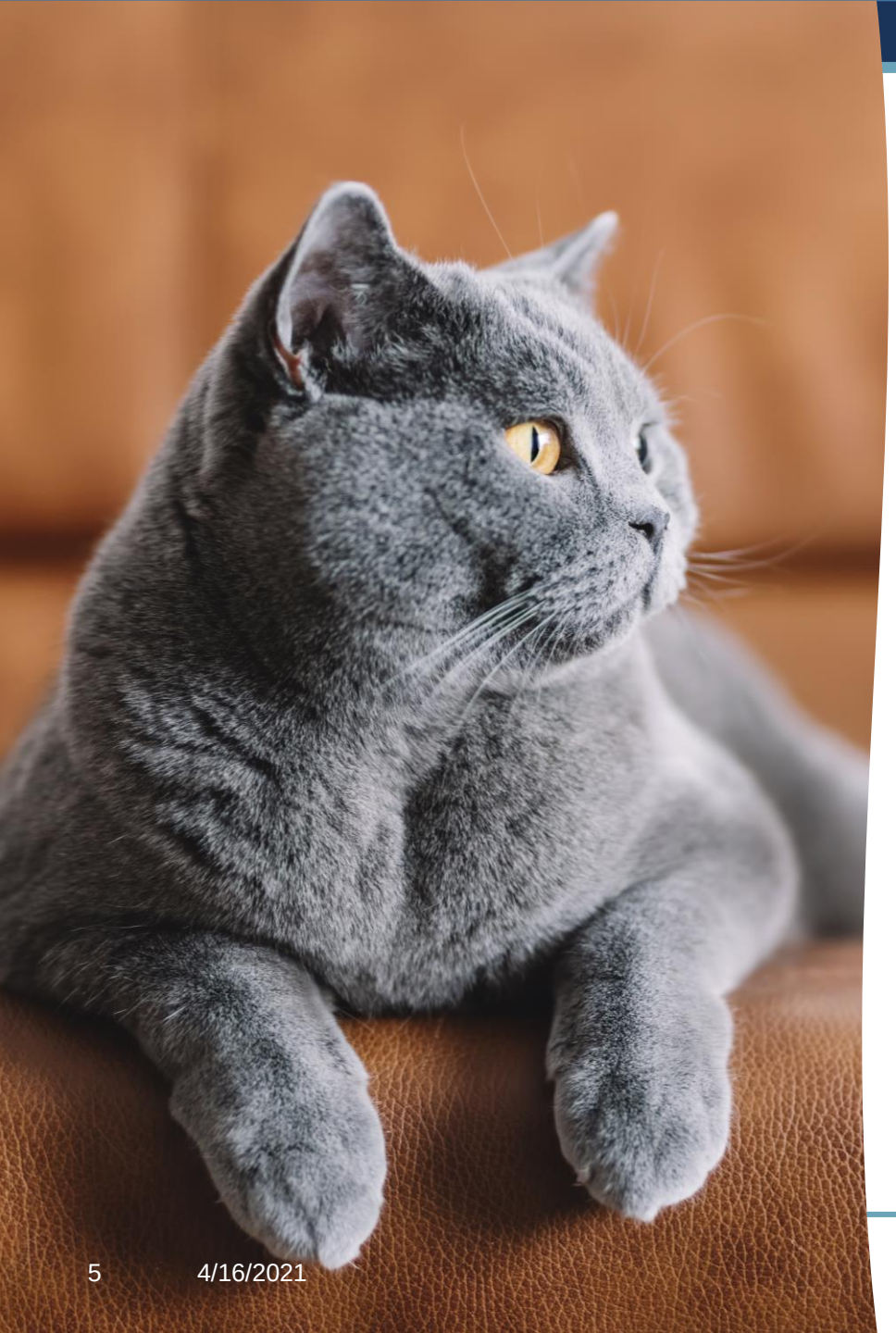
Mast cell disease

- 3rd most frequent cutaneous neoplasia in dogs.
  - Average age 8.2 years but range 6 months-18 years.
  - Labradors, Goldens, Cocker Spaniel, Boxers, Bostons, Bully breeds, Shar Pei.
- 2nd most frequent cutaneous neoplasia in cats.
  - Average age of 9 years.
  - Siamese, Ragdoll, Burmese, Russian Blue.
  - Cats have two histologic subtypes: mastocytic (similar to dog's mast cell tumors) and atypical (less common).

Mast cell disease

- Dogs:
  - Trunk and perineum: 40-50%.
  - Limbs: 30-40%.
  - Head and neck: 10-15%.
  - Multicentric disease: 11-14%.
  - Primary visceral: 8.5%.

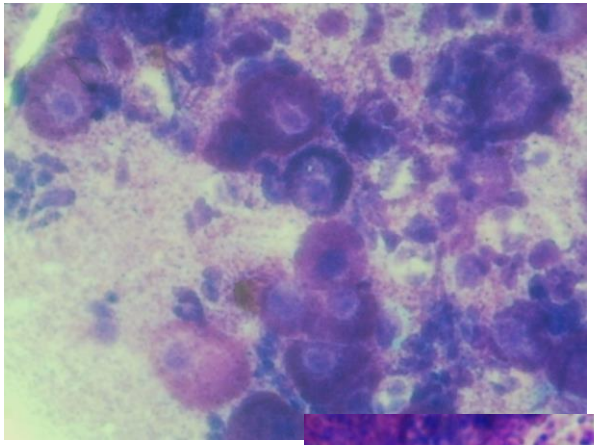
- Cats:
  - Skin of the head and trunk, spleen, intestine and lymph node most common.
  - Over 50% have visceral location (spleen).
  - 24% have multicentric disease.

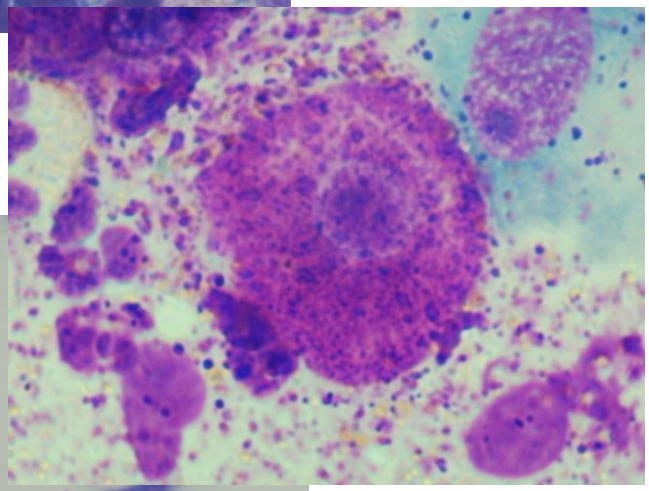


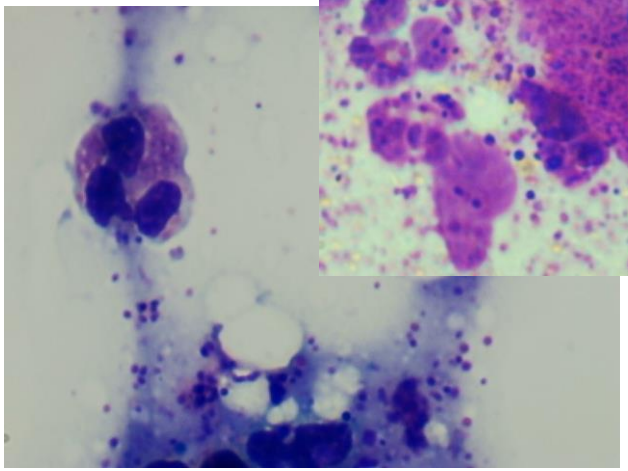
Mast cell disease

- Cytology.
- Histopathology.
  - Patnaik versus Kiupel.
  - Proliferation markers.
- Staging.

Cytology







- Diagnostic but not always prognostic.
- There are some features on cytology that can suggest low versus high grade.
- Remember that Diff Quik does not always stain mast cell granules.

Cytology

Cytologic Criteria for Mast Cell Tumor Grading in Dogs With Evaluation of Clinical Outcome

M. S. Camus[1], H. L. Priest[2], J. W. Koehler[3], E. A. Driskell[4], P. M. Rakich[5], M. R. Ilha[6], and P. M. Krimer[5]

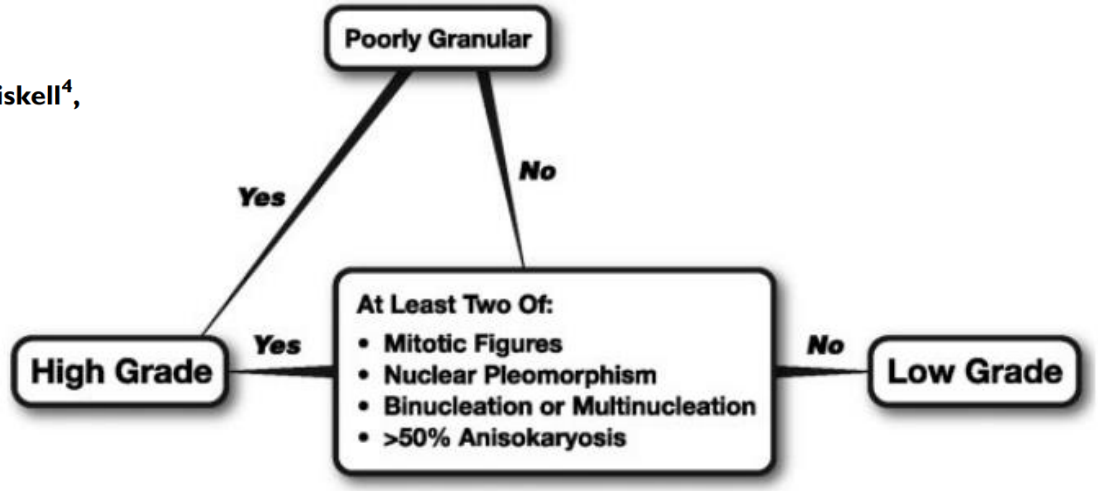


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Figure 5. Algorithm for rapid application of the cytologic grading scheme for canine cutaneous mast cell tumors.

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Histopathology

Canine Cutaneous Mast Cell Tumor Grading Systems

Patnaik Grading Criteria, 1984

Table 1. Summary of the Patnaik morphologic grading classifications for canine cutaneous mast cell tumors.[8]

	Tumor grade		
	I	II	III
Location	Dermis and interfollicular spaces	Infiltrate lower dermal and subcutaneous tissue; some extend to skeletal muscles or surrounding tissues	Replace subcutaneous and deep tissues
Cell morphology	Round, monomorphic, ample distinct cytoplasm with medium-sized granules	Round to ovoid, moderately pleomorphic, with scattered spindle and giant cells; most cells distinct cytoplasm with fine granules, but some with indistinct cytoplasm and large/hyperchromatic granules	Round, ovoid, or spindle shaped, pelomorphic, medium sized; cytoplasm indistinct with granules that are fine or not obvious; many giant cells and scattered multinucleated cells
Nuclear morphology	Round, condensed chromatin	Round to indented with scattered chromatin and single nucleoli; some with double nuclei	Indented to round vesiculated, with 1 or more prominent nucleoli; common binucleated cells
Architecture, cellularity, stromal reaction	Arranged in rows or small groups, separated by mature collagen fibers of the dermis	Moderately to highly cellular, arranged in groups with thin, fibrosvascular stroma (sometimes thick and fibrocollagenous with areas of hyalinization)	Cellular, arranged in closely packed sheets; stroma fibrovascular or thick and fibrocollagenous with areas of hyalinization
Mitotic figures	None	Rare (0–2/high-power field)	Common (3–6/high-power field)
Edema and necrosis	Minimal	Areas of diffuse edema and necrosis	Edema, hemorrhage, and necrosis common

Histopathology

Two-Tier Grading Criteria, 2011

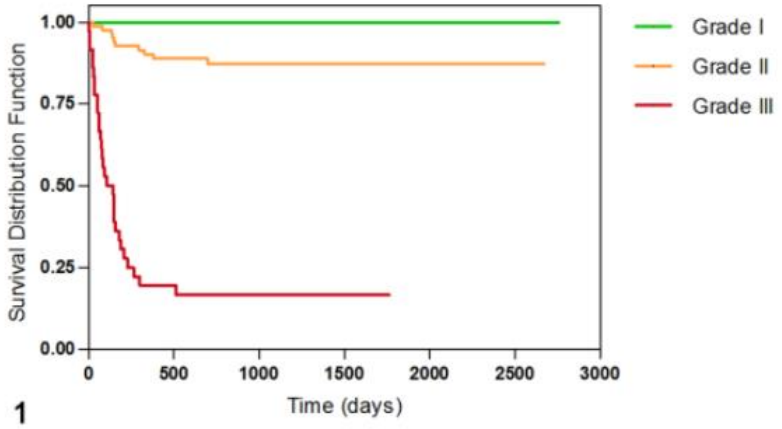
High-grade MCT is characterized by any one following criteria:

1. ≥ 7 MFs/10hpf
   - Evaluated in regions with highest mitotic activity
2. ≥ 3 multinucleated cells / 10hpfs
   - Where ≥ 3 nuclei constitutes a multinucleated cell
3. ≥ 3 bizarre nuclei / 10hpf
   - Highly atypical with marked indentations, segmentation, and irregular shape
4. Karyomegaly
   - Where at least 10% of neoplastic cells vary by 2-fold

Histopathology

Histologic Grading of Canine Mast Cell Tumor: Is 2 Better Than 3?

S. Sabattini[1*], F. Scarpa[1*], D. Berlato[2], and G. Bettini[1]



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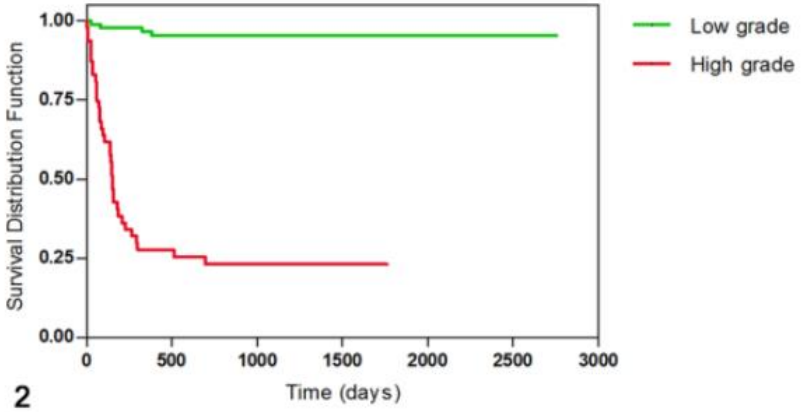

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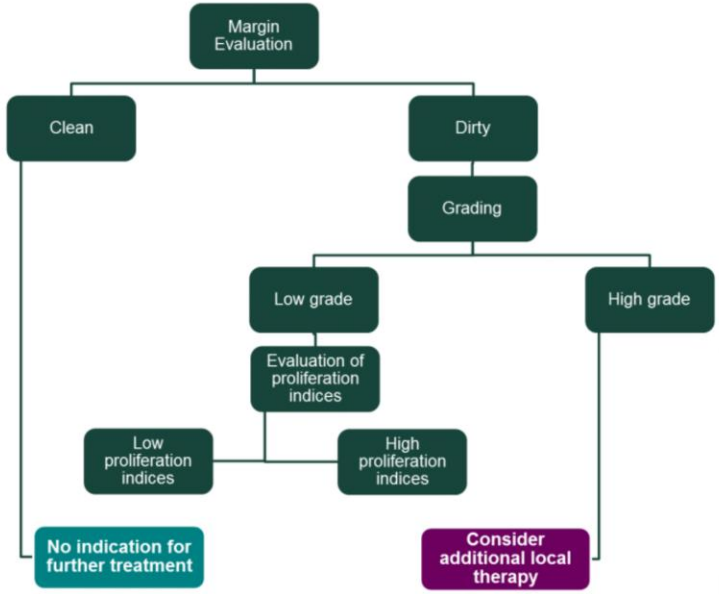
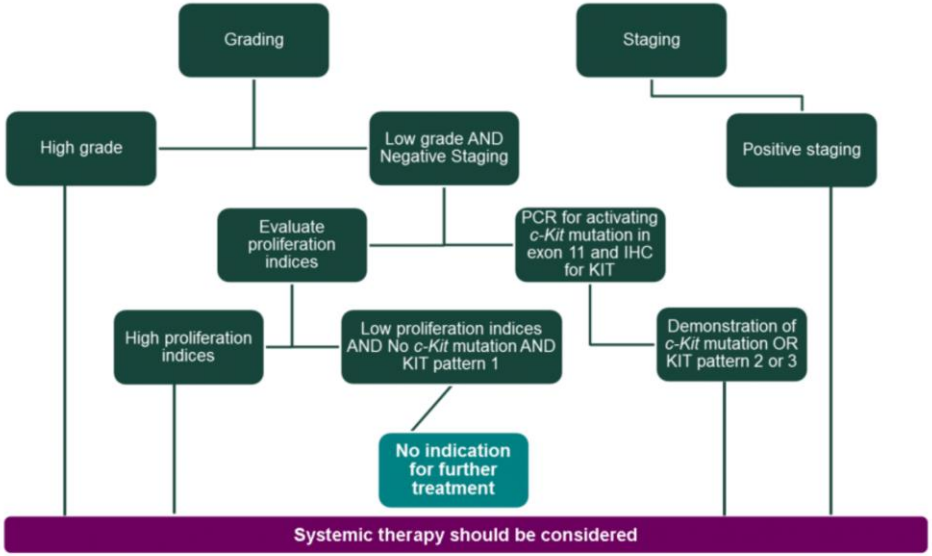
Histopathology

CONSIDERATIONS FOR INCLUSION OF ADDITIONAL LOCAL THERAPY IN TREATMENT OF DOGS WITH EXCISED CANINE CUTANEOUS MAST CELL TUMORS



CONSIDERATIONS FOR INCLUSION OF SYSTEMIC THERAPY IN TREATMENT OF DOGS WITH CANINE CUTANEOUS MAST CELL TUMORS



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Stage of disease

- Lymph node involvement?
- Distant metastatic disease?
- What about multicentric disease?

Table 2. World Health Organization Clinical Staging System for Mast Cell Tumors in Dogs[16]

Stage[a]	Description
0	Incompletely excised solitary tumors without regional node involvement
1	Solitary tumors confined to the dermis and without regional lymph node involvement
2	Solitary tumors confined to the dermis and with regional lymph node involvement
3	Multiple dermal tumors or large infiltrating tumors with or without regional lymph node involvement
4	Tumors with distant metastasis

[a]Substage a: no clinical signs are present; substage b: clinical signs are present.

Biologic behavior!!!

- Location?
- Size?
- Ulceration/degranulation event?
- Breedist unfortunately!

http://www.animalcancersurgeon.com/skin-tumors-mct

Degranulation event

Question

- Which of these breeds is NOT predisposed to mast cell disease?
  - 1. Shar Pei?
  - 2. Siamese?
  - 3. Poodle?
  - 4. Ragdoll?

Cases

Cases: Goldie

- Middle age spayed female.
- Doberman Mix.
- Owner noticed mass on back of leg that continued to grow, and she is clinically well.

https://qbiotics.com/pub/CandT_No_5598-final.pdf

Cases: Goldie

- Cytology: well differentiated mast cells.
- Lymph node: too many mast cells than comfortable with…
- Amputation?
- Radiation?

Cases: Goldie

- Staged clean for distant disease.
- Cytoreduction.
- Vinblastine blasts mast cells!
- Plan to give four doses once weekly along with prednisone and consider surgery.

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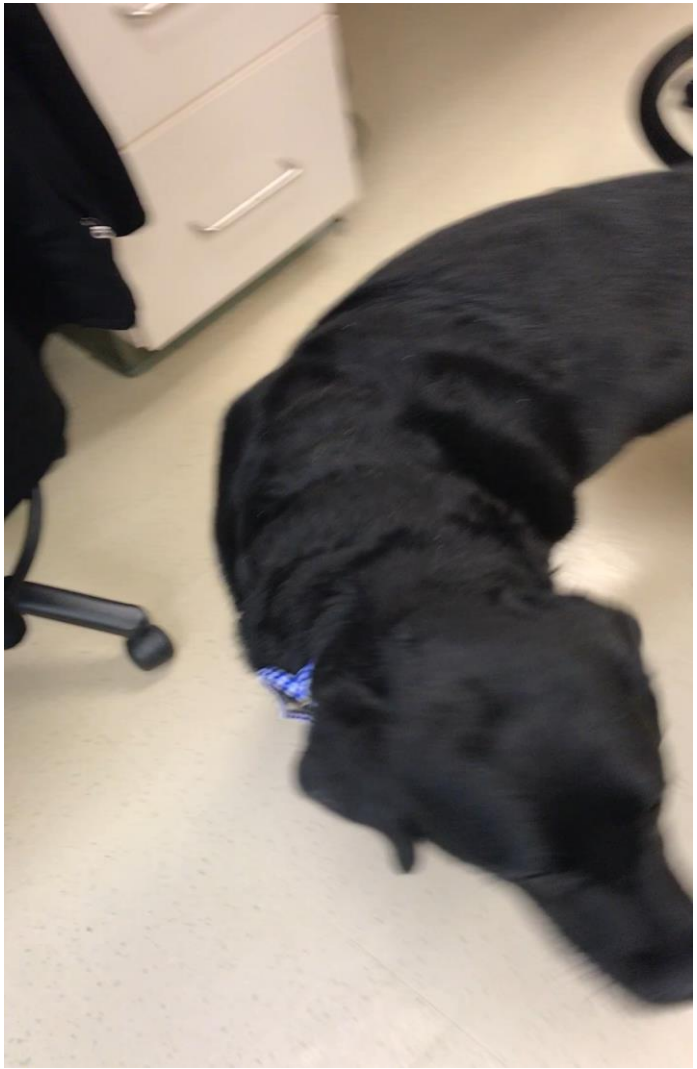
Cases: Goldie

- Reported 27% response rate with gross disease in Rassnick et al paper when used as single agent.
- Reported 47% response rate when used with prednisone in Thamm et al paper.
- Worth a try? Especially since we suspect LN is metastatic and would recommend chemotherapy after surgery or RT anyway?

Cases: Goldie



- 40% size reduction!
- Went to surgery to remove mast cell tumor and lymph node.
- Narrow but complete margins.
- Finished vinblastine protocol: 4 doses q 2 weeks.
- Lost to follow up but did not regrow in 6 months.

Cases: Rosco

- 9 year old MC Basset Hound-Shar Pei cross.
- First noticed mass as size of pea left carpus.
- Treated for lick granuloma.
- Continued to grow-quarter size. Became ulcerated.
- 6 weeks later biopsied-mild atypical round cell proliferation with numerous inflammatory cells…including many mast cells…
- Giemsa stain some of atypical round cells granules stained, diagnosing mast cell…comments were interesting…

Cases: Rosco

- Key points:
  - Patnaik grading grade II low grade.
  - BUT…groups of mitotically more active and less differentiated subpopulations would be indicative of higher grade malignancy…

In conclusion, the lesion present within the submitted specimen is most consistent with a sparsely cellular, poorly granular mast cell tumor. Applying the grading systems developed for cutaneous mast cell tumors the lesion is a grade II (Patnaik system) / low grade (Kiupel system), with a mitotic count of 1. However, please note that the presence of mitotically more active or less differentiated subpopulations in other areas of the lesion (which would be indicative of a higher grade malignancy), not represented in the sections, cannot be completely ruled out. Removal of the entire lesion with subsequent histologic assessment is recommended for a more definitive grading information.

Cases: Rosco

Cases: Rosco

- This case worries me…
- Ultrasound showed splenomegaly and hepatomegaly with increased echogenicity.
- Performed full staging with chest radiographs, abdominal ultrasound, aspirates of prescapular lymph node, spleen and liver.
- LN: metastasis.
- Spleen: Rare atypical mast cells.
- Liver: mast cell hyperplasia.

Cases: Rosco

Correlation of ultrasound findings, liver and spleen cytology, and prognosis in the clinical staging of high metastatic risk canine mast cell tumors

Alison P Book [1], Janean Fidel, Tamara Wills, Jeffrey Bryan, Rance Sellon, John Mattoon

Cytological comparison of fine-needle aspirates of liver and spleen of normal dogs and of dogs with cutaneous mast cell tumours and an ultrasonographically normal appearing liver and spleen

K Finora [1], N F Leibman, M J Fettman, B E Powers, T A Hackett, S J Withrow

Cases: Rosco

- Discussed amputation versus marginal excision and radiation therapy.
- Discussed need for chemotherapy due to metastatic disease.
- Owner went to MedVet Columbus for second opinion.
- They performed marginal excision with lymph node stripping.

Cases: Rosco

- Excisional biopsy shows low grade two but still has aggressive features that could be consistent with Kuipel high grade….
- Lymph nodes just show hyperplasia at first glance.
- Giemsa stain shows few mast cells in prescapular lymph node but clusters in axillary consistent with metastasis.

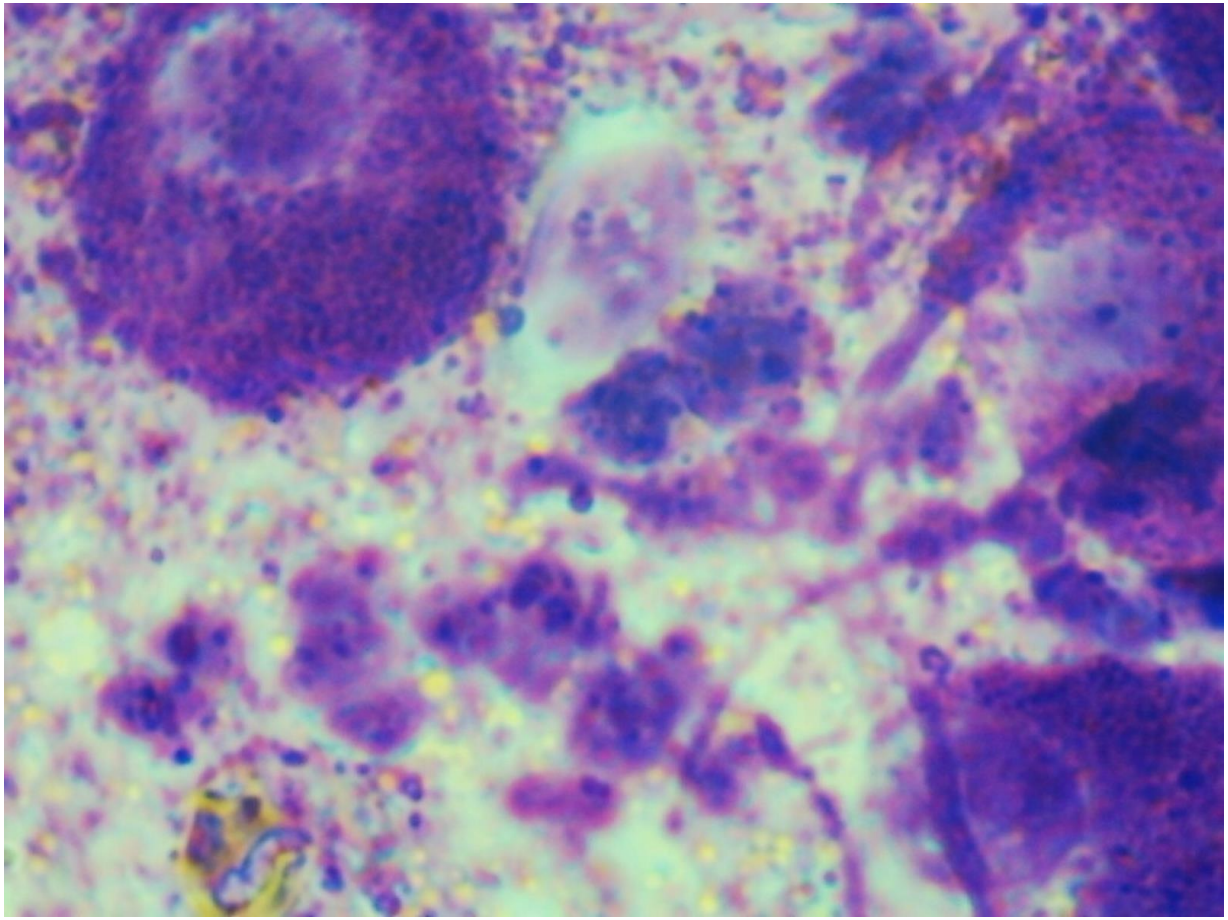
Cases: Rosco

- Started Palladia within a week after surgery.
- Would have considered vinblastine as my first-choice post op.
- Tolerated drug well.
- Recheck ultrasound with aspirates two months after surgery: hepatomegaly with increased echogenicity (steroid), aspirates of liver and spleen NO MAST CELLS!
- Plan to continue Palladia for at least a year.

Cases: Rosco

- 9 months later after surgery and chemo….
- Owner emails and sends pictures because Rosco has developed “skin infection” over his cancer leg.
- Not responding to topical therapy and antibiotics…these are the pictures I see…

Cases: Rosco



Cases: Rosco

- Discussed amputation as the only surgical option at this point and worried disease is traveling up lymphatics.
- Radiation would be a good option: treat much larger areas.
- Attempt chemotherapy to try and control disease.
  - Discussed multidrug protocol due to aggressive disease.
  - Vinblastine and lomustine.

Cases: Rosco

- Continued to progress despite chemotherapy drugs.
- Owner did not want to pursue amputation.
- Moved and may pursue radiation therapy but is PALLIATIVE at this point.

Question

- Which below is NOT a common sign of degranulation event?
  - 1. Bruising/swelling?
  - 2. Coughing?
  - 3. Vomiting?
  - 4. Gastric ulceration?

Cases: Sam

- 8-year-old MN Golden Retriever.
- Two weeks prior owner had noticed mass on foot.
- Mast cell present between 3rd and 4th digits right front.
- Was not started on any medications and cytology diagnosing mast cell tumor was only testing done.

Cases: Sam

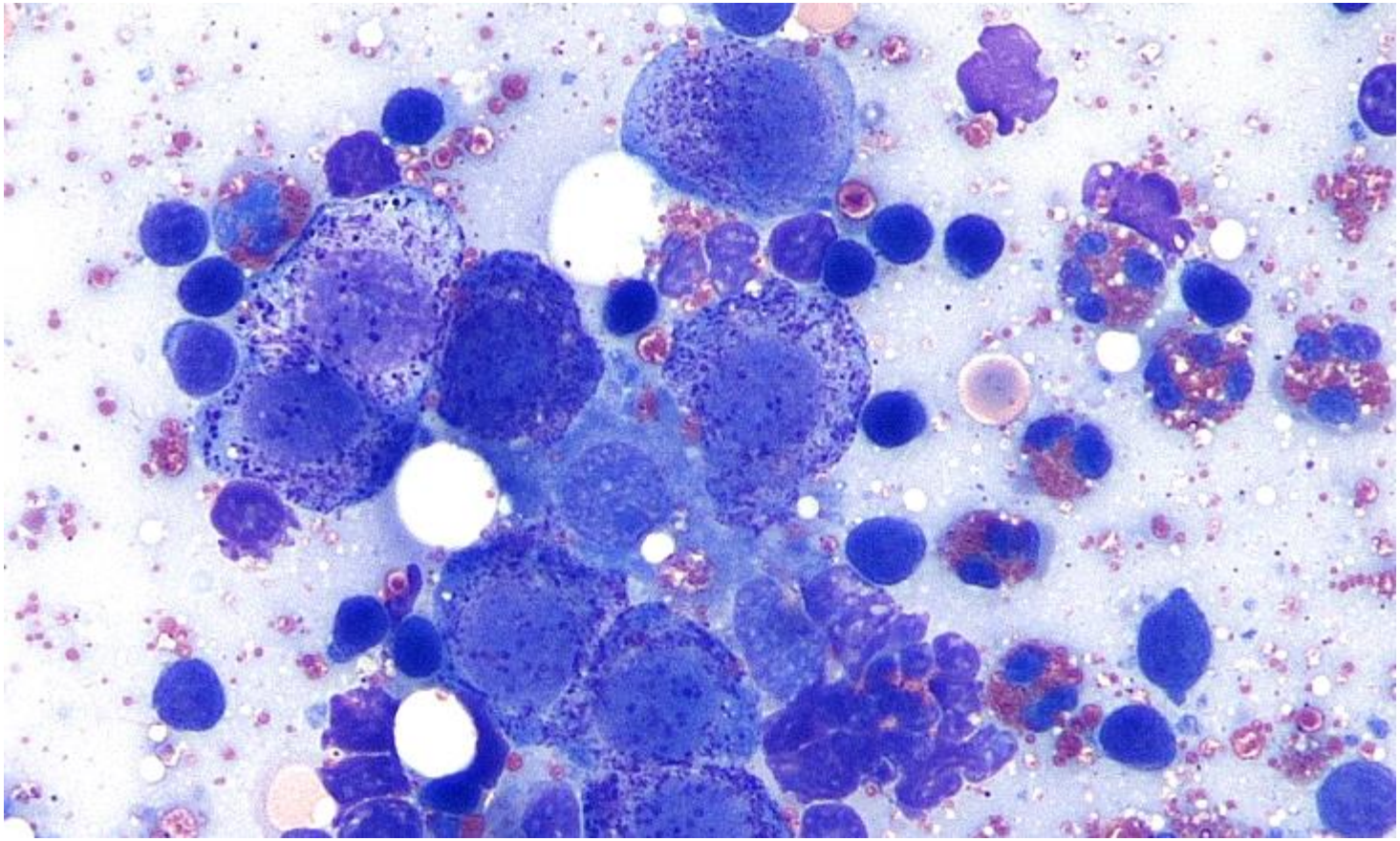
- PE mass on right front foot measures 2.2x1.3 cm but lymph nodes feel normal.
- Was able to aspirate sample of PS lymph node.
- Chest rads taken: normal.
- Cytology result would determine next step moving forward.
  - + then ultrasound.
  - - then surgery.
- Placed on Benadryl, Prilosec, and prednisone in hopes to shrink mass some.

Cases: Sam

MICROSCOPIC FINDINGS: LYMPHOID HYPERPLASIA AND REACTIVITY WITH MILD NEUTROPHILIC EOSINOPHILIC LYMPHADENITIS AND MILD MAST CELL INFILTRATE

COMMENTS:
The mild mast cell infiltrate in a patient with a mast cell tumor results in primary consideration for early metastatic disease. However, the number of mast cells does not allow for cytologic confirmation of metastasis and is still within limits for an inflammatory infiltrate. Neutrophilic-eosinophilic lymphadenitis is attributed to a paraneoplastic response, given the clinical history. Neutrophilic-eosinophilic lymphadenitis may also result from infection (i.e. bacterial, fungal, parasitic, protozoal, etc.) or drainage of a hypersensitivity reaction. Histopathologic evaluation would be necessary to confirm early metastatic mast cell neoplasia and definitively rule out an inflammatory infiltrate.

Cases: Sam



https://www.cliniciansbrief.com/article/image-gallery-lymph-node-cytology

Cases: Sam

- Since not convincing for mets and if so early, elected to proceed with surgery and depending on biopsy features consider further work up.
- Had surgery with Dr. Callard here. Plan to remove mass as well as prescapular lymph node.
- Knew going in that surgery was going to involve 3rd digit amputation to try and get better margins.
- Did well and had normal recovery.

Cases: Sam

Diagnosis:
Lymph node: Early metastatic mast cell tumor

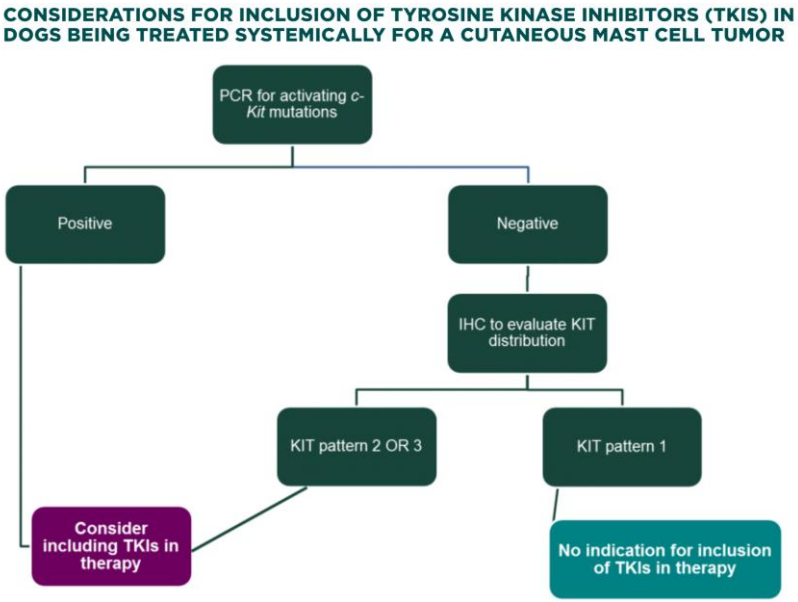
Digit: Mast cell tumor, grade 2/low grade, appears excised

Comment:
The mast cell tumor is consistent with grade 2 using the Patnaik grading scheme and low grade using the 2-tiered grading scheme. Early metastatic mast cell tumor is identified in the lymph node sections. The neoplastic cells appear to be completely excised in the digit and within the lymph node.

Cases: Sam

- Elected to perform abdominal ultrasound to stage for distant disease.
  - No evidence of metastatic disease, cystitis.
  - Elected not to pursue aspirates due to low grade nature.
- Submitted biopsy for Michigan State Mast Cell Prognostic Panel to give us more information and select chemotherapeutic.
- Bandage changes and some minor setbacks on healing but overall did well.

Cases: Sam



- MSU prognostic panel evaluates:
  - Proliferation indices AgNOR (speed of proliferation) and Ki-67 (number of proliferation).
  - ITD mutations of exon 11 and exon 8 of c-KIT.
  - Aberrant KIT pattern expression.
  - All shown to be correlated to survival and metastasis plus tells us are TKIs (Palladia) the best drug for the job.

Cases: Sam

- Sam's prognostic panel:
  - Ki-67: 5.0.
  - AgNOR: 2.2.
  - AgNOR x Ki-67: 10.9.
  - KIT pattern 2.
  - PCR negative for ITD mutation in c-KIT exon 11 and 8.
- What this means:
  - MCT with AgNOR x Ki-67 indices of <54 and Ki-67 of <23 were not associated with poor prognosis.
  - KIT pattern 2 in 20% of cases had dogs that were dead of MCT in 10 months.
  - Negative for c-KIT mutation means that Palladia may not be the best option for Sam.

Cases: Sam

- Elected to start vinblastine therapy.
- Dose once weekly for 4 weeks, and then every other week for 4 more doses.
- Sam tolerated it well and finished protocol.

Cases: Sam

- Saw Sam in October 2020 for recheck and restaging.
- No signs of regrowth and no evidence of metastasis.
- New lumps and bumps but no MCT.
  - 10-20% of dogs that develop 1 MCT will develop more!

Cases: Charlie

- Almost 10 year old MN Labrador retriever.
- Had a 4 cm mass removed from right side of prepuce August 2019.
- Diagnosed as completely excised MCT grade 3!
- 5 months later owners notice a swelling at previous surgical site.
- Cytology was submitted and results: poorly granulated MCT with probable LN effacement.

Cases: Charlie

Morphologic Diagnosis:

Skin, ventral abdomen: Poorly differentiated mast cell tumor with local tissue invasion into the Subcutaneous tissue. The tumor is large, densely packed and featured moderate anisokaryosis and scattered flame figures. The tumor is ulcerated on the surface and well circumscribed. Mitotic Count (# mitotic figures/2.37mm2) = 48. (Grade 3)

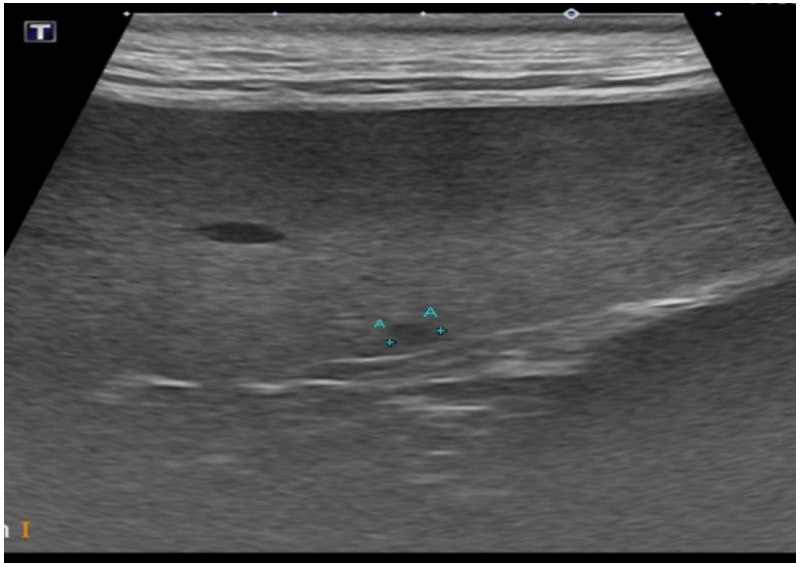
Interpretation/Comment:

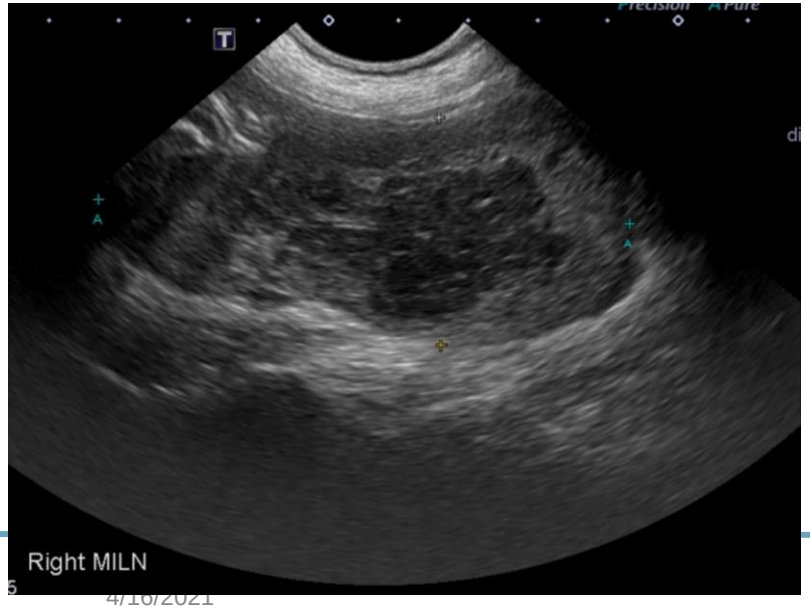
Poorly differentiated (Patnaik grade III of III) mast cell tumors have a generally poor prognosis. They are characterized by a high likelihood of local recurrence and distant metastasis. In one study, 94% of dogs with grade III mast cell tumors died of this disease within two years (Vet Pathol 1984, 21, 469-474). *Excision appears complete* Tumor cells are between 2mm and 5mm from the margin.

Cases: Charlie

- PE:
  - 9.5 cm subcutaneous mass right inguinal area with superficial erythema and what appears almost like ecchymosis lesions (inguinal lymph node).
  - Few historical lipomas.
  - Otherwise, happy!

Cases: Charlie





- Staging prior to pursuing further therapy.
- Chest radiographs normal.
- Abdominal ultrasound showed:
  - Marked sublumbar LN enlargement.
  - Splenomegaly with subtle nodules.
- Aspirated the spleen.
  - If spleen involved systemic treatment only may be best option.

Cases: Charlie

MICROSCOPIC DESCRIPTION:
Four smears are submitted for evaluation. The smears have a low to moderate cellularity with a moderate amount of blood. Nucleated cells consist predominantly of small lymphocytes, with many individualized to occasionally aggregated, poorly-granulated mast cells (~40-60%), as well as scattered late erythroid precursors, intermediate to large lymphocytes, and macrophages. The mast cells exhibit moderate anisocytosis and anisokaryosis with round to oval, eccentric nuclei with coarse chromatin. Occasional binucleation is seen. These cells have a moderate amount of lightly basophilic cytoplasm that contains few small, metachromatic granules.

MICROSCOPIC INTERPRETATION:
Metastatic mast cell tumor.

Cases: Charlie

- Owners wanted to be aggressive with chemotherapy.
- Elected to do combination vinblastine and Palladia.
- With prednisone and supportive H2 blockers.
- Understood prognosis is poor overall with likely 7-month survival.

Cases: Charlie

Combination vinblastine, prednisolone and toceranib phosphate for treatment of grade II and III mast cell tumours in dogs

Jaime A. Olsen ✉, Maurine Thomson, Kathleen O'Connell, Ken Wyatt

First published: 24 May 2018 | https://doi.org/10.1002/vms3.106 | Citations: 7

Cases: Charlie

- Started prednisone before chemotherapy.
- Reduction in mass size by 15% with prednisone alone.
- Vinblastine q 2 weeks for 8 dosages. Started out modest dosage.
- Palladia @ home on MWF.
- Reduced prednisone dosage slightly due to diarrhea.

Cases: Charlie

- At his third dose the LN had < by 84%!!!
- Dose increased slightly with vinblastine.
- Stayed stable throughout vinblastine protocol at around 2.5 cm.
- After finishing vinblastine staying on Palladia.

Cases: Charlie

- At one month after finishing vinblastine the results were phenomenal.
- Inguinal node 1.5 cm.
- Splenic changes basically resolved.
- Sublumbar lymph nodes drastically reduced.
- Charlie's quality of life is awesome!

Cases: Charlie

- In august 2020…
- Six months after starting chemotherapy and a year after his original surgery his LN came back with a vengeance…
- Started single agent lomustine q 3 week but his cancer is likely to be highly resistant.
- At recheck 3 weeks later worsened along skin with many satellite nodules.
- Charlie was very uncomfortable.

Cases: Charlie

Safety and efficacy of intralesional triamcinolone administration for treatment of mast cell tumors in dogs: 23 cases (2005–2011)

Ashley Case, Kristine Burgess

PMID: 29244608 DOI: 10.2460/javma.252.1.84

Cases: Charlie

- Had to add on more pain medications because he was getting increasingly uncomfortable.

- QOL continued to decline and we euthanized Charlie 9 months after we first saw him.

Cases: Tas Tas

- 13 year old MN mixed breed that came from the streets of South America.
- Mass had been present 1.5 years on right ventral chest/axilla.
- Was not aspirated and thought to be a lipoma….
- Within a few months it grew quickly.
- Antibiotics were no help, scheduled surgery.

Cases: Tas Tas

- Blood work showed leukocytosis and mild anemia.
- Chest radiographs no signs of mets.
- When performing surgery marble sized masses in a chain cranial to main mass.
- These not removed to conserve skin.
- Behavior tells us this is not going to be good….

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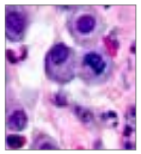
Cases: Tas Tas

MICROSCOPIC DESCRIPTION:
This mass is characterized by a poorly circumscribed subcutaneous population of round cells which are non-encapsulated and rarely extend into the dermis. These cells contain deeply staining basophilic intracytoplasmic granules, a central round nucleus and an indistinct nucleolus. Mild numbers of eosinophils are associated with these loose cords of cells. There is mild anisocytosis, anisokaryosis and rare binucleation. Intramural and perivascular oedema is also noted.

MICROSCOPIC INTERPRETATION:
Subcutaneous mast cell tumour; excision complete

Mitotic count: 2 per 10 HPF
Margins: Microscopic- Deep: 1.7 mm including one muscle fascial plane ; Closest Lateral: 3.2 mm
Vascular/lymphatic invasion: Not seen

Cases: Tas Tas

	Subcutaneous mast cell tumors	
Mitotic count (previously referred to as "mitotic index") 	• As compared to MC = 0, MC > 0 but ≤ 4 associated with: – 5.59 times higher risk of local recurrence – 3.72 times higher rate of MCT-related death • As compared to MC = 0, MC > 4 associated with: – 36.05 higher rate of MCT-related death – 130.21 times higher risk of local reoccurrence – Increased risk of and decreased time to metastasis	
Presence of multinucleated cells	• Multinucleation was significantly associated with decreased survival times (hazard ratio = 3.40) • Associated with increased distant MCT occurrence rate by 2.24 times	• Predicted MST: – Infiltrative tumor, MC > 4, and multinucleation: 140 days – Infiltrative tumor, MC > 4, but no multinucleation: 950 days
Growth pattern	• Infiltrative tumors: – 3.18 times higher rates of MCT mortality than well-circumscribed tumors – Significantly higher rates of MCT disease (local reoccurrence, distant MCT occurrence, and metastasis) than both circumscribed and combined patterns	
Surgical margins	• In general, completely excised well-circumscribed SCMCTs are unlikely to recur • Recurrence rate: – With complete excision: 2% – With incomplete excision: 12%	• Predicted time to local reoccurrence: – Incompletely excised SCMCTs with infiltrative pattern: 70 days – Completely excised SCMCTs with infiltrative pattern: 1,000 days – Incompletely excised well-circumscribed SCMCTs: 365 days

https://www.idexx.com/files/canine-mct.pdf

Cases: Tas Tas

- Within two weeks a baseball sized mass grows back over surgical site.
- Ulcerates, bleeds, becomes secondarily infected.
- Then he develops subcutaneous masses all along his ventrum from the sternum to the inguinal region.

Cases: Tas Tas

- On exam extensive firm, subcutaneous mass effect from sternum to inguinal area.
- Larger mass on right ventral chest, 8.5 cm, ulcerated, draining, necrotic center.
- Masses are erythematous, hot to the touch, bruised in some areas, almost rope like.
- He seems painful.

Cases: Tas Tas

Cases: Tas Tas

- Aspirated mass to confirm was actually mast cell regrowth.
- Cells were poorly granulated but mast cells for sure.
- Ran blood work and was still anemic and had leukocytosis.

Cases: Tas Tas

- Discussed that surgery is not an option.
- Could consider radiation therapy would be palliative.
- Discussed palliative chemotherapy, discussed either going aggressive like Charlie but Tas Tas not feeling as well.
- Therefore, settled on single agent vinblastine.
- Of course, prednisone, Benadryl and omeprazole as well.

Cases: Tas Tas

- After first vinblastine the masses were less erythematous and warm.
- He was not eating well.
- Started appetite stimulant.
- Gave another dose of vinblastine with slightly increased dose as no neutropenia noted.

Cases: Tas Tas

- Masses became larger.
- Very painful so added in gabapentin.
- Vinblastine did not seem to be helping after the first dose.
- Mass was again becoming necrotic and secondarily infected.
- Discussed humane euthanasia as I felt he was having degranulation events making him feel miserable.

Cases: Tas Tas

Cases: Scarlet

- 4-year-old FS Boxer.
- Presented to referral veterinarian 2 weeks prior to oncology consult for mass on sternum.
- Another mass over left rib cage had been noted historically as well.
- Aspirated sternal mass and the mass on the rib cage became inflamed and bruised after aspirate.
- Mass on sternum diagnosed as mast cell tumor.
- Owners also noted new mass over dorsal shoulder.

Cases: Scarlet

- On physical exam found all three masses:
  - Over sternum cutaneous mass.
  - Over left rib dermal mass.
  - Over dorsal shoulder dermal mass.

- No enlarged lymph nodes or organ enlargement.

Cases: Scarlet

- Discussed likely multicentric mast cell disease.
- Boxers are prone to developing multiple low grade mast cell tumors.
- All are independent of one another, not mets.
- Generally, will develop multiple tumors over lifetime.
- Low rates of metastasis and generally good prognosis overall.

Cases: Scarlet

- Discussed a few different options:
  - Surgical removal with board certified surgeon.
  - Punch biopsy marginal removal with oncology.
  - Or new exciting therapy….

Cases: Scarlet

Welcome to STELFONTA®

An innovative and effective treatment for mast cell tumors (MCTs) in dogs

https://vet-us.virbac.com/home/stelfonta/for-veterinary-professionals

Cases: Scarlet

STELFONTA® Indication

FDA-approved local treatment for non-metastatic Mast Cell Tumors

Indicated for the treatment of:

- Non-metastatic cutaneous mast cell tumors
- Non-metastatic subcutaneous mast cell tumors located at or distal to the elbow or the hock in dogs

Tumors must be less than or equal to 10 cm^3 in volume, and must be accessible to intratumoral injection.

Cases: Scarlet

- Biologically-active small molecule.
  - Forbol ester.
  - From the Australian rainforest: native blushwood plant.

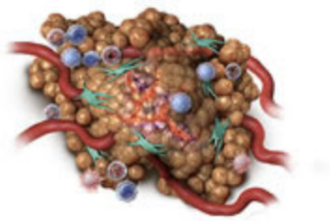
- Effects:
  - Oncolytic lysis of tumor cells in direct contact with tigilanol tiglate.
    - Due to disruption of mitochondrial signaling.
  - Activates protein kinase c signaling cascade.
    - Propagates throughout tumor causing acute inflammatory response.
  - Direct effects of increased permeability of tumor vasculature.
    - Leads to direct damage of tumor vessels leading to tumor destruction.

https://www.theguardian.com/society/2014/oct/08/cancer-tumours-destroyed-by-berry-queensland-rainforest

Cases: Scarlet

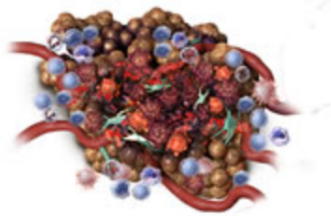
See **STEL**FONTA® start to work within hours,[1] with tumors typically destroyed by Day 7

Day 1



Acute inflammatory response with swelling and erythema to the tumor margins and immediate surrounds[1]

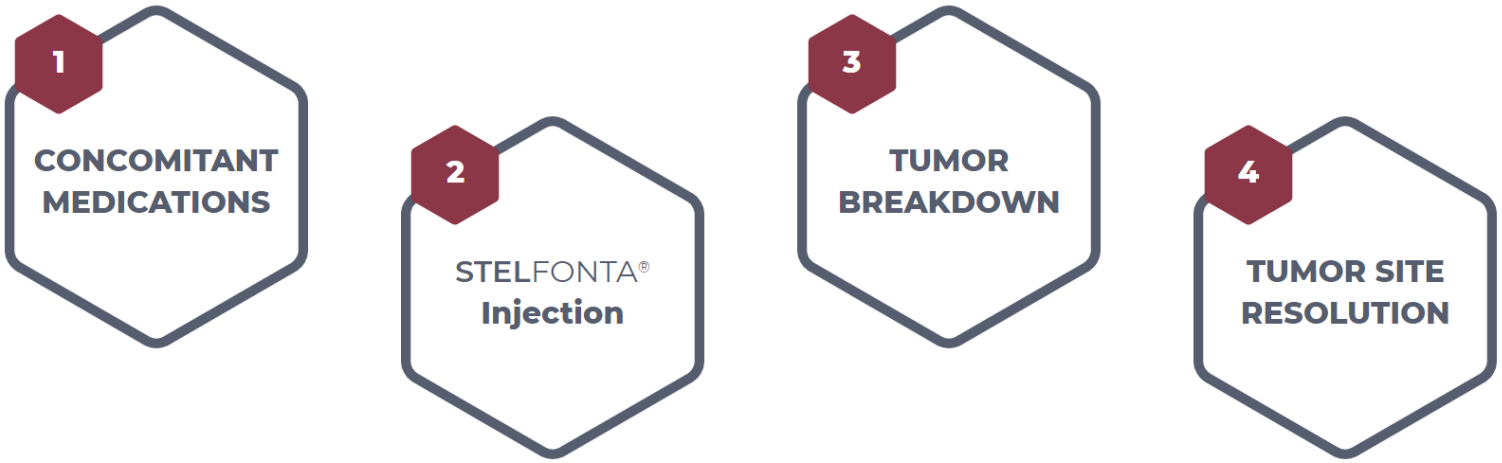
Day 7



Necrotic destruction is seen – in dogs this means blackening, shrinkage and leakage of thick discharge

Cases: Scarlet

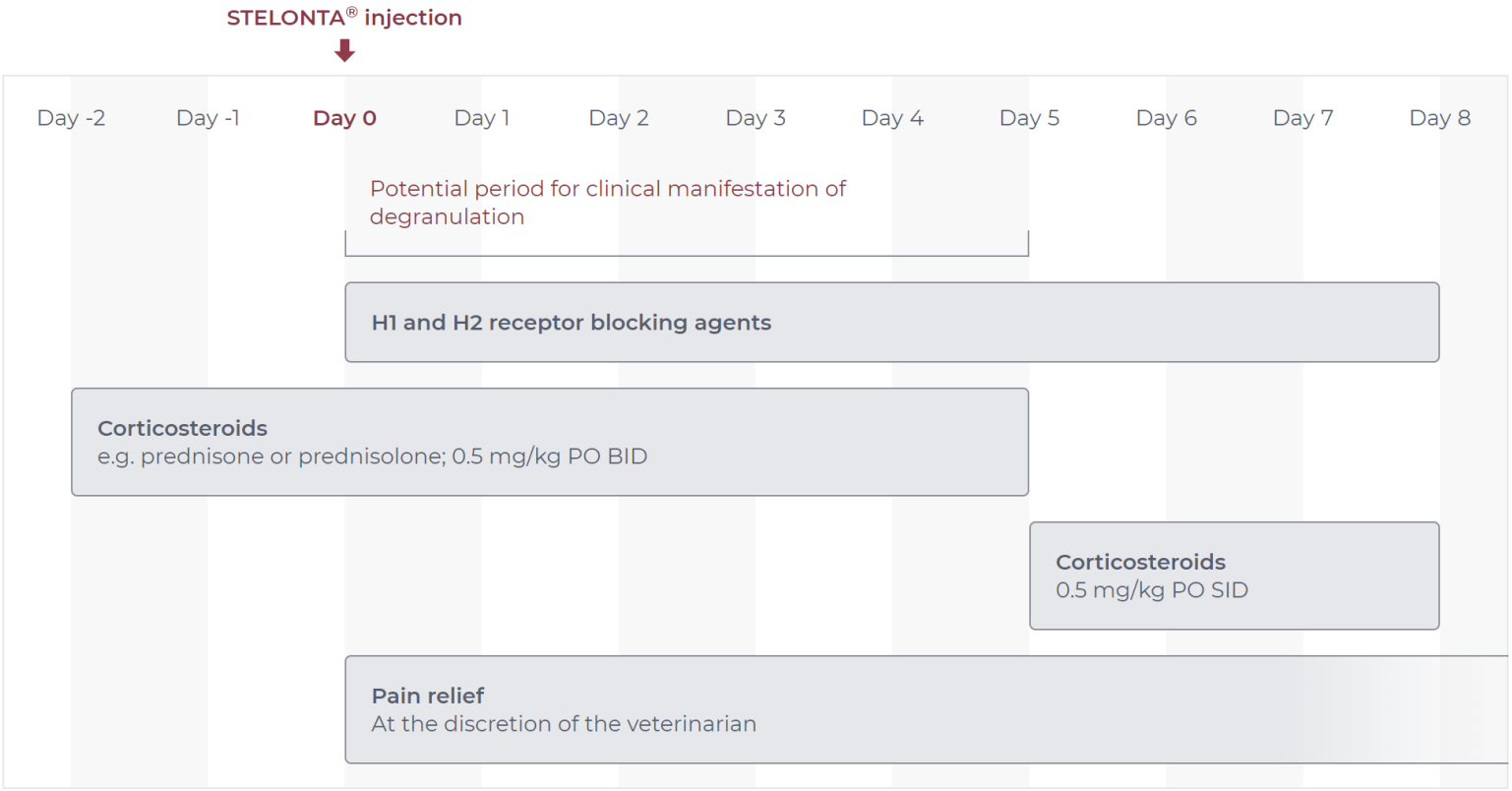
4 stages to treatment success with **STEL**FONTA®



MEDVET

Cases: Scarlet

Concomitant medication dosing schedule



Cases: Scarlet

Calculate the dose and inject **STEL**FONTA® directly into the tumor

To administer **STEL**FONTA®:

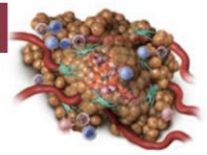
Accurately measure the length, width and height of the tumor (in cm)
Determine the volume of the tumor:
Volume of tumor (cm^3) = ½ x [length (cm) x width (cm) x height (cm)]
Then determine the correct dose:
Dose (mL) = **tumor volume (cm^3)** x ½

Using a sterile, luer-lock syringe with a 23-gauge needle and wearing appropriate protective equipment (glasses and gloves), inject the dose by inserting the needle into the tumor mass through a single injection site, moving the needle back and forth in a fanning manner to help ensure the treatment reaches all aspects of the tumor.

Cases: Scarlet

Tumor breakdown is a sign **STEL**FONTA® is working

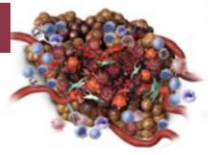
Day 1



Oncolytic and inflammatory effect begins

Within hours: STELFONTA® starts to work, with changes visible at the tumor site. The cells in the tumor and tumor blood vessels will begin to break down resulting in a change of color in the tumor and swelling at the treatment site.

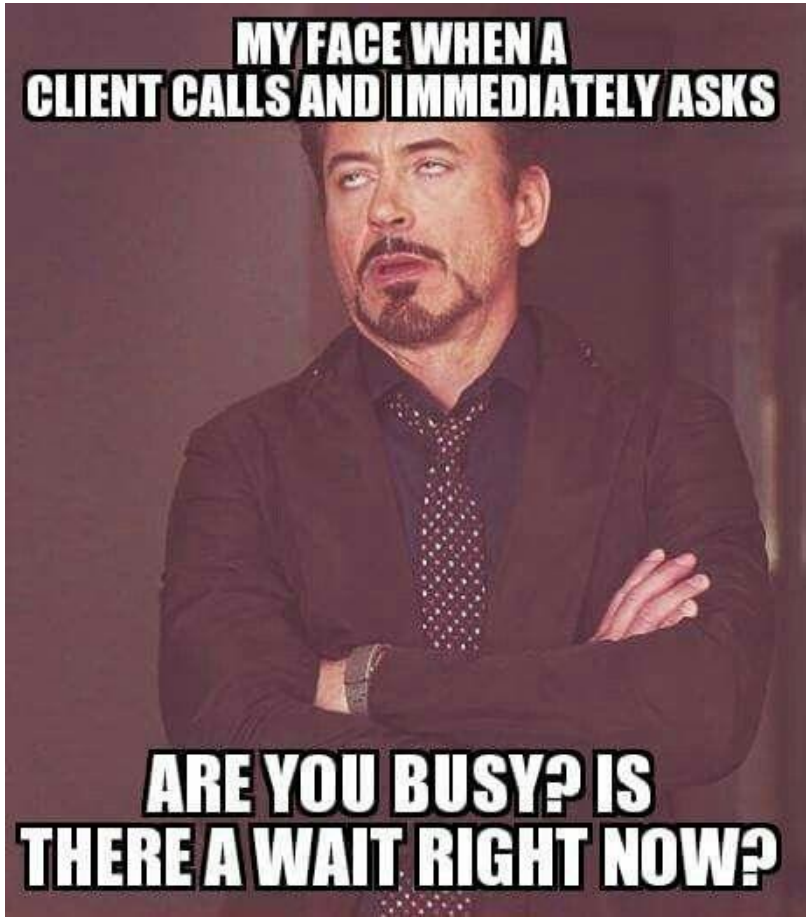
Day 4



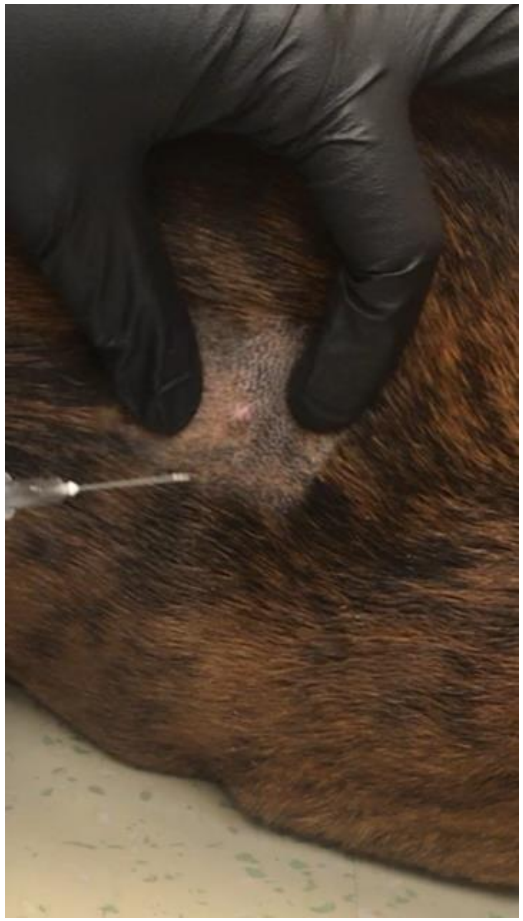
Increased permeability of tumor vasculature

Within days: The tumor may turn black. The surface may become soft and fluid may leak from the tumor as it continues to break down. Swelling at the treatment site may continue and cause some discomfort to the dog.

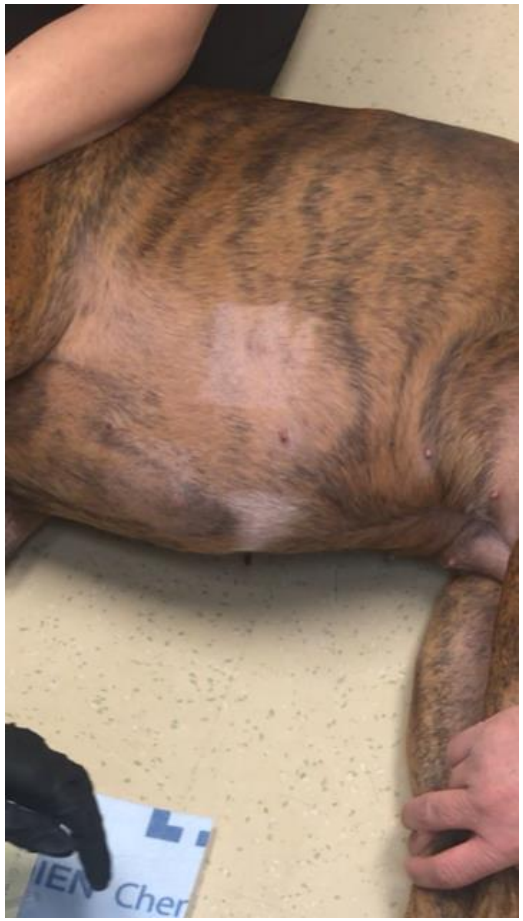
Cases: Scarlet



Cases: Scarlet



Cases: Scarlet

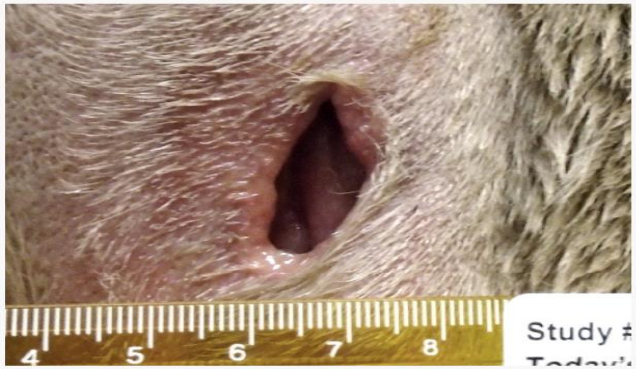


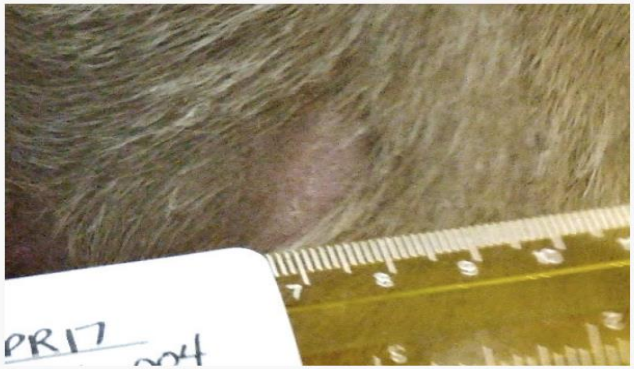
Cases: Scarlet

Cases: Scarlet

Wound healing via second intention with minimal intervention*

- As the tumor breaks down further, a "pocket" or deficit may develop where the tumor once was
- A healthy layer of new granulation tissue will be seen, indicating healing by second intention
- 96% of tumor sites healed by Day 84





* *Minimal intervention. Antibiotics, bandages, and eCollar aren't usually required.*

Common adverse events

- Most common adverse events such as wound formation, injection site pain/bruising/erythema/edema, lameness in a treated limb are related to **STEL**FONTA®'s mode of action at the tumor site
- Formation of wounds is a secondary intention to treatment with **STEL**FONTA®

Cases: Scarlet

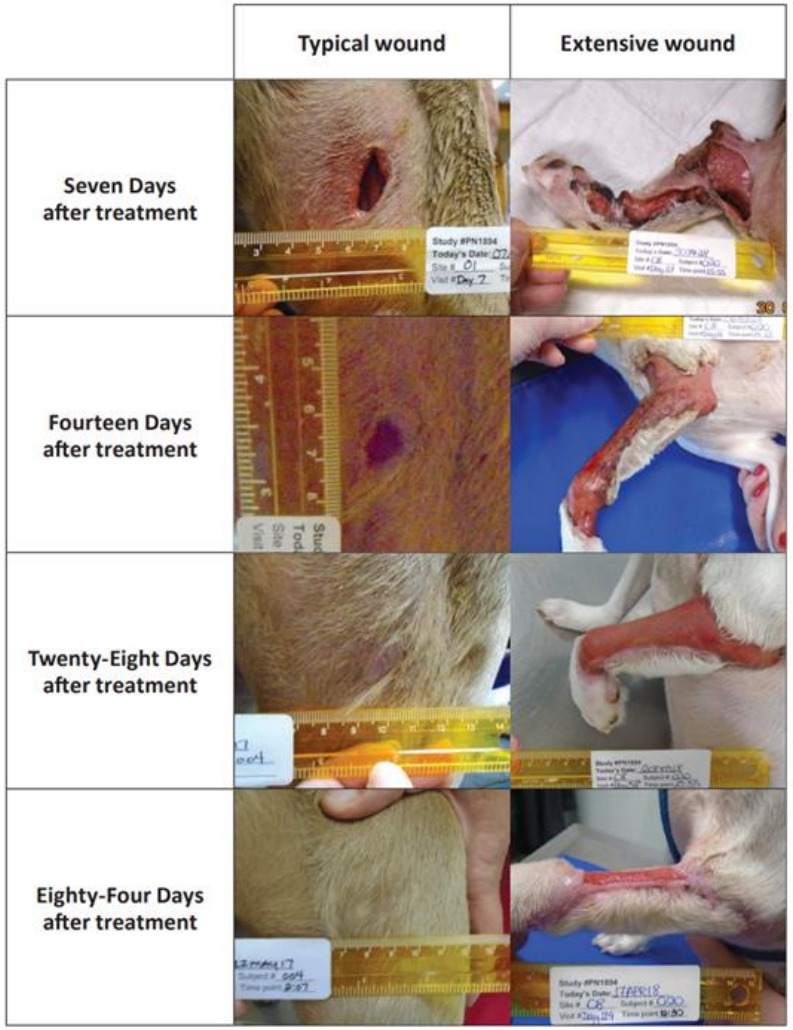
ADVERSE REACTIONS

Human Exposure

There was one human exposure during the field study where the veterinarian had a needle stick injury to the thumb at completion of tumor treatment and was injected with an unknown amount of STELFONTA. The incident resulted in pain and necrosis of the center of the thumb at the point of needle stick. The wound healed over a period of three months. See Pictures 1 and 2 below. A separate needle stick injury was reported with a maximum potential dose of 0.1 mL tigilanol tiglate into the distal extremity of the left index finger, resulting in a localized burning sensation, local inflammation, bruising, muscular pain up the left arm, and localized tissue necrosis. Muscular pain resolved in the first 12-24 hours and the wound healed in 8 weeks. There have been other needle stick injuries reported, with at least one injection into a thumb, with minimal (stinging, pain, and swelling) to no adverse events associated with these accidental self-injections.

Picture 1. Thirteen days after self-injection

Picture 2. Seventy-four days after self-injection



Question

- Which of the following chemotherapeutics is a common mast cell tumor treatment?
  - 1. Doxorubicin?
  - 2. 5-fluorouracil?
  - 3. Carboplatin?
  - 4. Vinblastine?

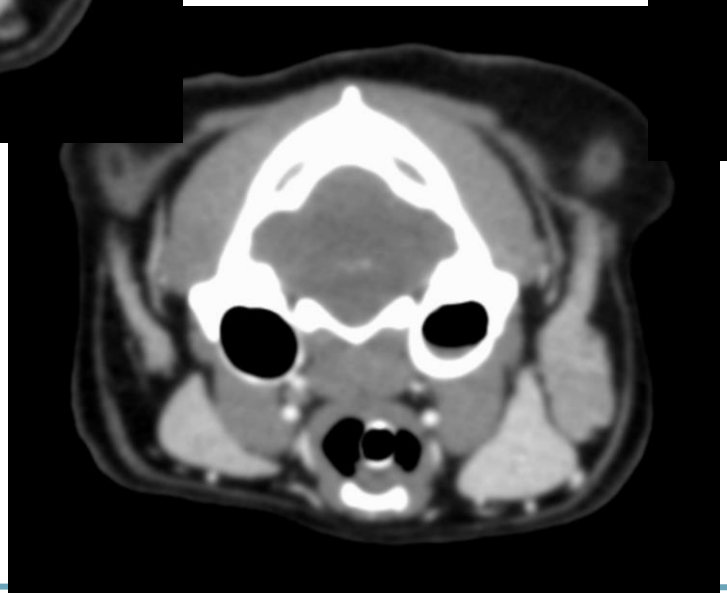
Cases: Miles

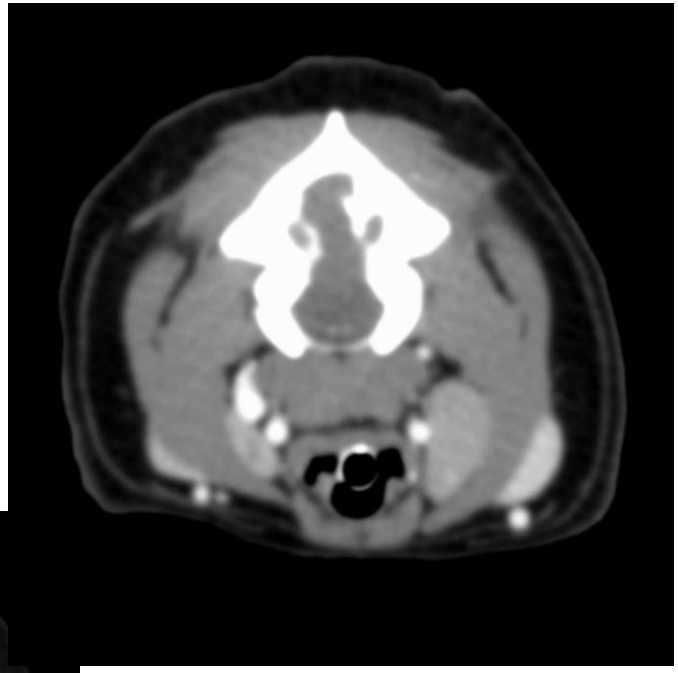
- 8 year old MN DSH.
- Presented to our surgery service for suspected inner ear polyp or mass.
- Has historically had issues with his left ear for about two years.
- Had a “polyp” removed from the ear by referring veterinarian October 2020.
- Owner saw growth in left ear and some discharge recur.
- Seen by dermatologist in February who visualized a mass and referred him to a surgeon.

Cases: Miles

- Was receiving Synotic drops in ear which helped symptoms.
- Had received Depo Medrol injection in February 2021 which always seemed to make Miles feel better.
- On physical exam he was found to be obese and had bloody crusting discharge from his left ear.
- A mass is visualized in the horizontal canal.

Cases: Miles





Cases: Miles

**Update 3/16/2021:
Toluidine blue staining highlights metachromatic granules in many of the neoplastic cells, though there are large areas with sparse staining, as well. Overall, these results support the previous suspicion of mast cell neoplasia.

This is very likely a mast cell neoplasm.

The mitotic count in this case is greater than 5, could suggest some risk for more aggressive behavior. A recently proposed grading scheme (Veterinary Pathology 2019, Vol. 56(1) 43-49) would consider this to be low grade if the overall mass is < 1.5 cm and high grade if > 1.5 cm when combined with the features than can be assessed from the samples provided. In that study, the 15 (24%) high-grade cMCTs had reduced survival time (median, 349 days; 95% CI, 0–739 days) vs the 48 low-grade tumors (median not reached; P < .001).

Whether this is the same process occurring in the retropharyngeal lymph node or salivary gland would require evaluation of those tissues to differentiate from another process (such as salivary neoplasia).

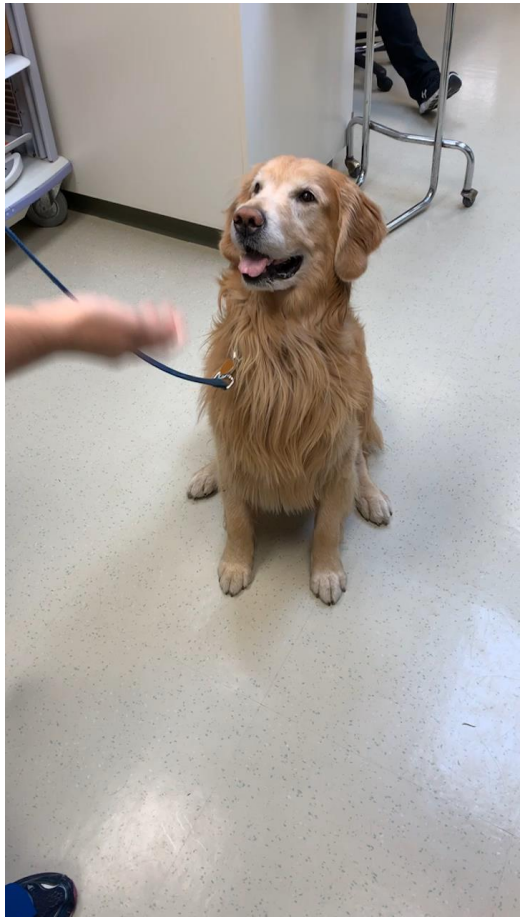
MICROSCOPIC DESCRIPTION:

Left ear canal: The dermis is expanded and infiltrated by a neoplasm composed of sheets of neoplastic round cells supported by thin collagenous stroma. Multifocally small numbers of eosinophils and lymphocytes are admixed. The neoplastic cells have round to oval central nuclei with coarsely stippled chromatin one to several prominent nucleolus. They have moderate amounts of well demarcated, faintly granulated cytoplasm. There is mild anisocytosis and anisokaryosis with 6 mitotic figures in 10 HPF. Infrequently, the neoplastic cells appear to enter the

Cases: Miles

- 1. Surgery.
- 2. Radiation therapy.
- 3. Chemotherapy.
- 4. Palliative care.

Wrap it up!



Questions????