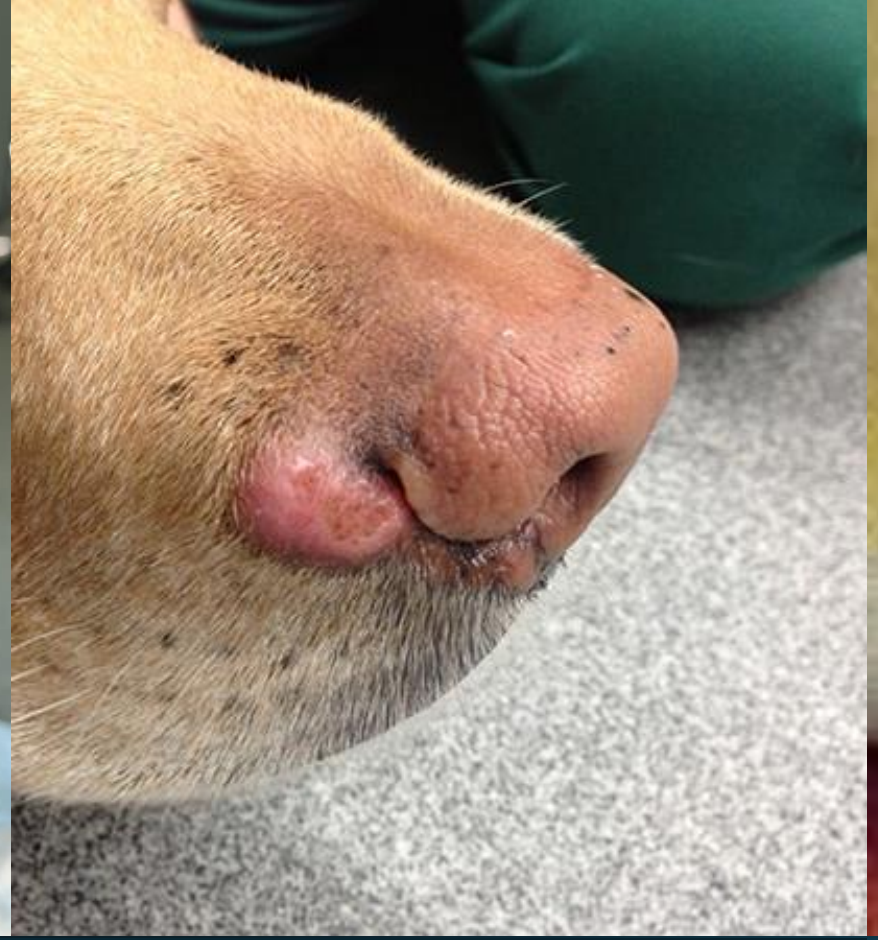
내과 발표

비엔동물전문의료센터
BIEN ANIMAL MEDICAL CENTER

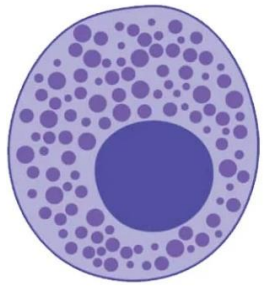

MCT

- malignant skin tumor 16-21%

- Age 8-9 years

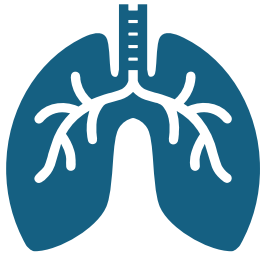
- Boxer, Staffordshire Bull Terrier, Boston Terrier, Bulldog, Labrador Retriever , Beagle, Scottish Terrier, Weimaraner, Rhodesian Ridgeback, German Short-Haired Pointer, Chinese Shar-Pei, and Schnauzer

MCT



Mast cell 비만세포

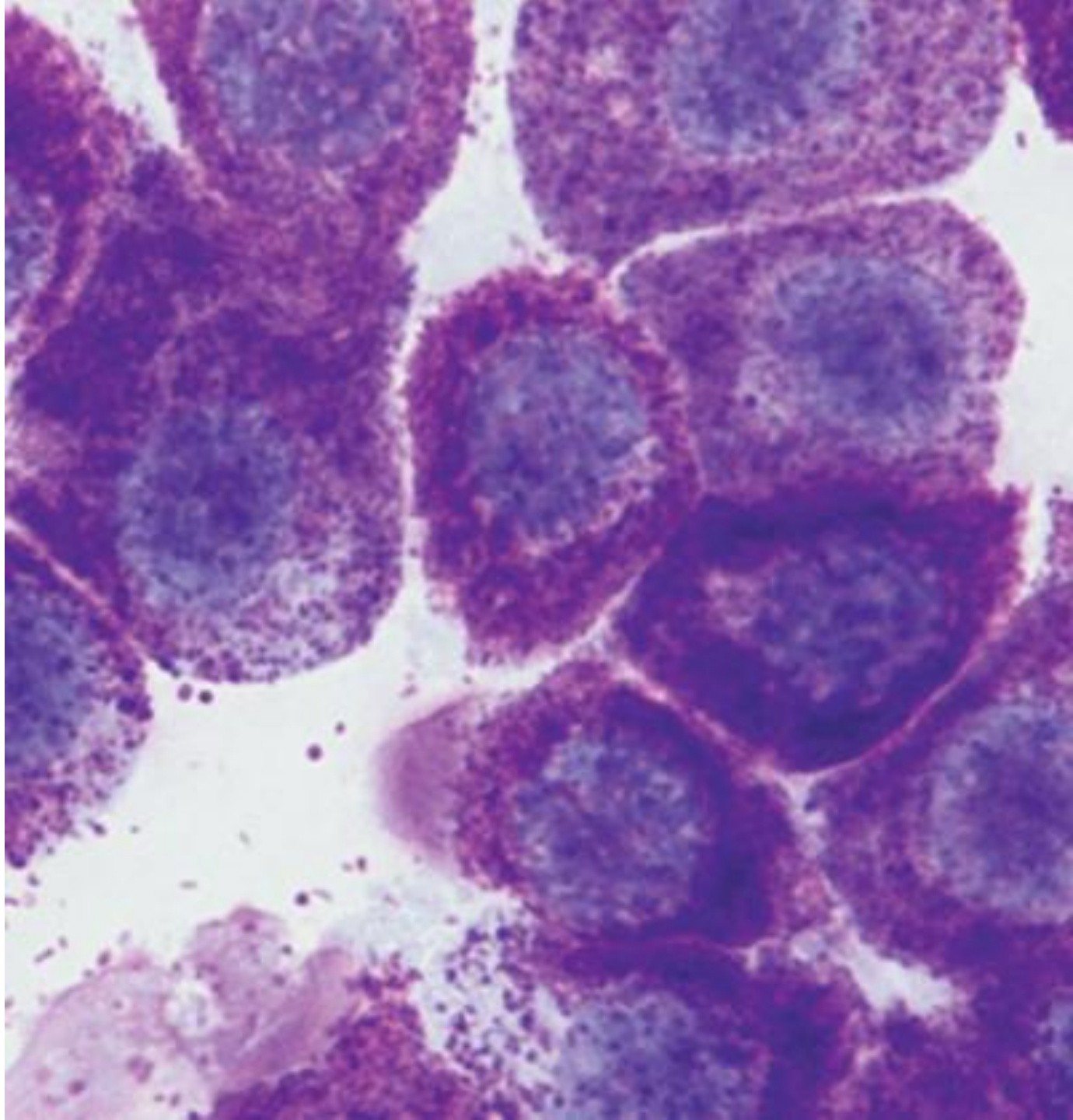
정상적인 면역계를 유지하는데
이용, myeloid 계열 세포에서 분화



피부, 폐 위장관등의 조직에서
정상적으로 분포

MCT

- Mast cell tumor=mast cell의 비정상적인 증식
- 과립(histamine, heparin)의 기능이 과항진되어 임상증상 유발
- 피부,피하,점막,장기 내로 발생 가능
- C-kit gene이 변이되어 비만세포종 발생 가능



MCT toxicity

Histamine hyperactivation

H1: anaphylactic reaction(chlorpheniramine, dexa)

H2: gastirc acid stimulation(famo, ome)

MCT stage

Stage	
0	One tumour incompletely excised from the dermis, without regional lymph node involvement
I	One tumour confined to the dermis, without regional lymph node involvement
II	One tumour confined to the dermis, with regional lymph node involvement
III	Multiple dermal tumours; large, infiltrating tumours with or without regional lymph node involvement
IV	Any tumour with distant metastasis, including blood or bone marrow involvement
Substage	
a	Without systemic signs
b	With systemic signs

MCT stage

Grade of malig-nancy	Cell morphology			Mitotic index	Surrounding tissues
	Shape	Cytoplasm	Cell nucleus		
I	round	high amount of cytoplasm with numerous granules	round with condensed chromatin	–	slight oedema and necrosis
II	round to oval, occasionally giant or spindle-shaped	moderate amount of cytoplasm with delicate granules, occasionally scanty cytoplasm with large, hyperchromatic granules	round, with loose karyoplasm and single nucleolus, less frequently double nuclei	low, 0–2 per high power field	regions of significant tissue oedema and necrosis
III	moderate size, round, oval or spindle-shaped, many giant cells	poorly distinguished cytoplasm containing poorly visible or invisible granules	round, vesicular cell nucleus with a single or multiple nucleoli, frequent bi- or multinuclear cells	high, 3–6 per high power field	frequently noted: oedema, congestion and necrosis

High-grade if any one of the following criteria is present:	
≥7 mitoses/10 HPFs	In regions with the highest mitotic activity
≥3 multinucleated cells/10 HPFs	Multinucleated cells defined as cells with 3 or more nuclei
≥3 bizarre nuclei/10 HPFs	Highly atypical with marked indentations, segmentation, and irregular shape
Karyomegaly	At least 10% of neoplastic cells vary by 2-fold

Abbreviation: HPF, high-power fields (400× magnification).

Treatment: stage 1,2

Surgery

Low grade vs. High grade

-> radiation or chemo(toceranib, vinblastine, CCNU..)

Treatment: beyond stage 2

Surgery-> adjuvant therapy

Adjuvant therapy->surgery

Prognosis

Cutaneuous MCT

- Low grade, 10% 미만 전이, MST 2년 이상
- High grade, 80% 이상 전이, MST 4달 미만

Mucosal MCT

- 예후 불량

Subcutaneous MCT

- 예후 양호

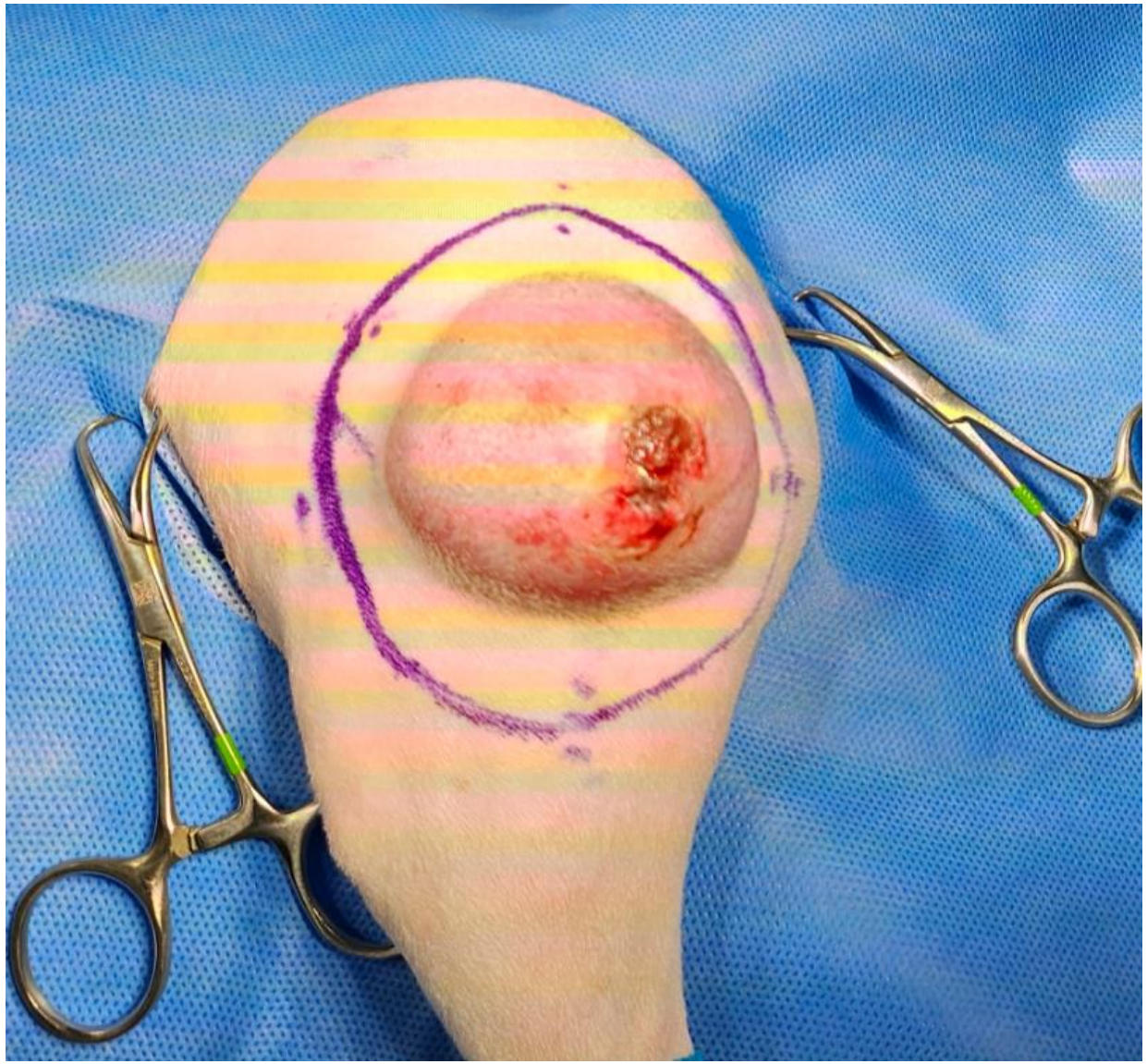
내부장기 MCT

- 피부보다 예후 불량, 전이율 높음

Case 1.

- 삼식이, 믹스, CM, 14y 1m
- 좌측 후지 MCT, 근육 침습 X, 좌측 서혜부 림프절 미약한 종대

Surgery



Histopathologic examination

COMMENTS:
Subcutaneous mast cell tumors (SCMCTs) are located exclusively within the subcutis, or may also mildly extend into the overlying deep dermis. It is important to distinguish these mast cell tumors (MCTs) from cutaneous mast cell tumors (CMCTs), which are located within the dermis, with/without involvement of the underlying subcutis, as more than 90% of SCMCTs are controlled by surgical excision alone (Thompson et al., 2011). However, 10% of dogs with SCMCT die of MCT-related disease, 11% develop a second SCMCT distant from the primary site, 8% recur, and 5% metastasize (Kiupel, 2017).

Grading: The Patnaik and Kiupel grading systems were developed for CMCTs, and do not apply to SCMCTs. However, certain morphologic features including increased mitotic count, infiltrative growth pattern, and presence of multinucleation, have been associated with a more aggressive biologic behavior, assisting the identification of the small subset of biologically more aggressive SCMCTs (Thompson et al., 2011). For more details regarding the prognostic significance of these features please refer to the IDEXX Diagnostic Update for Canine Mast Cell Tumors (2017): www.idexx.com/mct.

Assessment of the features associated with biologically more aggressive SCMCTs:

Mitotic count (MC, number of mitotic figures per 10 high power fields): 6

Growth pattern: Infiltrative

Multinucleation: Absent

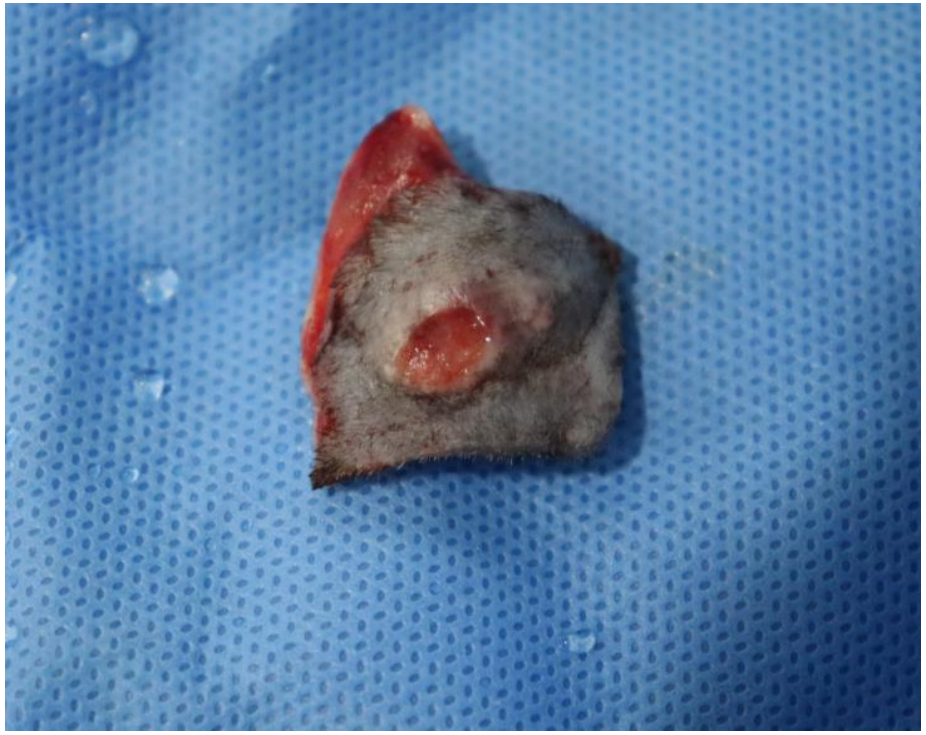
In this case, the morphologic features are suggestive of a biologically more aggressive variant of SCMCT.

Surgical margins: As a general rule, if a SCMCT is well-circumscribed and excision was complete, then the tumor is unlikely to recur (Kiupel, 2017). A study showed only 2% recurrence rate with complete excision, and only 12% recurrence rate even with incomplete excision. Risk factors for local tumor recurrence of SCMCTs include MI greater than 0, incomplete margins, and infiltrative growth pattern. The predicted time to local reoccurrence for cases having incomplete margins and infiltrative pattern is 70 days, compared to 1,000 days for completely excised infiltrative tumors, and 365 days for incompletely excised
circumscribed tumors (Thompson et al., 2011).

Case 2.

- 시월이, 노르웨이 숲, CM, 8y 3m
- 우측 귀 끝 MCT susp w/ 양측 하악 림프절, 덧액와 림프절 경미한 종대

Surgery



Histopathologic examination

Rt ear pinna mass (it is identified 8 months ago).
Cytology: Mast cell tumor.
Mild enlargement of bilateral mandibular LN (on CT exam).
Please evaluate the surgical margin.
Suspected: MGT.
Size of Lesion: 1.45 x 0.58 x 1.1 cm.

INTERPRETATION:
Pinna, right: Cutaneous mast cell tumor
Mitotic count: 0 in 2.37 mm2
Vascular invasion: Not observed
Surgical margins: Closest surgical margin, 1.1 mm

COMMENTS:
Histopathology of this skin mass is most consistent with a feline cutaneous mast cell tumor. Mast cell tumors (MCT) account for approximately 20% of cutaneous neoplasms in the cat. While most feline cutaneous MCT present as solitary lesions, a multicentric presentation is not uncommon, with clusters of lesions in an anatomic region or more widespread cutaneous distribution.

A recent study has proposed a histologic grading scheme for feline cutaneous MCT, grouping tumors into low and high grades (Sabattini et al., 2019). High grade classification was based on a mitotic count of greater than 5 mitotic figures in 2.37 mm2, and at least two of the following criteria: tumor diameter greater than 1.5 cm, irregular nuclear shape, and nucleolar prominence/chromatin clusters. In this study, high grade feline cutaneous MCT were associated with significantly reduced survival times, with a median survival time of 349 days (versus "median not reached" for low grade tumors). The tumor in this case is low grade according to this grading scheme.

(The histologic grading system for canine mast cell tumors is not used for feline mast cell tumors because it has been shown in various studies that it does not correlate with prognosis in cats.)

References: Sabattini S et al. (2019), Vet Pathol 56(1):43-49; Meuten, ed. (2017), Tumors in Domestic Animals, 195-199; Melville K et al. (2015), J Feline Med Surg 17(6):486-493

HISTOPATHOLOGIC DESCRIPTION:
Pinna, right: The specimen is characterized by a densely cellular , mostly well circumscribed mass, composed of sheets of well- differentiated mast cells supported by pre-existing collagenous stroma. The mast cells exhibit minimal pleomorphism. They are round to oval with distinct cell borders, and a moderate amount of eosinophilic cytoplasm which exhibits occasional faint basophilic cytoplasmic granularity. Nuclei are round, central to paracentrally placed, with a finely stippled chromatin pattern, and 1 to occasionally 2, small, indistinct, amphophilic nucleoli. There is minimal anisocytosis and anisokaryosis, and no mitotic figures are counted in 2.37 mm2. There is no evidence of lymphatic/vascular invasion. Scattered within the mass are rare eosinophils. Tumor diameter is 1.3 cm.

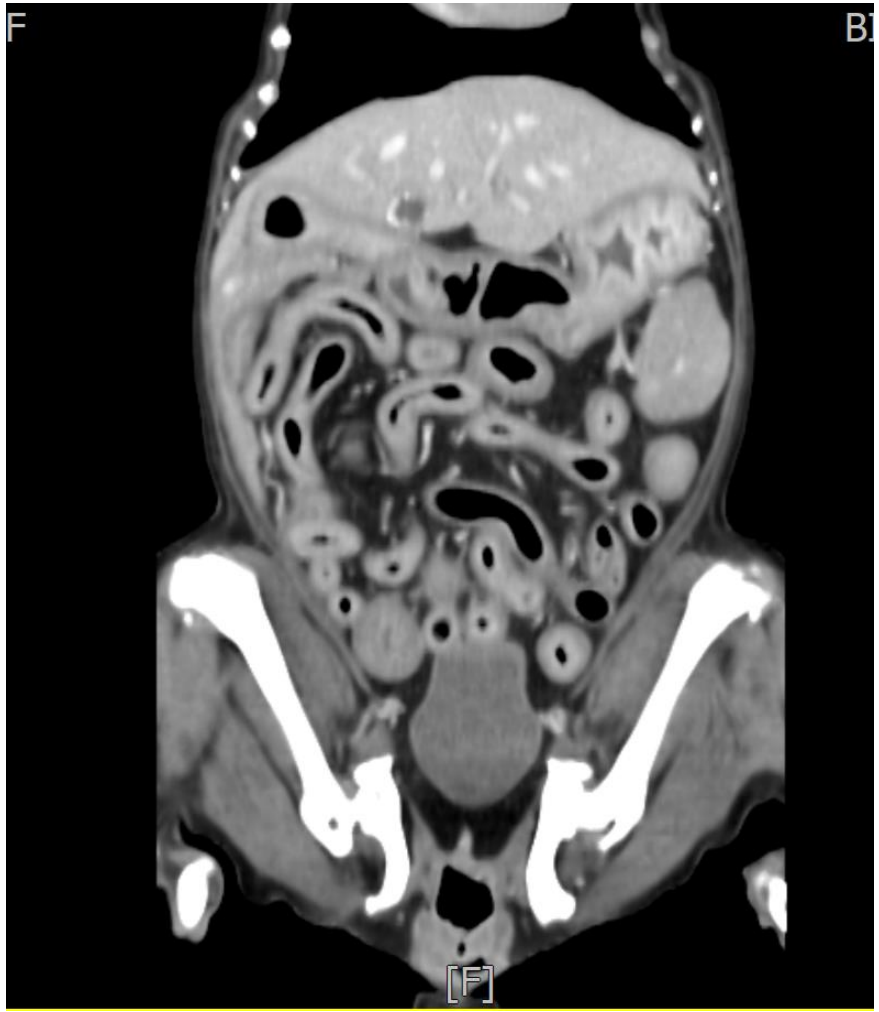
Case 3.

- 아미, 시츄, F.S, 13살2개월

- CC: 설사 및 체중감소, 식욕저하
- 타원에서 검사 치료 후 호전 없어 리퍼병원 내원

- 검사상 장종양 확인되어 CT촬영, FNA의뢰.

CT



Surgery

Pathology

COMMENTS:
Intestine (jejunum):
This is a poorly differentiated round polygonal cell neoplasm with abundant eosinophilic inflammation with differential diagnosis of a poorly differentiated mast cell tumor or lymphoma. Special stains are pending to try and further differentiate this round cell population described. The findings of the special stains and any additional comments if warranted will be reported in the final report. If the special stains fail to highlight intracytoplasmic granules then immunohistochemical markers may be warranted to try and further characterize the neoplastic round cell population and those suggestions will be given in the final report if needed.

Lymph node (jejunum):
Changes throughout the incisional sample lymph node show hyperplastic and reactive changes. There appears to be drainage numerous eosinophils likely from the mass described. If there are draining neoplastic cells is difficult to determine given the abundant inflammation and pre-existing parenchyma.

HISTOPATHOLOGIC DESCRIPTION:
Intestine (jejunum): Tissue consists of irregular sections of small intestine with marked, segmental and transmural effacement by a neoplastic round to polyhedral cell which is moderately cellular admixed with myriad eosinophils on a fine fibrovascular stroma. Cells have variably distinct cell borders, minimal eosinophilic cytoplasm and hyperchromatic irregular nuclei. Anisocytosis and anisokaryosis are moderate. Rare cells are multinucleated. The mucosal surface is ulcerated elevated with cell debris and fibrin. Intact sections of villi moderate numbers of eosinophils in lamina propria villi tips are rarely greater subjacent congestion. They are moderate to large areas of necrosis throughout the mass.

Lymph node (jejunum): Tissue consists of a representative wedge section of lymph node parenchyma with surrounding fibrocollagenous stroma and peripheral sampling of lymphoid cortex with prominent lymphoid follicles with prominent germinal centers. Medullary sinuses and subcapsular sinuses are expanded by numerous eosinophils with fewer lymphocytes plasma cells and mottled cells. Eosinophils and the minimal adjacent collagenous stroma.

SPECIAL STAIN RESULTS:

Giemsa: Negative.

INTERPRETATION:
Intestine (jejunum): Round to polyhedral cell neoplasm with severe eosinophilic inflammation (see comments)
Mitotic count: 40 per 10 400x fields
Margins: Masses on appear to extend linear surgical margins 140 mm in 120 mm away from the mass lesion. The mass extends close (less than 1 mm away) to be serosal surgical margins multifocally.
Vascular invasion: There is no definitive evidence of lymphovascular invasion in the sections of tissue reviewed histologically.

ADDITIONAL COMMENTS:

The mast cell special stain does not highlight intracytoplasmic granules throughout neoplastic cells described. This may suggest a mast cell tumor is less likely. The differential diagnoses considered following negative mast cell special stains with lymphoma. Additional study via the use of immunohistochemistry may be helpful in this case. This immunohistochemical testing is available at IDEXX for an additional charge.

Pathology

Immunohistochemistry Report

2/16/2024 8:45 AM

RESULTS:
CD3: The neoplastic cells are diffusely negative.

PAX5: The neoplastic cells are diffusely negative.

cKIT: Approximately 80% of the neoplastic cells exhibit moderate cytoplasmic immunoreactivity.

INTERPRETATION, COMMENTS:

The immunochemical staining panel supports a diagnosis of intestinal mast cell tumor. Primary intestinal mast cell tumors are commonly associated with anemia, hypoproteinemia, mastocytemia, and gastrointestinal ulceration. In a retrospective study of mast cell tumors in the GI tract of dogs, miniature breeds, especially Maltese, were most frequently affected, and the average age of affected dogs was 9.7 years. The most frequently affected sites were in the upper digestive tract, and the prognosis was very poor. According to the Veterinary Society of Surgical Oncology (VSSO), intestinal mast cell neoplasia is associated with a 100% metastatic rate, with metastatic sites including regional lymph nodes (common), liver, spleen, heart, and lungs. A median survival time of 16 days has been reported, with 100% tumor-related mortality within 2 months of diagnosis.

Reference: Mast Cell Tumors of the Gastrointestinal Tract in 39 Dogs (Vet Pathol 39:557564, 2002).

VSSO-intestinal MCT

- **Signalment**: purebred male dogs of miniature breeds
- **Clinical signs**: anorexia, lethargy, vomiting, and diarrhea
- **Hematology:** anemia, hypoproteinemia, and mastocytemia are common
- GI ulceration is a common finding
- 100% metastatic rate with metastatic sites including regional lymph nodes (common), liver, spleen, heart, and lung

- **+ CLINICAL SIGNS**
- Anorexia, weight loss, intermittent vomiting, and diarrhea
- Severe, persistent vomiting is occasionally observed if proximal small intestinal tumor causes obstruction

VSSO-intestinal MCT

- **SURGERY**
- Debilitation and hypoproteinemia may complicate treatment
- Exploratory celiotomy with resection and end-to-end anastomosis with 4-8 cm margins and serosal patching
- Mesenteric and regional lymph nodes should be assessed ± aspirated

- **+ CHEMOTHERAPY**
- Chemotherapy is recommended for intestinal MCT

- **+ PROGNOSIS**
- MST 16 days with 100% tumor-related mortality within 2 months of diagnosis
- 100% metastatic rate

Chemotherapy

- Tyrosine kinase inhibitor: toceranib
- Vinblastine
- CCNU

Prognosis

- POD-3 month: intestinal MCT recurrence susp.

- Rx)
- Toceranib 2.5mg/kg EOD
- +metro 10mg/kg BID
- Ome 0.5mg/kg BID
- Meto 0.3mg/kg BID
- Almagate 1ml/kg BID

Prognosis

- POD-7 month 항암중단
- POD-8 month 아이 사망

감사합니다

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