A microscopic image of lung tissue stained with hematoxylin and eosin (H&E). The image shows alveolar spaces filled with red-stained erythrocytes, indicating pulmonary hemorrhage. The surrounding lung parenchyma is pink, and the nuclei of various cells are stained blue.

Sudden unexpected natural death of three dogs with pulmonary hemorrhage

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COI

We have no personal or financial interests to declare.

We have no financial support from an industry source at the current presentation.

Background

Pulmonary hemorrhage (PH)

■ Causes

Hemorrhagic diathesis (thrombocytopenia, rodenticide, etc.)

Septicemia

DIC

Severe congestion

Pulmonary hypertension

Trauma

Neoplasm (e.g. hemangiosarcoma) etc.

Objective

- Cause of death
- Cause of PH
- Clarify relationship between these

Methods

- 3 dogs with PH
- Full autopsy and histopathology (including CNS)
- Histochemistry (Gram, PAS, PTAH)
- Bacterial culture (tissue swab)
- Broad-range PCR for bacteria and fungi on FFPE specimens

① "Donald"
(Pomeranian)



② "Bingo"
(Toy Poodle)



③ "Dress"
(Yorkshire Terrier)



Results

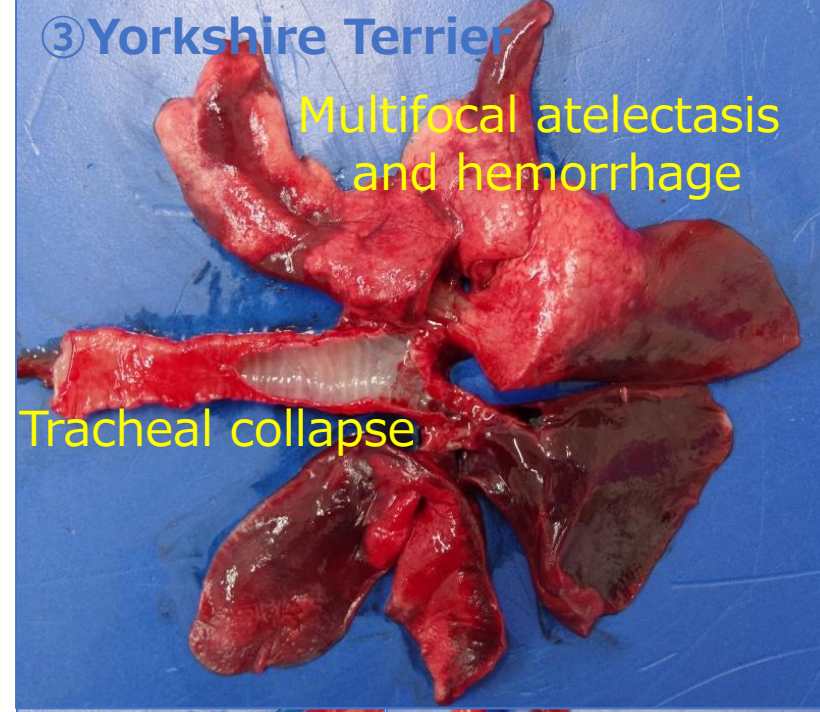
Signalment and clinical information

Case #	①	②	③
Breed	Pomeranian	Toy Poodle	Yorkshire Terrier
Age	2m 3w	6y 5m	12y 4m
Sex	Intact male	Castrated male	Spayed female
Vaccination	Unknown	Once a year, combined vaccine	Last shot >4 yrs ago, type unknown
Household had	5 other dogs	Only this dog	Only this dog
BW and BCS	760g, 2.5~3/5	2.7kg, 3/5	1.25kg, 3/5
History	<ul style="list-style-type: none"> <input type="checkbox"/> Soft stool <input type="checkbox"/> Anorexia and lethargy <input type="checkbox"/> Coccidial oocysts in feces <input type="checkbox"/> Parvovirus (-) <input type="checkbox"/> BUN slightly ↑ 	<ul style="list-style-type: none"> <input type="checkbox"/> Hct 60-65% <input type="checkbox"/> Being dull recently <input type="checkbox"/> Lost 1 kg in past 1 year on low-fat diet 	<ul style="list-style-type: none"> <input type="checkbox"/> Tracheal collapse <input type="checkbox"/> IMHA (3y 3m ago) <input type="checkbox"/> Pyometra (2y 8m ago) <input type="checkbox"/> Suspected hepatitis with icterus (8 m ago) <input type="checkbox"/> Suspected rheumatoid arthritis (4m ago)



Main gross findings

HW and HW/BW ratio (avg. 0.71%)



7 grams, 0.9%

30 grams, 1.1%



15 grams, 1.2%



Main histopathologic findings

① Pomeranian

② Toy Poodle

③ Yorkshire Terrier

Adventitial hemorrhage
w/o medial thickening

Adventitial hemorrhage
w/o medial thickening

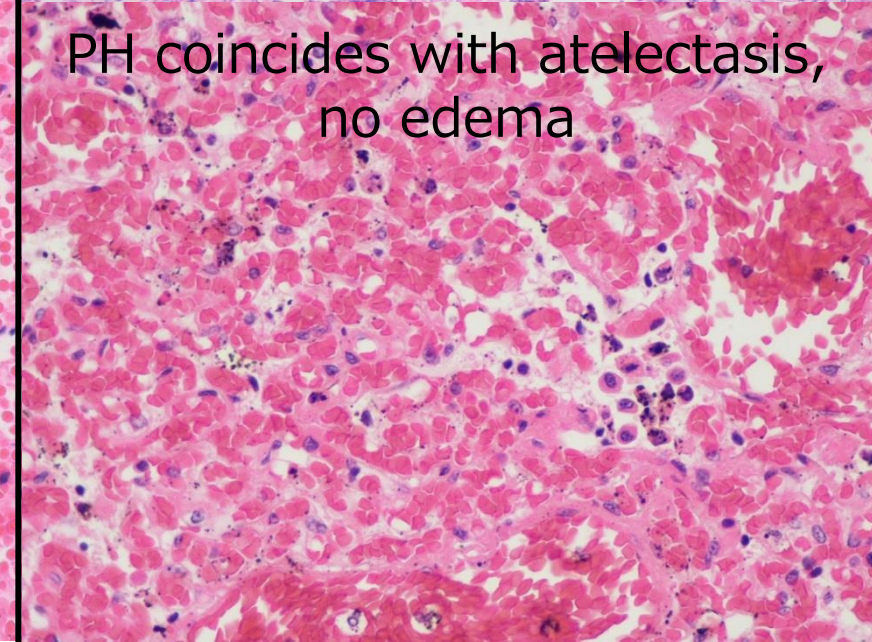
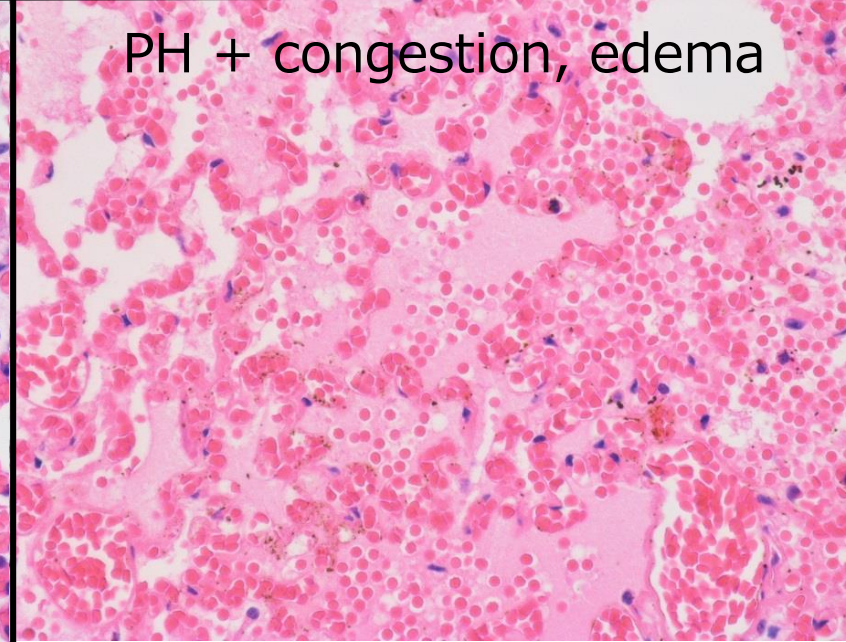
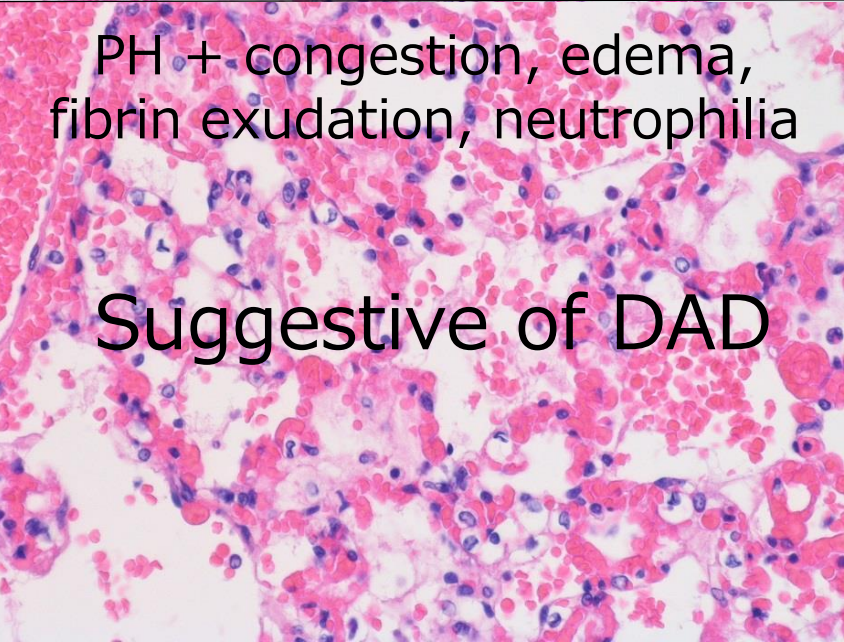
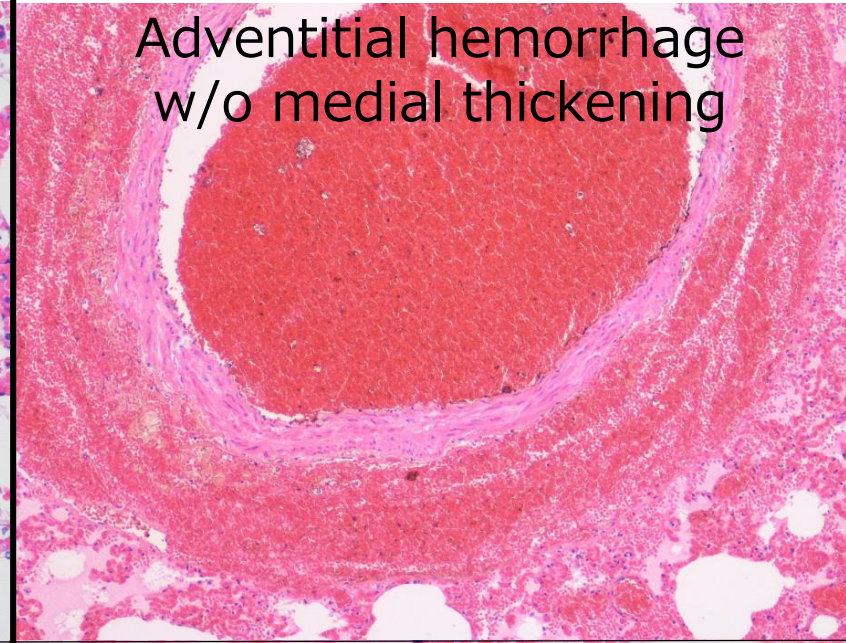
No perivascular lesions

PH + congestion, edema,
fibrin exudation, neutrophilia

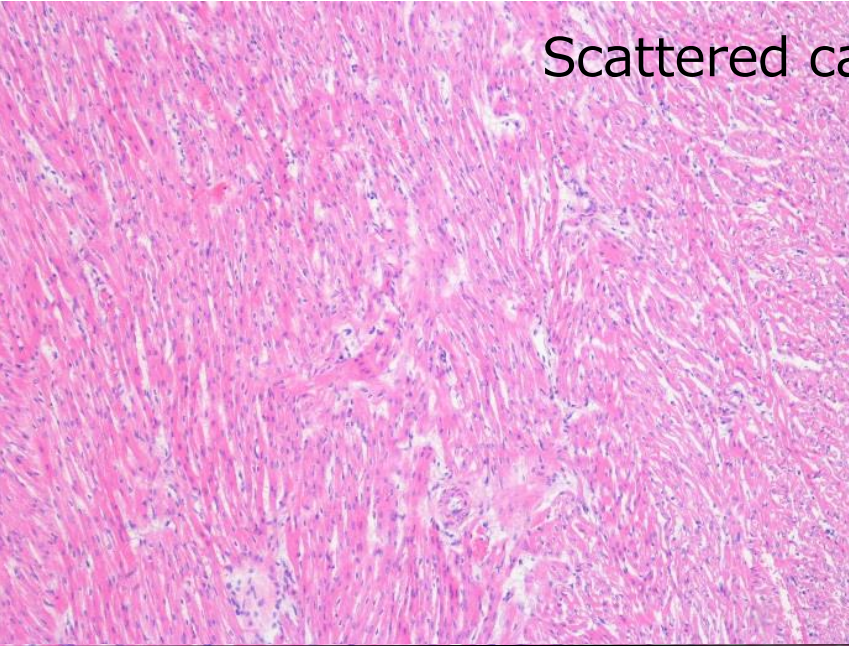
PH + congestion, edema

PH coincides with atelectasis,
no edema

Suggestive of DAD

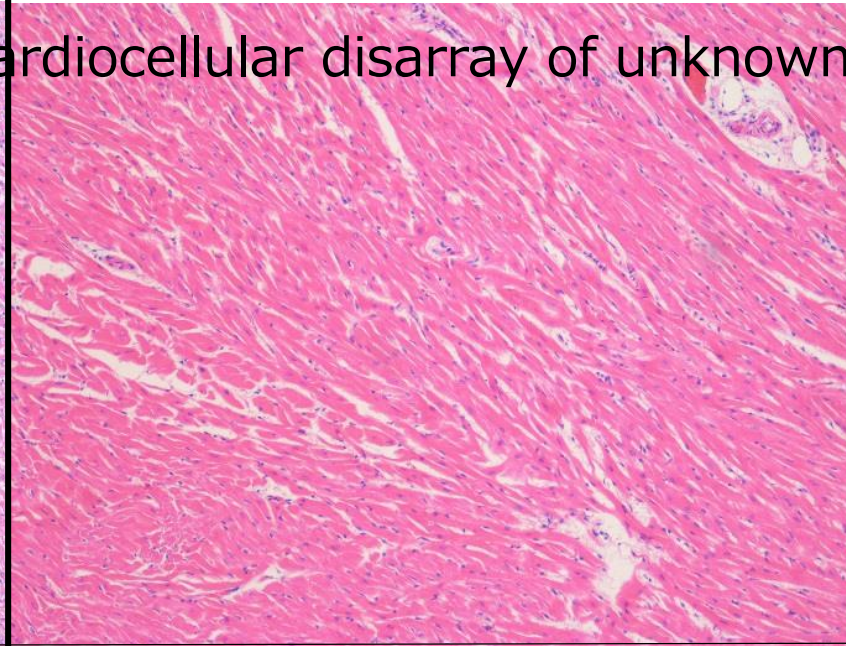


① Pomeranian



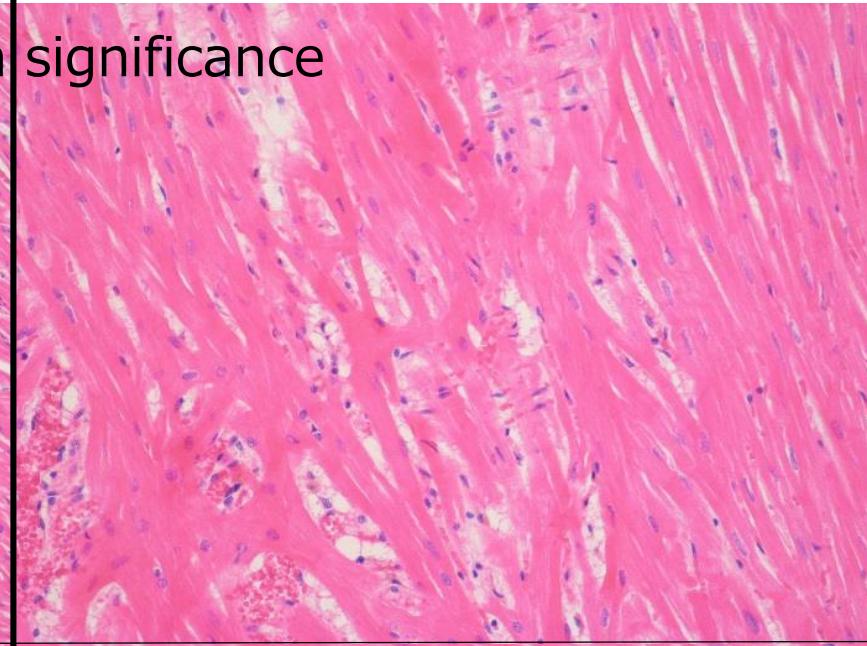
Scattered cardiocellular disarray of unknown significance

② Toy Poodle

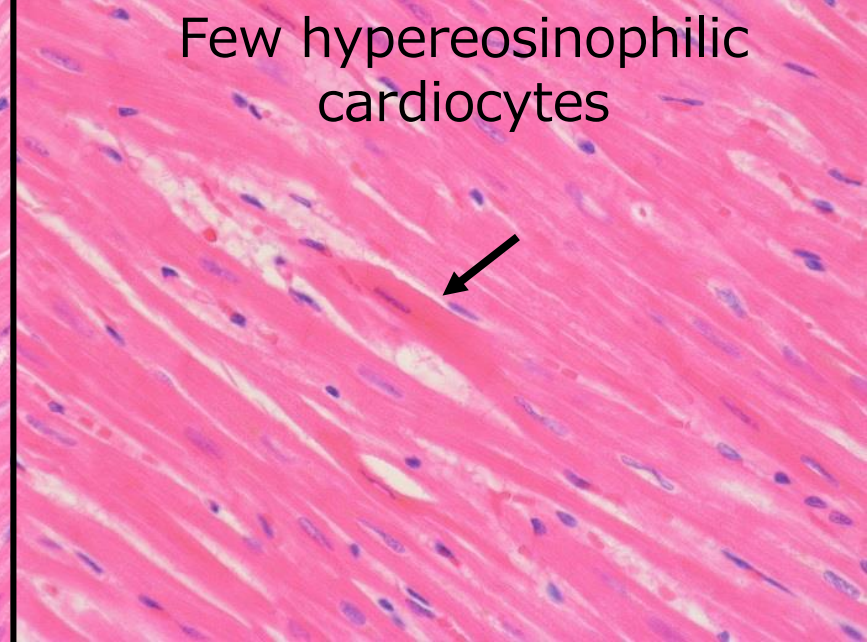
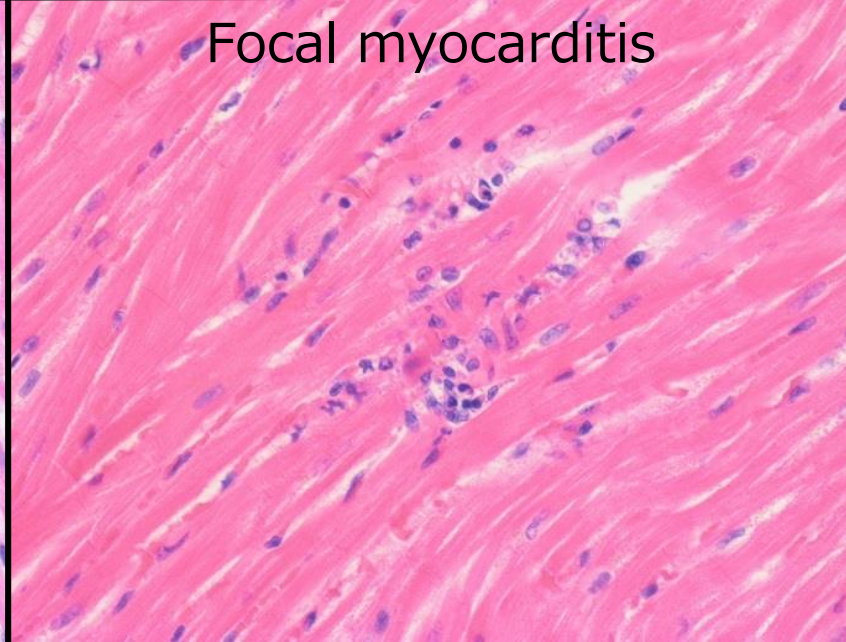
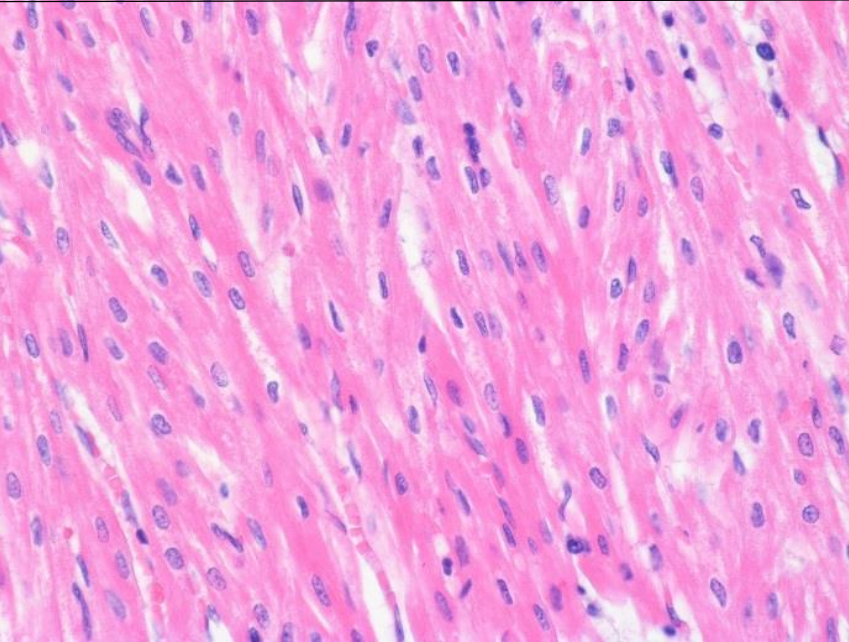


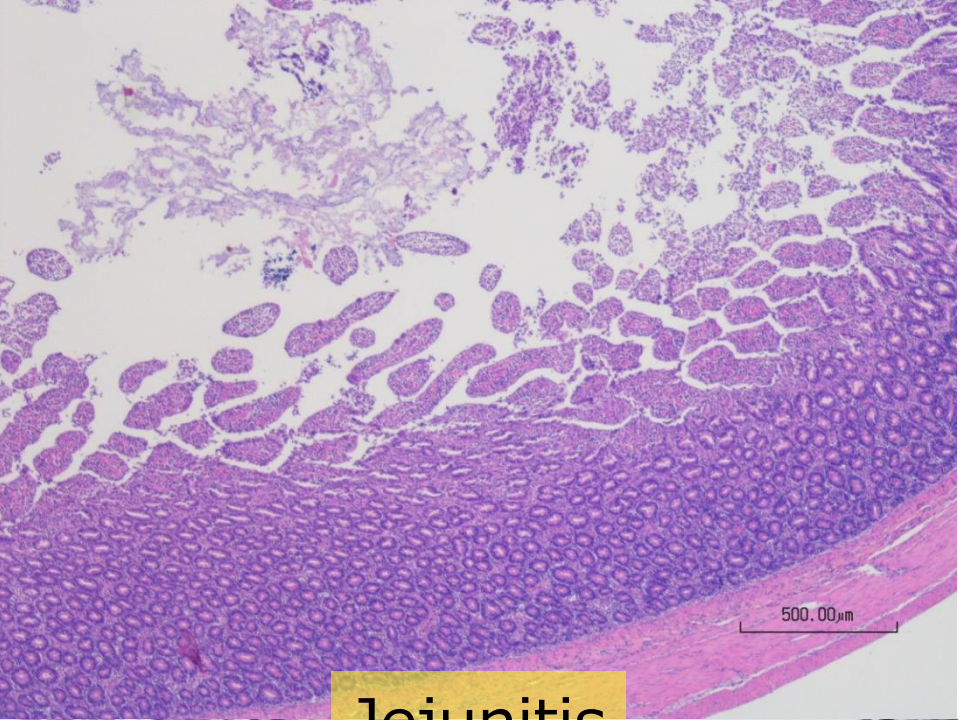
Focal myocarditis

③ Yorkshire Terrier

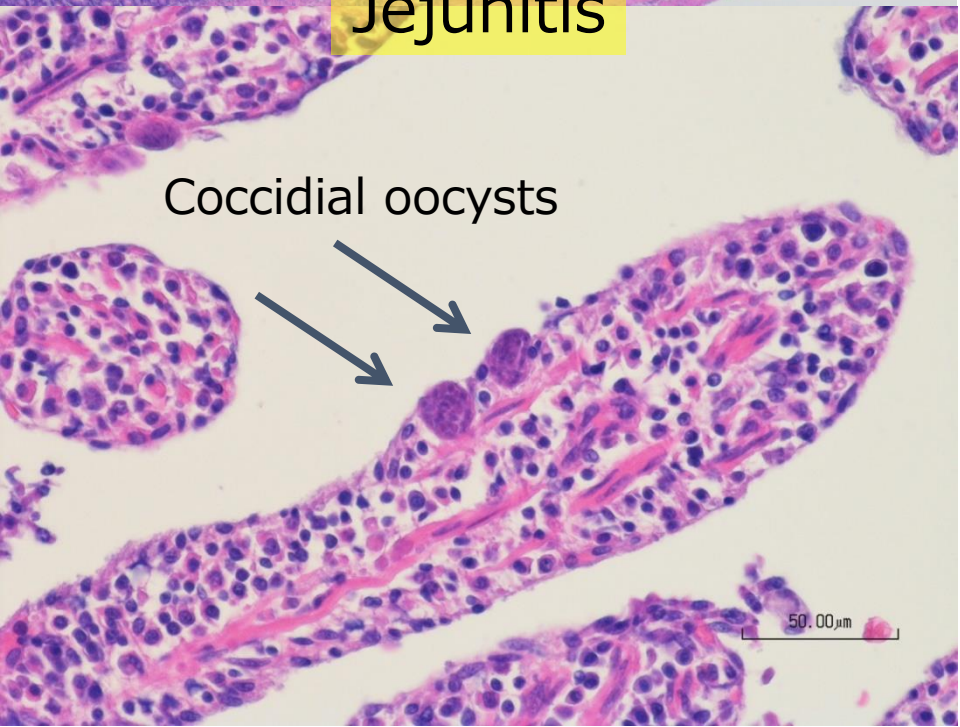


Few hyper-eosinophilic cardiocytes





Jejunitis

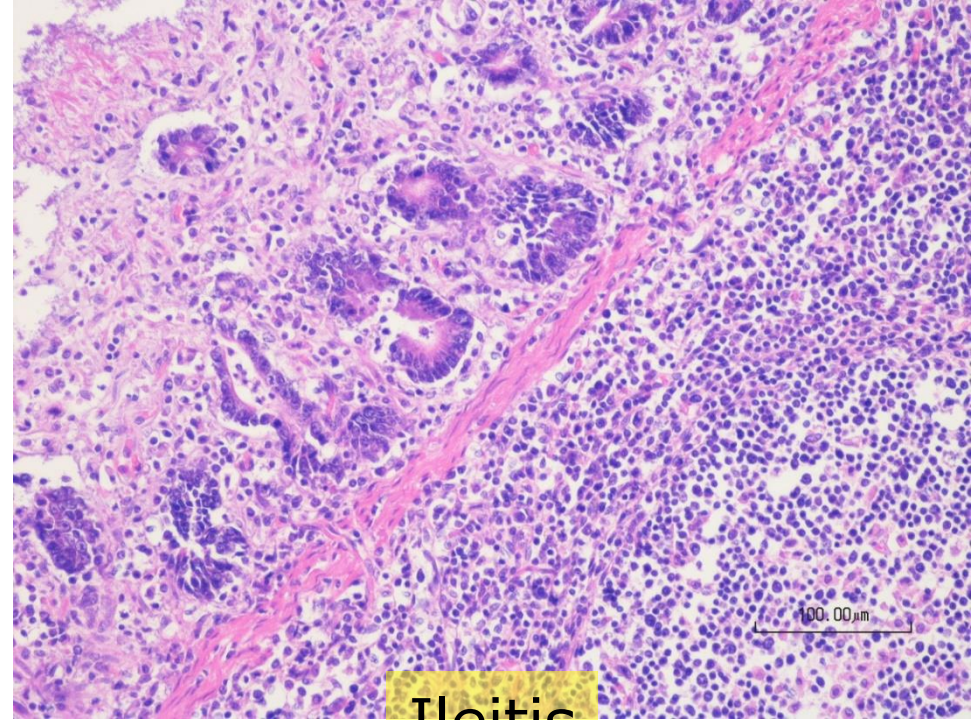


Coccidial oocysts

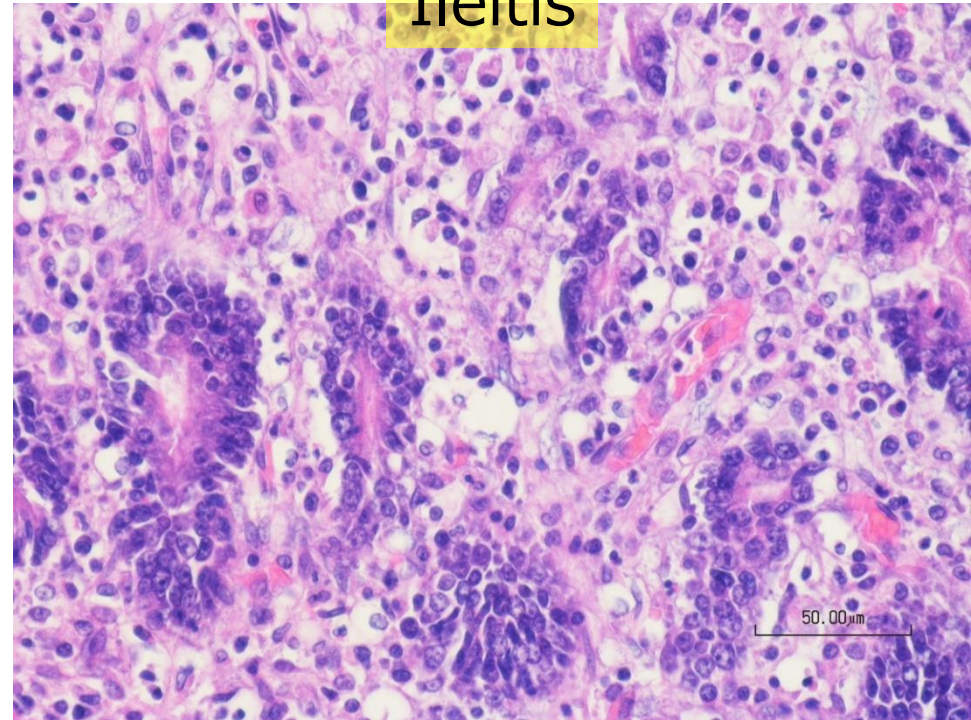
① Pomeranian

Mild coccidial jejunitis

Superficial necrotizing ileitis
(entry locus for bacterial translocation?)

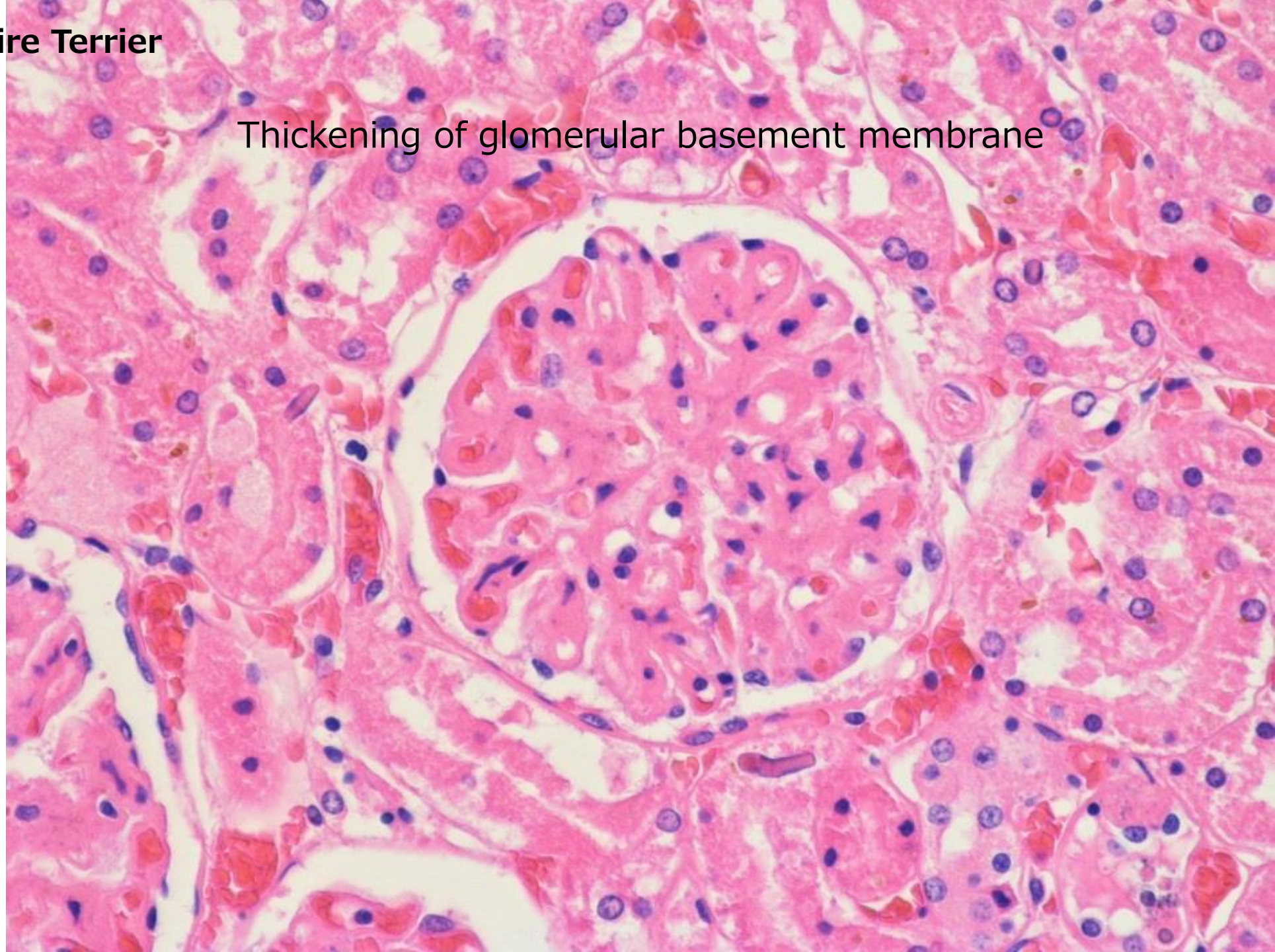


Ileitis



③ Yorkshire Terrier

Thickening of glomerular basement membrane



Results of ancillary tests

	①Pomeranian	②Toy Poodle	③Yorkshire Terrier
Bacterial culture	<ul style="list-style-type: none"> ❑ Lung: (–) 	<ul style="list-style-type: none"> ❑ Lung : <i>P. multocida</i> ❑ Trachea : (–) 	<ul style="list-style-type: none"> ❑ Lung : <i>Proteus mirabilis</i>, MRSA ❑ Liver : <i>Enterobacter sp</i>, <i>Enterococcus faecium</i>
Special stain of lung	<ul style="list-style-type: none"> ❑ Gram, PAS : no infectious organisms ❑ PTAH : no fibrin thrombi 		
16S rRNA broad-range PCR of lung	<ul style="list-style-type: none"> ❑ Bacterium: (–) ❑ Fungus: positive but identification failed possibly due to overlap of multiple species 		

Cause of death, pulmonary hemorrhage, and their relationship

	①Pomeranian	②Toy Poodle	③Yorkshire Terrier
Suspected (immediate) cause of death	Diffuse alveolar damage	Acute pulmonary edema	Tracheal collapse
	Acute respiratory failure		
Suspected cause of PH	Septicemia (bacterial translocation)	Sudden arrhythmia (surge of left ventricular preload)	Tracheal collapse (shear stress btw apposing alveolar epithelia)
Relationship between death and PH	Likely	Likely	Unlikely (PH too mild)

Discussion (1/2)

Leptospiral pulmonary hemorrhagic syndrome

- ❑ Well recognized in human medicine but pathogenesis elusive
- ❑ Proposed mechanism: vascular damage by leptospiral toxin, immunologic mechanisms, or DIC
- ❑ 15 dogs with severe acute pulmonary hemorrhage
- ❑ PCR detected *Leptospira*-specific gene in 3 dogs
- ❑ Pathogenesis of severe pulmonary hemorrhage still unknown

Case Report

Veterinary Medicine International, volume 2010, article ID 928541.

An Emerging Pulmonary Haemorrhagic Syndrome in Dogs: Similar to the Human Leptospiral Pulmonary Haemorrhagic Syndrome?

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A. Mayer-Scholl,³ and A. D. Gruber¹

Discussion (2/2)

Diffuse pulmonary hemorrhagic syndrome of human

◆ Goodpasture syndrome

- Autoantibodies against noncollagenous domain of the $\alpha 3$ chain of collagen IV
- Glomerulonephritis
- 40-60% patients develop necrotizing hemorrhagic interstitial pneumonitis

◆ Idiopathic pulmonary hemosiderosis

- Pathogenesis unknown
- Some patients develop other immune disorders

◆ Polyangitis with granulomatosis (formerly Wegener granulomatosis)

- Necrotizing or granulomatous vasculitis affecting small- to medium-sized vessels
- T-cell-mediated hypersensitivity response
- Anti-proteinase-3 antineutrophil cytoplasmic antibodies (PR3-ANCA) elevate

Conclusions

- ❑ Etiology of canine PH is diverse and its determination requires laborious laboratory work.
- ❑ Causation between PH and other organ's abnormality should be carefully sought for possible discovery of novel animal syndrome.

Limitations

- ❑ Lack of
 - Perimortem clinical data
 - Glomerular EM and special stains
 - Endotoxin or cytokine detection to prove septicemia
 - Exam of cardiac conduction system

References

- ❑ An emerging pulmonary haemorrhagic syndrome in dogs: similar to the human leptospiral pulmonary haemorrhagic syndrome? R. Klopfleisch et al., *Veterinary Medicine International*, volume 2010, article ID 928541.
- ❑ Robbins and Contran Pathologic basis of disease, 9th ed., V. Kumar et al. eds., p.701-702, 2015, Elsevier.
- ❑ Pathology of domestic animals, 6th ed., M.G. Maxie et al. eds., 2015, Elsevier. (pulmonary hemorrhage; Vol.2, p.490-491: heart weight/body weight ratio; Vol.3, p.13)

Acknowledgements

□ **All animal owners and referring veterinarians**

□ **Dr. Kaoru Kai** (tissue trimming)

□ **Fujifilm Monolith Co., Ltd.** (HE slide preparation, bacterial culture)

□ **Shikoku Cytopathological Laboratory Co., Ltd.** (histochemistry)

□ **Kaho Techno Co., Ltd.** (PCR testing)

Any questions?

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食品サンプル iPhone ケース!