

Case Report / Olgu Sunumu

Pulmonary Veno-Occlusive Disease in a Cat with Lymphoma

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Abstract: Pulmonary veno-occlusive disease (PVOD) is an uncommon disease in humans and animals caused by pulmonary hypertension (PH). The aim of this study was to investigate pathomorphological findings of PVOD in a cat. A mass was detected in the right atrium with echocardiography in an 11-year-old male cat. Following treatments, necropsy of the cat was performed after death due to respiratory failure. Macroscopically, masses were detected in mesenteric lymph node, mediastinal lymph node and, heart. Congestion and consolidated areas with edema were seen in the examination of the lung. Histopathologically, neoplastic lymphoid cells were observed in intestine, lymph nodes and heart. In lung, vein lumens were almost completely occluded by mostly loose intimal fibrosis. Near affected veins, increasing in number of the capillaries was observed. While intimal fibrosis was detected by Masson's trichrome staining, the occluded veins were demonstrated by Verhoeff-van Gieson staining. In this case report, pathomorphological evaluation of PVOD was performed and as a result of clinicopathological examinations; PVOD, intestinal lymphoma, and cardiac metastasis were described in a male cat.

Keywords: Cardiac, histopathology, intestinal, lymphoma, Pulmonary Veno-Occlusive Disease.

Lenfomalı Bir Kedide Pulmoner Veno-Oklüzif Hastalık

Özet: Pulmoner Veno-Oklüzif Hastalık (PVOH) pulmoner hipertansiyonun (PH) neden olduğu, insanlarda ve hayvanlarda nadir görülen bir hastalıktır. Bu olgu ile bir kedide gözlenen Pulmoner Veno-Oklüzif Hastalık'ın patomorfolojik yönden incelenmesi amaçlanmıştır. 11 yaşlı erkek kedinin ekokardiyografisinde sağ atriumda kitle gözlemlendi. Tedavilerin ardından solunum güçlüğüne bağlı ölen kedinin nekropsisi yapıldı. Makroskopik olarak, mezenteriyal ve mediastinal lenf yumrularında ve kalpte kitleler ile karşılaşıldı. Akciğer muayenesinde ödem ve konjesyon ile konsolide alanlar görüldü. Histopatolojik olarak bağırsak, lenf yumruları ve kalpte neoplastik lenfoid hücreler gözlemlendi. Akciğerde şiddetli intimal fibrozise bağlı venlerin lümenlerinde daralma ve tıkanmalar dikkati çekti. Etkilenen çoğu damarların çevresinde kapillarizasyon gözlemlendi. Masson trikrom boyamasıyla intimal fibrozis tespit edilirken, tıkalı damarlar Verhoeff-van Gieson boyamasıyla gösterildi. Bu olguda bir kedide PVOH patomorfolojik yönden değerlendirilmiş ve klinikopatolojik incelemeler sonucunda erkek bir kedide PVOH, intestinal lenfoma ve kardiyak metastazi tanımlanmıştır.

Anahtar sözcükler: Bağırsak, histopatoloji, kardiyak, lenfoma, Pulmoner Veno-Oklüzif Hastalık.

Pulmonary veno-occlusive disease (PVOD) is a rare pathological change seen in both humans and animals. Pulmonary veno-occlusive disease occurs as a severe and uncommon variant of pulmonary hypertension (PH) which remains a miscellaneous problem (8, 13, 18). According to the World Health Organization (WHO), PH is generally classified by the underlying cause: pulmonary arterial hypertension (PAH), Left Heart Disease, chronic obstructive pulmonary disease, chronic pulmonary thromboembolic disease, and unclear multifactorial mechanisms (11). In veterinary medicine, as well as the

poor understanding of the determination and causes of PH; PVOD has been reported only once in dogs (18). A definite diagnosis of PVOD requires pathologic examination of lungs. And, the significant finding of PVOD is occlusion of pulmonary veins by fibrous tissue. Also, alveolar capillary congestion and capillary proliferation are observed (6, 10, 16).

Lymphoma is one of the neoplasms that occur frequently in domestic animals, especially in cats. Lymphomas have usually malignant character and consist of lymphocytes or lymphoid cells. They can be classified

grossly according to anatomical distribution such as multicentric, alimentary, mediastinal, miscellaneous. Besides being the most encountered tumor in cats, alimentary/intestinal lymphoma is more common than other anatomical forms (12, 15, 17). While no cause can be determined for most intestinal lymphomas, the indirect role of Feline immunodeficiency virus (FIV) on lymphomagenesis and the direct role of Feline leukemia virus (FeLV) as an oncogenic retrovirus are known to be effective in the etiology of intestinal lymphomas in cats (9, 15).

The objective of this case was to evaluate clinicopathological of Pulmonary veno-occlusive disease detailed first time in a cat with metastatic intestinal lymphoma. So, owing to the pathomorphological examination, a relationship was established between the mentioned diseases.

An 11-year-old, 5,6 kg, neutered male cat living indoors was presented to the emergency room with a 3 day history of escalated respiratory distress, dyspnea following 20 days of anorexia. All of the mucous membranes were pale to cyanotic. During the clinical examination, the cat

was found to be dyspneic and mildly dehydrated. Thoracic auscultation revealed no breath sounds from left part of the thorax.

Initial diagnosis was made with a complete blood count and biochemical profile (Erba XL-600, ERBA Diagnostics Mannheim, MA, USA), and thoracic radiographs. The blood panel showed some abnormalities including a leukocytosis of $22,2 \times 10^9$ cells/l (reference interval [RI] 5,5–19,5) elevated alanine aminotransferase (230,3 IU/l; RI 6–83), elevated aspartate aminotransferase (156,8 IU/l; RI 26–43), elevated creatinine kinase (703,3 IU/l; RI 56–130), uremia (155,6 mg/dl; RI 15–64,2), elevated creatinine (5,23 mg/dl; RI 0,8-1,8).

Severe pleural effusion was prominent in the thoracic radiographs. At this stage, an echocardiography (Hitachi ARIETTA 60 OH, USA) was performed, which revealed the presence of a large pericardial effusion, both anterior and posterior to the heart. Also a mass which was suspected to be a tumor or a thrombus was detected in the right atrium (Figure 1-a). 250 ml of serosanguinous fluid was yielded with ultrasound-guided thoracosynthesis.

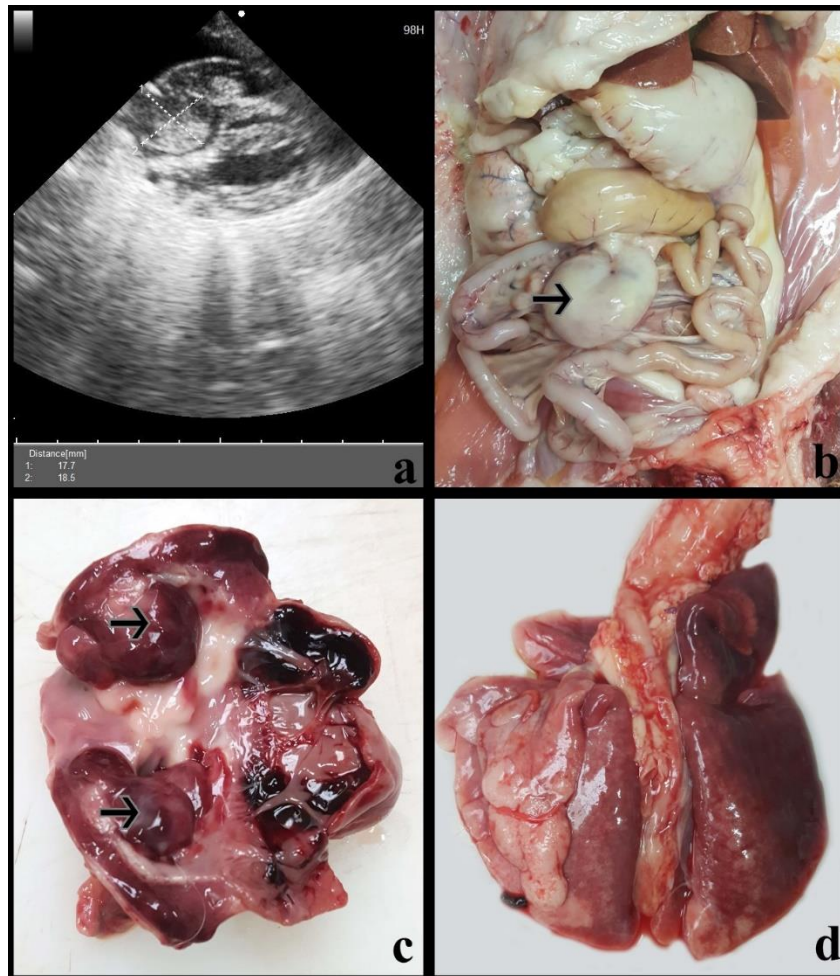


Figure 1. Echocardiogram and macroscopic findings, cat.

a. Mass in right atrium on echocardiogram. **b.** Mesenteric lymph node near caecum (arrow). **c.** Reddish mass in right atrium (arrows). **d.** Pale-coloured on the lung parietal surface.

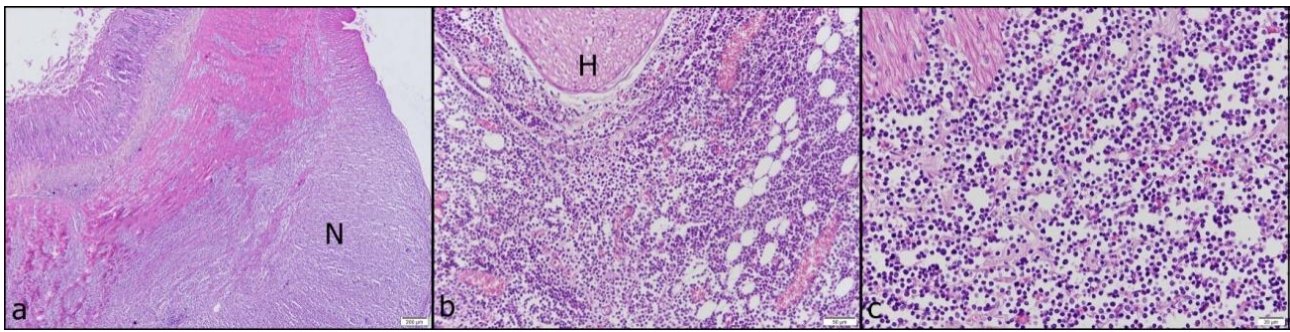


Figure 2. Microscopic findings, cat.

a. Appearance of lymphoma (N) in intestine. HE. **b.** The neoplastic cells (N) extended to His bundle (H) in heart, HE. **c.** General appearance of neoplastic cells at high magnification in heart, HE.

Furosemide 2 mg/kg IV was administered first. This was repeated 3 hours later at 3 mg/kg, and no changes were observed in the respiratory rate. Additionally, the cat was started on crystalloid fluids at 15 ml/kg/h, ampicillin sulbactam 25 mg/kg q12h IV and enalapril 1,25 mg PO. After 15 days, marked abdominal respiration, respiratory distress, lethargy and loss of appetite signs appeared again. 250 mL of fluid was removed by thoracosynthesis and pericardiosynthesis and then inspiration relaxed. After 8 days, because of severe excessive respiratory distress and heart failure, the patient died.

The necropsy was performed in Department of Pathology. Sections from lesions of organs were fixed in 10% neutral buffered formalin and routinely processed. Formalin-fixed, paraffin-embedded tissues were sectioned at 4-6 μ m, and stained with haematoxylin and eosin (HE), Masson's trichrome staining, and Verhoeff van Gieson (VVG). The stainings were performed according to routine process (5).

Macroscopically, mesenteric lymph node near caecum appeared to be a huge mass with 8x3x3 cm diameter (Figure 1-b). The cut surface was necrotic. Other mesenteric lymph nodes were also increased in volume. When the chest cavity was opened, a huge mediastinal lymph node was noticed. While examining the heart, the right atrium was prominently enlarged. On the cross-section, a mass, attached from pericardium to myocardium, was seen. The mass was approximately 1 cm diameter and had reddish color and elastic consistency (Figure 1-c). In lung examination, consolidated areas with edema and congestion were seen (Figure 1-d).

Microscopically, in the mesenteric and mediastinal lymph nodes, follicular architecture was replaced by a population of uniformly lymphoid cells which were round to oval in shape. They generally had narrow cytoplasm and hyperchromatic nuclei. Not only the mesenteric lymph nodes but also the aggregate lymph follicles in intestines had malignant features (Figure 2-a). They were diagnosed

as malignant lymphoma. Additionally, the centrum of the mesenteric lymph node was severely necrotic and had neutrophil leukocyte infiltration and pyknotic cells. Also, the mass in the heart showed neoplastic lymphocytic cells. These cells extended from the pericardium to the myocardium, even to the His bundles (Figure 2-b), had round to ovoid shape with generally hyperchromatic nucleus with narrow cytoplasm (Figure 2c).

In lung, vein lumens were almost completely occluded by mostly loose intimal fibrosis (Figure 3-a, b). This part of the vein is stained green/blue color with Masson's trichrome staining (Figure 3-c). With Verhoeff-van Gieson staining, in veins, single elastic lamina scattered due to fibrosis, was detected (Figure 3-d). Near affected veins, increasing in number of the capillaries was recognized. Severe edema and emphysema were seen. Also, alveolar macrophages in bronchial lumen, neutrophil leukocytes in vessel lumen were detected. In liver, severe fatty degeneration was observed.

Pulmonary veno-occlusive disease (PVOD) is one of a clinicopathological findings which is rarely seen. It was first described in 1934 by Dr. J. Hora in a 48-year-old man and until today, lots of cases were reported in human medicine about PVOD (2). According to literatures, even though some factors has been considered as possible causes like genetic factors, toxic causes, autoimmune disorders, lung diseases and heart failures; the exact cause is still unknown. But, it is acceptable as a variant of PH (7, 8). PVOD was also reported in a few dogs with hypertension (18). And, it is a known fact that prevalence of hypertension and heart failure are higher in dogs than cats (14). In the present case, PVOD was seen in a cat. The PVOD phenomenon was also reported in a Persian cat, and although that case was associated with cardiomyopathy, the main reason also remained confidential (3). In the presented case, the cause of heart failure that indirectly leads to PVOD was a cardiac metastasis of alimentary lymphoma.

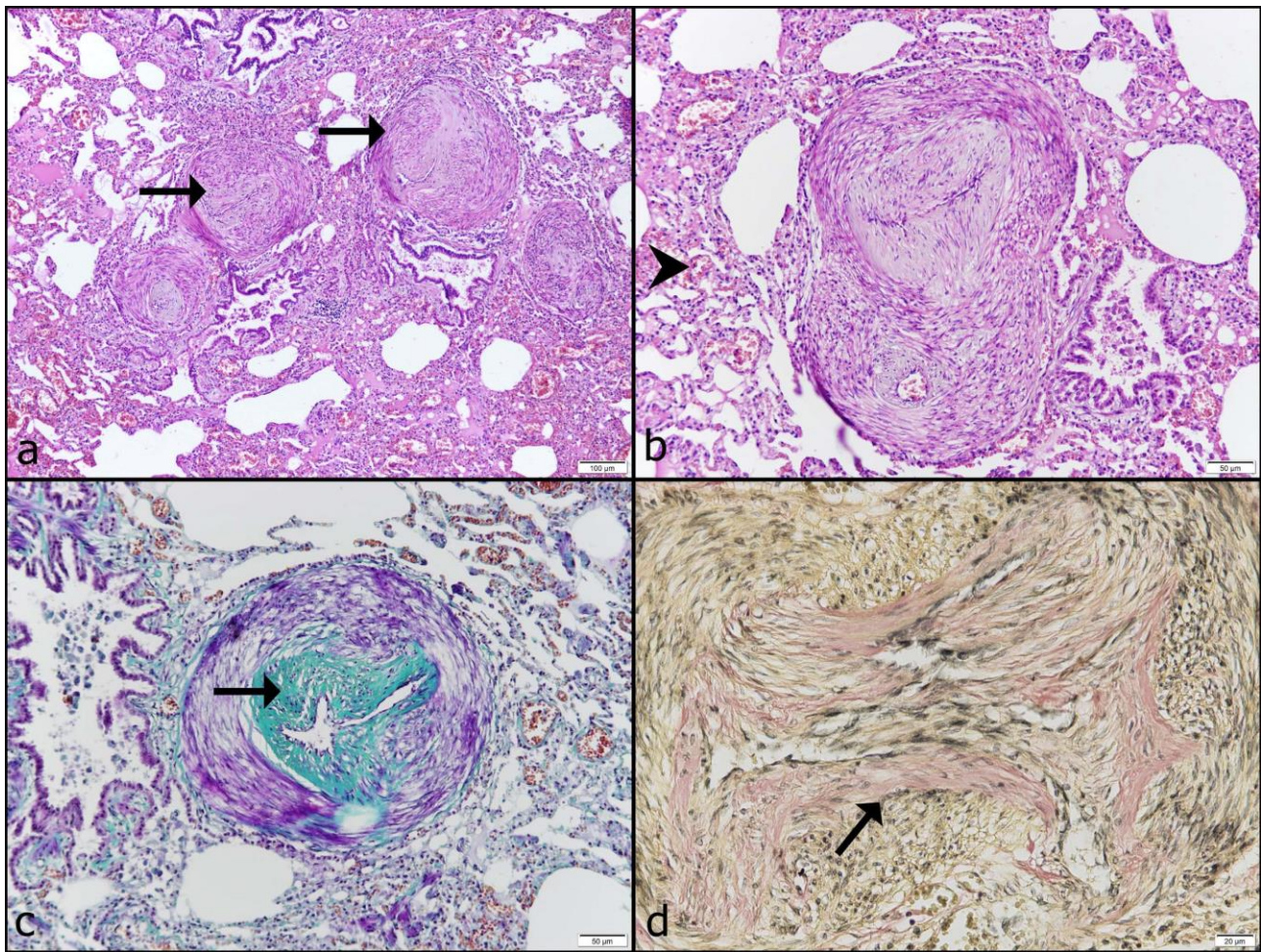


Figure 3. Microscopic findings, cat.

a. Occluded veins in lung (arrows), HE. **b.** Occluded vein lumens (arrows) and alveolar capillary congestion (arrow head), HE. **c.** Occluded vein lumens by intimal fibrosis (arrow) in lung, Masson's trichrome staining. **d.** Scattered single elastic lamina (arrow) due to fibrosis in lung, Verhoeff-van Gieson staining.

In patients with PVOD, serum aspartate aminotransferase and alanine aminotransferase levels usually are within normal range (4). These values, which were high in this study, were attributed to liver fat, which was also observed histopathologically. But, presence of dyspnea and cyanosis were characteristic clinical signs of severe pulmonary disease including PVOD (18).

For a diagnosis of PVOD, histopathological examination is essential. As in human and canine PVOD, in the present case, occluded pulmonary vein lumens, capillarization and edema were evident (12, 18). Similar to the argument presented by Williams et al. (18), in the current case Verhoeff-van Gieson staining was used to distinguish veins from arteries. The occluded veins with a single elastic lamina were shown with this staining. Besides this, intimal fibrosis was detected by Masson's trichrome staining with green color of fibrous tissue.

Another thing that makes the case special is the occurrence of heart failure due to cardiac metastasis of alimentary lymphoma. Cardiac masses arising from the

heart generally have poor prognosis whether diagnosed as benign or malignant. Lymphoma has been observed in the heart of cats. According to a study conducted by Aupperle et al. (1), two cases of five secondary cardiac tumors were malignant lymphoma and, regardless from the type of tumor, depending on their anatomical location in heart, cardiac tumors can result in congestive heart failure as in the presented case.

In summary, pulmonary veno-occlusive disease, which is mostly seen in both humans and dogs, was reported for the first time in a cat with lymphoma. However, details of the development mechanism keep it uncertain, in present case; it was thought that the mass indirectly led to heart failure and PVOD formation in the lung.

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Ethical Statement

This study does not present any ethical concerns.

Conflict of Interest

The authors declared that there is no conflict of interest.

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