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Generalized Intravascular Proliferation in Two Cats: Endotheliosis or Intravascular Pseudoangiosarcoma?

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Summary

Two cats had unusual occlusive vascular endothelial proliferations in several organs. The newly formed cells were strictly intraluminal and of endothelial origin, as shown by positive immunohistochemical staining with factor VIII-related antigen.

Unusual vascular proliferative lesions were seen in two cats necropsied within a 6-week period. The affected animals had been submitted from different parts of Switzerland and had had no contact.

Case 1. This male, 9-month-old Maine Coone cat had several attacks of diarrhoea and vomiting. It was killed humanely after painful oedema of the cornea and loss of pupillary reflexes had developed. At necropsy there were signs of cardiac insufficiency: hydrothorax, hydropericardium, dilatation of the atrium and ventricle of the right heart with a white infarct (1.5 cm diameter) in the apex of the heart and lung oedema (perhaps enhanced by death). In addition the cat was anaemic and there were haemorrhages in the anterior chambers of the eyes. Other organ systems were macroscopically normal.

Case 2 was a male, 2-year-old domestic short-haired cat, presenting with vomiting, dilatation of the pupils, haematuria and anaemia 2 days before death. The clinician’s tentative diagnosis was “plant poisoning”. Necropsy revealed only petechiae in the mucous membranes of the urinary bladder, blood coagula of unknown origin on the liver surface and extensive lung oedema with emphysema of the lung margins.

Histological examination of the organs of both cats revealed identical unusual vascular lesions in several organs (Table 1). Proliferations of cells of endothelial type filled the lumina of small arteries and veins, forming cords. Other vessels contained glomerulus-like whorls with small capillary spaces (Fig. 1). The newly formed cells were strictly intraluminal and always in contact with the endothelium. Their nuclei were dark, elongated, and of irregular shape; the nuclear-cytoplasmic ratio was normal, but mitosis was more frequent than usual. There were some bizarre mitotic figures.

To identify further the proliferating cells, immunohistochemical examination for factor VIII-related antigen was carried out. After digestion of the tissue sections for 5 min with 0.1 per cent Pronase, a rabbit anti-human factor VIII-related antigen (Dako A/S Denmark) was used in a dilution of 1 in 100,
### Table 1
Generalized intravascular proliferation in three male cats

| Case                                      | Age (years) | Sites showing intravascular proliferation                                                                 | Further investigations                        |
|-------------------------------------------|-------------|----------------------------------------------------------------------------------------------------------|-----------------------------------------------|
| 1 (this paper)                            | 0-75        | Intestine, lymph nodes, spleen, brain, eye, pancreas, myocardium                                         | Negative for FIP, FIV, FeLV                    |
| 2 (this paper)                            | 2           | Intestine, lymph nodes, spleen, kidney, bone marrow                                                     | Liver, spleen and kidney bacteriologically negative |
| Described by Rothwell et al. (1985)       | 6           | Intestine, lymph nodes, meninges, kidney, eye, pancreas, myocardium, adrenal, thyroid, liver             | Electron microscopy revealed cells to be endothelial and pericyte-like |

Fig. 1. Arteriole with glomerulus-like whorl in myocardium. Haematoxylin and eosin. × 440.

followed by the routine procedure of the rabbit anti-human Dako PAP Kit™. Factor VIII-related antigen is an established cell marker for endothelial cells in human and animal tissues (von Beust et al., 1988). Staining for factor VIII-
related antigen was positive in about 50 per cent of the intraluminal cells, evidence that these proliferations were indeed of endothelial origin. Many of the affected vessels contained fibrinoid thrombi, but there was no inflammatory reaction. Normal vessels were in close proximity. The liver and lungs of neither animal had vascular changes. Diffuse haemosiderosis and marked extramedullary haemopoiesis in the spleen was seen in both cats.

The only comparable case was reported by Rothwell et al. (1985) in Australia. At necropsy a 6-year-old male domestic cat with neurological signs revealed generalized vascular lesions of the same type in the myocardium, meninges, adrenal cortex, pancreas, thyroid, intestine, kidney, eyes and lymph nodes. Changes were very moderate in the liver and the lungs, and they were absent in the skin. Immunohistochemical and electronmicroscopical examination showed the proliferations to consist of endothelial and pericyte-like cells. The Australian authors likened the changes to "neoplastic angioendotheliomatosis" in man (Pfleger and Tappenheimer, 1959; Janda and Vaněk, 1978; Haneke and Vigneswaran, 1988; Pièrard et al., 1988; Parent et al., 1989), a disease which has also been described in the dog (Dargent et al., 1988).

Angioendotheliomatosis is currently regarded as an angiotropic lymphoma since the tumour cells, which are not attached to the vascular endothelial lining, are immunohistochemically negative for factor VIII-related antigen and positive for the leucocytic common antigen (LCA) (Dolman, 1986). In contrast the proliferating cells in the two cats described here and in the Australian case were positive for factor VIII-related antigen and negative for LCA. This suggests a true endothelial cell proliferation. Furthermore, the histological picture and the immunohistochemical findings rather resemble those described in "intravascular pseudoangiosarcoma of man (Kuo et al., 1976). Pseudoangiosarcoma consists of solitary vascular knots in the skin, remains strictly intravascular and is rarely accompanied by inflammation. The histogenesis is still not clear. If it is not a neoplasm, hyperplasia of endothelial cells with a toxic aetiology should be considered. In all three cats, however, the lesions were generalized. The wide range of age in the affected cats (9 months to 6 years) suggests an infectious or toxic aetiology, as the animals were too young for a neoplasm to develop, and the lesions, had they been congenital, were too severe to have permitted prolonged survival.

Human beings with acquired immunodeficiency syndrome (AIDS) may develop Kaposis sarcoma and this should be borne in mind in cats with feline immunodeficiency virus (FIV) infection. In Kaposis sarcoma, proliferations develop from vessel endothelium, but they do not remain intravascular and are accompanied by severe inflammation (Lattes, 1982). Only the Maine Coone cat was tested for viral infection. Four weeks before death it was serologically negative for FIV, feline leukaemia virus (FeLV) and feline coronavirus (FIP). These negative results do not totally exclude seroconversion, but in view of the necropsy findings, infection with one of these viruses was considered unlikely.

As the two cases from Switzerland were unrelated and only one comparable case has been described (Rothwell et al., 1985), we assume that these striking systemic vascular proliferations are either very rare, or that they may be a new occurrence.
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