PATHOMORPHOLOGICAL LESIONS IN THE PANCREAS, KIDNEYS, AND LIVER OF A DOG WITH PHAEOCHROMOCYTOMA AND CHRONIC HYPOGLYCAEMIA – A CASE STUDY

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Abstract

A dog (male, dachshund, aged 16.5 years) was euthanised due to hypoglycaemia, which had lasted for about eight years. Macroscopic examinations revealed bilateral tumours of the following sizes 7 cm x 5 cm x 4 cm (right) and 6 cm x 5 cm x 3.5 cm (left) in the sublumbar area. The presence of these tumours was found with an ultrasound examination performed on the dog at the age of 8 years. At that time, the tumours were only half the size. Histopathologically, the tumours were classified as phaeochromocytoma. The morphology of the liver, extensive necrotic foci and hyperplasia of connective tissue in particular, contributed to the dog’s hypoglycaemia. The lesions could have developed as a result of damage to acinar cells of the pancreas and became advanced due to long-term glucocorticotherapy. In turn, originally, hypoglycaemia might have developed in the dog as a result of adrenal medulla failure induced by phaeochromocytoma.

Key words: dog, phaeochromocytoma, pancreas, kidneys, liver, pathomorphology.

Phaeochromocytoma is a neoplasm originating from chromaffin cells of the adrenal medulla that occurs relatively rarely in animals. It is most often diagnosed in dogs and cattle, less frequently in other animals (2, 5, 11, 14). Usually, it is a single-sided neoplasm and its bilateral tumours have been identified less often (2). It usually occurs locally; however, cases proceeding with metastases have been reported as well (2, 4, 5, 11, 13). It results in various disturbances in the production of catecholamines, which leads to the malfunction of carbohydrate metabolism (3, 8).

Literature provides ample descriptions of phaeochromocytoma itself; however, data is lacking on the description of the morphological lesions in internal organs accompanying both its presence as well as concomitant long-term hypoglycaemia. Therefore, an attempt was made to present the pathomorphological pattern of the internal organs of a dog, especially of the pancreas responsible for carbohydrate metabolism, with bilateral phaeochromocytoma and chronic hypoglycaemia observed in the dog for about eight years.

Material and Methods

A male dog of the smooth-haired dachshund breed (castrated, with a body mass of 14.2 kg and age of 16.5 years) was euthanised due to chronic hypoglycaemia.

At the age of 8 years, a reduced blood glucose level was observed in the dog for the first time. In 2003–2006, the level of glucose accounted for: 48.2, 48.9, 50.4, 42.0, 58.7, 62.7, 46.7, 49.5, 51.9, 62.6, 59.8, and 59.8 mg/dl (in subsequent analyses carried out every 3–4 months). The level was maintained below the recommended values stipulated for dogs, i.e. 70–120 mg/dl (15).

A routine ultrasound examinations (USG), performed in that period in about 6-month intervals, revealed bilateral tumour-like formations on both sides of the animal, in the sublumbar area. The tumours increased progressively from ca. 3.5 cm x 3.9 cm to 6.7 cm x 4.4 cm (just before the euthanasia). The dachshund survived over 8 years owing to the treatment and appropriate managing.

The macroscopic examination and collection of the material for microscopic and ultrastructural analyses were done immediately after the dog’s euthanasia. For
Histological examination revealed large pleomorphism in the area of both tumors. Microscopic lesions did not display macroscopically noticeable pathological degeneration and congestion. The liver was characterized by parenchymatous brownish heterogeneous appearance and colour from grey to red—locally reddened and with lighter hues, of a firm consistency. The kidneys, with the sizes of 7 cm x 5 cm x 4 cm (right) and 6 cm x 5 cm x 3.5 cm (left), were brown-grey, locally reddened and with lighter hues of a firm consistency. On the cross-section, they demonstrated a heterogeneous appearance and colour from grey to red-brownish.

The liver was characterized by parenchymatous degeneration and congestion. The other internal organs did not display macroscopically noticeable pathological lesions.

In the area of both tumors, microscopic examinations revealed large pleomorphism of phaeochromocytes with distinct anisocytosis (Fig. 1). In some cells, there were vacuoles and grain-like structures observed. Cells with large hyperchromatic nuclei and giant cells with cytoplasm rich in hyaline drops occurred sporadically. Mitoses were not very frequent. The connective tissue sometimes attained the form of trabeculae. In addition, some sites were observed with plentiful blood vessels. The overall pattern was typical of phaeochromocytoma (Fig. 1) – a neoplasm derived from adrenal medulla cells.

In the pancreas, out of the retrogressive lesions, necrosis of acinar cells was observed in 8 out of the 20 sections examined (Figs 2 and 3). Each time, it covered several cells in the visual field and was assessed as one in the KY scale. In addition, some of the mentioned cells were the subject to partial vacuolar degeneration (noted in 3 sections) and atrophy (observed in 12 sections) – Fig. 3. Oedema was assessed mainly as 2 (in KY scale) and appeared in every section, whereas those assessed as 3 in 6 sections were seen locally (Fig. 4). Small, usually spot extravasations at an intensity level of 1 in the KY scale were observed in 14 sections and those with an intensity of 2 – in one case. The presence of fibrin and proliferation of connective tissue in lobular septa were noted in 15 sections (Fig. 5). Infiltrations of single lymphoid cells were visible in 14 sections (1 in the KY scale) – Figs 4 and 5.

Relatively often, the acinar cells were characterized by ultrastructural lesions, though prevailing areas with their correct structure were observed simultaneously. Out of the lesions presented, the most often identified one appeared to be necrosis of these cells. It involved mainly their small clusters (Fig. 6). In addition, it occurred within single acinar cells where it was very distinct (Fig. 7) or signalled by the presence of myelin-like structures (Figs 8 and 9). Around such lesions, there were agglomerates of phagocytic cells and sometimes a few binuclear acinar cells in the visual field (Fig. 10).

Outside the area of acinar cells with necrotic lesions, sometimes cells having altered mitochondria – mostly oedematous, with damaged crests and atrophy of mitochondrial matrix, were observed (Figs 10 and 11). Usually, next to them, rough endoplasmic reticulum (RER) with dilated canals, sometimes subject to acinar transformation and sometimes with concentric arrangement, defragmentation, or concentrated contents was observed (Figs 8, 12, and 13). In some of the acinar cells, the Golgi apparatus was excessively developed or with widened cisterns (Fig. 13). Zymogen granules were diversified in terms of shape and number (Figs 11 and 12). Some of the acinar cells were very rich in them, whereas others were poor or completely devoid of these grain-like structures (Figs 9 and 10).

In the mitochondria of the pancreatic insulin cells, the concentration of mitochondrial matrix or blurring of the crests was observed sporadically.

The epithelium of the excretory ducts was free of morphological lesions. Sometimes, proliferated connective tissue was located in the proximity of the ducts and the lumen of the ducts was relatively small. The endothelium of blood vessels relatively often demonstrated swelling, and sometimes damage. In some cases, at these sites, erythrocytes were outside of the blood vessels.

In intercellular spaces, proliferated connective tissue and fibrin were observed relatively often. They were sometimes accompanied by lymphocytes. Acinar cells located near such a tissue were atrophic in character. The overall lesions indicated sclerosis of the pancreas.

Results and Discussion

Autopsy revealed two tumors located near the kidneys, 20 sections from the pancreas (from head, body, and caudal segments), as well as five from the kidneys and five from the liver, whereas for analysis under an electron microscope – three sections from the pancreas were taken. Samples taken for microscopic examination were fixed in 10% neutral formalin and embedded in paraffin blocks. The sections were stained with haematoxylin—eosin (HE). Examinations were performed on five preparations stained with HE from each section.

The sections for ultrastructural examination were fixed in 2.5% glutaraldehyde on a 0.2 mol/L phosphate buffer, pH 7.4, and embedded in Epon 812. Semi-thin sections were stained according to the method described by Levis and Knight (10) and assessed under a light microscope to identify the appropriate site for preparing ultra-thin sections. The ultra-thin sections were contrasted with uranyl acetate and lead citrate.

Submicroscopic analysis was conducted using an Opton 900 PC TEM (Germany).

In the microscopic characteristics of the pancreas, the evaluation scale by Kyogoku et al. (9) – KY was used. Following the criteria adopted by these authors, microscope preparations were observed at a magnification of 200x (20x objective and 10x eyepiece) and determined for necrosis: 0 – lack, 1 – less than 5% in visual field (in v.f.), 2 – 5 – 20% in v.f., 3 – more than 20% in v.f.; for stromal oedema: 0 – lack, 1 – dilating of interlobular septum, 2 – dilating of intralobular septum, 3 – separating of single acinar cells; for extravasations: 0 – lack, 1 – 1-2 in v.f., 2 – 3-5 in v.f., 3 – more than 3 foci in v.f.; and for leukocytic infiltration: 0 – lack, 1 – less than 20 cells in v.f., 2 – from 20 to 50 cells in v.f., and 3 – more than 50 cells in v.f.
Fig. 1. Microscopic pattern of phaeochromocytoma - large polymorphism of phaeochromocytes with their distinct anisocytosis. HE, A - 150x, B - 500x.

Fig. 2. Necrosis and atrophy of single acinar cells, presence of binuclear acinar cells (arrows), congestion, disruption of blood vessel wall continuity (short arrows). HE, 500x.

Fig. 3. Necrosis, vacuolar degeneration and atrophy of single acinar cells (cells with pycnotic nucleus), presence of binuclear acinar cells (arrows). HE, 500x.

Fig. 4. Oedema, the presence of fibrin, and infiltration of lymphoid cells in the lobular septum. HE, 150x.

Fig. 5. Hyperplasia of connective tissue and infiltration of lymphoid cells. HE, 500x.

Fig. 6. Disorganisation in the cytoplasm of acinar cells indicating the onset of necrosis. 7 500x.
Fig. 7. Necrosis of acinar cells 7500x.

Fig. 8. Concentric arrangement of the rough endoplasmic reticulum, myelin-like structures (arrows) in the cytoplasm of an acinar cell. 12000x.

Fig. 9. Acinar cells with oedematous and damaged mitochondria (asterisks) and mitochondria containing myelin-like structures (arrows), poor in zymogen granules. 12000x.

Fig. 10. Binuclear acinar cell with myelin-like structures, without zymogen granules. 5000x.

Fig. 11. Diversity of shape and number of zymogen granules, damage of mitochondria (asterisks). 7500x.

Fig. 12. Defragmentation of the rough endoplasmic reticulum in acinar cells, diversified size of zymogen granules. 7500x.
In the microscopic preparations of the kidneys, there were vast fields with necrosis of renal tubules epithelium observed, with parenchyma and hyaline degeneration (Fig. 14). These lesions were usually accompanied by circulatory disorders: congestion, haemostasis, and extravasations. Haemosiderosis was present in all sections. Hyperplasia of connective tissue was noted especially in the wall of blood vessels and in renal glomerules. Relatively often, the lesions were accompanied by the infiltration of lymphocytes. The presence of membranous glomerulonephritis was observed as well (Fig. 15).

In all sections of the liver, there were observed steatosis simplex, parenchymatous, and vacuolar degeneration. Necrosis covered single hepatocytes or occurred in the form of foci (Fig. 16). It was observed in 12 sections. Often, these lesions were accompanied by haemostasis or congestions, the latter mostly with extravasation. In most sections, there was hyperplasia of connective tissue in the wall of the blood vessels, infiltration of leukocytes, and proliferation of stellate cells and binuclear hepatocytes (Fig. 16).

Both the macroscopic and microscopic pattern of the phaeochromocytoma in the described dog was typical of that neoplasm. Worthy of notice is also the fact that in ca. 8-year period it was subject to a twofold increase and did not give metastases. In contrast, in the literature no case was found of concomitant occurrence of that neoplasm and persistent chronic hypoglycaemia. However, hypoglycaemia was only described as following removal of phaeochromocytoma (5). On the contrary, phaeochromocytoma produces catecholamines, releasing them periodically to the blood circulation (3, 12), which in turn leads to temporary hyperglycaemia (2).

Thus, it may be concluded that the described case is rather unusual. It was demonstrated that in the dog examined, a reduced level of blood glucose was
maintained for ca. 8 years. Hypoglycaemia is not a disease entity, but a symptom of homeostasis disorder in the body (5-7). In the presented cases, it was not induced by morphological lesions of the endocrine portion of the pancreas. That organ did not demonstrate a considerable extent of lesions in acinar cells and was subject to hypertrophy with connective tissue. It was undoubtedly the morphological condition of the liver that contributed to the hypoglycaemia – the vast necrotic foci in particular. The lesions observed herein could have developed as a result of the described damage to dog pancreas and been intensified by chronic glycocorticotherapy (1). In turn, originally, hypoglycaemia could have developed in the dog along with adrenal medulla failure evoked by phaeochromocytoma. This could have contributed to disorders of adrenaline production and normal production of noradrenalin. Hypoglycaemia develops precisely upon adrenal medulla failure.

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References