ADRENAL INCIDENTALOMA: A COINCIDENCE OF A SERIOUS PROBLEM?

In the last decennium, the diagnosis of adrenal incidentaloma (AI) has become increasingly prevalent contemporaneously with advances in imaging techniques. In human medicine, AI is defined as an adrenal mass discovered serendipitously by radiologic evaluation in the absence of clinical features suggestive of adrenal disease. The definition encompasses lesions larger than 1 cm that are detected outside the work-up for staging of known cancers [1].

In humans, the prevalence of AI is 2-4% and increases with age. In dogs, there is only one study about the prevalence and the clinical features of AI. Cook et al. (2003) reported AI in 4% of dogs, which were referred to ultrasonographic examination in a 3-year-period [2]. Adrenal masses were more likely in dogs older than 9 years and masses exceeding 2 cm in maximum dimension were malignant. An important finding of this study is, that non-adrenal malignant neoplasia was present in 28.5% of dogs. In cats, adrenal masses are not so frequent as in dogs and there are no reports about their prevalence (so far).

The essential question when dealing with AI is whether the adrenal mass requires intervention (malignant and/or hormonally active) or it can be left untreated (benign and hormonally silent) [3]. The first step in clinical practice, and a paramount importance in a patient with AI, is a thorough clinical evaluation to detect the signs of an underlying secretory tumor and the signs of malignancy. As an AI is usually unilateral, careful evaluation of the contralateral adrenal gland is important. Hormonally active or functional tumors may arise from the adrenal cortex or the medulla and over-secrete mineralocorticoids, glucocorticoids, sex-steroids and catecholamines. Non-functional adrenal tumors are either benign or malignant. An important differential diagnosis for enlarged adrenal gland is metastatic disease, with pulmonary, prostatic and mammary carcinoma being the most common. Another adrenal abnormalities that can present as AI are: hemorrhage, hemomata, cyst [3].

Pheochromocytoma is commonly initially diagnosed as an AI. Next to the increasing use of diagnostic imaging in the diagnostic procedure, there is also the availability of endocrine testing for a pheochromocytoma [3,4]. Clinical signs and symptoms of a pheochromocytoma are subtle and related to cardiovascular, neuromuscular, gastrointestinal system or less commonly to a space-occupying lesion [5]. The biochemical diagnosis is based on measurements of catecholamine metabolites, called metanephrines. Urinary normetanephrine:creatinine ratio and plasma normetanephrine are to be the most sensitive, although the proper reference ranges in dogs remain the problem for both methods [4]. The treatment of choice of a pheochromocytoma is adrenalectomy. Surgery is planned after 2-3 weeks of medicinal therapy with α-adrenergic antagonist phenoxybenzamine [6]. This therapy does not affect catecholamine release, but reverses the effect of catecholamine excess and is beneficial during surgical manipulation of the tumor, but also in dogs, which cannot be treated surgically. In cats, pheochromocytoma is extremely rare.

Cortisol-secreting adrenocortical tumors (ATs) occur in dogs and cats and occasionally present as an AI. Clinical signs and symptoms in dogs with cortisol-secreting AT are associated with hypercortisolemia and include pu/pd, polyphagia, abdominal enlargement, alopecia and other well-known signs associated with Cushing’s syndrome [7]. In cortisol-secreting ATs which present as an AI, the AT-tissue may only be moderately active and therefore the clinical signs of hypercortisolemia are usually mild. Especially in large ATs, steroidogenesis tend to be incomplete and instead of cortisol, its precursors are secreted. The diagnosis of glucocorticoid-secreting AT is a two-step procedure. First, endocrine testing with UCCR combined with HDDST, or LDDST should be performed. Non-suppressive results of testing are not yet diagnostic for an AT. Further work-up includes measurement of basal ACTH concentration and diagnostic imaging. The CT scan of the pituitary and adrenals is the preferred approach and can be expanded to the thoracic scanning in order to be able to detect the metastasis. Adrenocortical adenomas and carcinomas are reported to occur with equal frequency, but the differentiation is cumbersome even by histological examination. Carcinomas tend to be larger than 2 cm and are characterized by invasive growth into adjacent blood vessels, but the only straightforward characteristic of a carcinoma is the presence of metastasis. In about 10% of cases, cortisol-secreting AT is associated with...
a pituitary tumor. The treatment of choice of cortisol-secreting AT is adrenalectomy [8].

When surgery is not possible due to the metastasis and/or invasive growth, the AT is managed medically by either the adrenocorticoalytic drug mitotane (o,p’-DDD) or the adrenocorticostatic drug trilostane. Both treatments are effective in controlling the clinical signs of cortisol excess and mitotane therapy will lead to the complete tumor remission and even disappearance of metastasis (when complete adrenal destruction protocol is used) [9]. Because mitotane treatment is associated with severe side effects and there is an increasing awareness of its toxicity in humans and animals, it has been replaced by trilostane. While this drug is much better tolerated, it has no effect on the tumor tissue. Trilostane therapy is only palliative.

Aldosterone-producing tumors in cats are much more common than in dogs [10]. Predominant feature of hyperaldosteronism is hypokalemia, followed by polyuria, polydipsia and hypertension. Endocrine diagnosis is made based on the measurement of plasma aldosterone:renin ratio. Initial treatment should be directed towards alleviation of hypokalemia and hypertension by using an aldosterone antagonist and a calcium channel blocker and substituting potassium as needed. Subsequent adrenalectomy is the treatment of choice for animals without tumor metastasis. When adrenalectomy is not feasible, palliative medical treatment is continued.

When hormone-secretion is diagnosed in an AI, the terminology is adjusted based on the hormone secretion to cortisol-secreting AT, pheochromocytoma, etc. Basically, only hormonally inactive adrenal masses are supposed to be called AI.

Hormonally inactive adrenal masses are becoming an increasing problem in veterinary medicine and the discussion about the treatment approach is ongoing. While a benign AI deserves no treatment, a malignant AI should be removed as soon as possible. Aspects of malignancy of AI include: (1) size, (2) invasive growth, and (3) presence of metastasis. A size cut-off threshold for malignancy is unknown, but most of the authors agree that a size of more than 2 cm is suggestive of malignancy. Invasion of the AT in the adjacent blood vessels is commonly seen in large adrenal masses and there is no consensus whether this is a marker of malignancy or “just” an invasion of a benign mass to the surrounding tissue with little resistance. Metastasis are the only straightforward sign of malignancy and are mostly detected in the liver, adjacent lymph nodes and/or lungs. The differentiation between benign or malignant adrenal mass by fine needle aspiration biopsy (FNAB) is not possible and the procedure itself is not without risks. The only indication for FNAB is a suspicion of metastasis in the adrenal gland. In that case, excluding a pheochromocytoma beforehand is essential [3].

References