Insulin-secreting tumors, more commonly known as insulinomas (INS) originate from endocrine cells from the islets of Langerhans in the pancreas. INS are uncommon in dogs and very rare in cats. Primary canine INS are commonly solitary tumors and their diameter is usually smaller than 2.5 cm. Most INS are located in the left or right pancreatic lobe. In general canine INS are considered to be malignant in more than 95% of cases, because they almost always tend to metastasize, even though they may lack histological criteria of malignancy. INS hypersecrete insulin and cause an increased insulin concentration in the blood. Normally when blood glucose concentrations decrease, insulin secretion is inhibited. Neoplastic cells are less sensitive to the negative feedback of low blood glucose concentrations and secrete inappropriately high amounts of insulin despite declining blood glucose concentrations resulting in a profound hypoglycemia. Clinical signs of canine INS often occur intermittently. In the initial stages hypoglycemic episodes are preceded by fasting, exercise, excitement or stress, because those situations lead to increased glucose utilization. Between hypoglycemic attacks affected dogs usually do not have clinical signs. The mean duration of clinical signs prior to diagnosis is 3.6 months (range, 1 day – 3.5 years).

Physical examination findings are usually unremarkable in dogs with INS. The presumptive diagnosis of canine INS is not defined by hypoglycemia alone, but commonly based on signalment and history, combined with the fulfillment of Whipple’s triad: Presence of clinical signs, hypoglycemia and relief of clinical signs after glucose administration or feeding.

The plasma insulin concentration should be determined and with INS circulating insulin concentrations are typically within the reference range or higher despite hypoglycemia.

Diagnostic imaging techniques, like transabdominal ultrasonography (US), computed tomography (CT), single-photon emission computed tomography (SPECT) and somatostatin receptor scintigraphy (SRS) can be of great help for the identification and preoperative staging of INS. More recently dual-phase CT angiography (CTA) techniques have been developed and the use of dynamic CTA for the presurgical localization has been reported to be successful. To date the gold standard, however, remains exploratory laparotomy. Careful inspection and palpation of the pancreas and adjacent structures reveals most INS and metastases.

INS therapy can be divided into medical management and surgical treatment. Surgery, if needed combined with postoperative medical management, is the treatment of choice for long-term management, because this treatment strategy results in longest survival times. Dogs with INS should be fed four to six small meals a day of a high-protein, high-fat and high-complex-carbohydrate diet. This type of diet decreases postprandial hyperglycemia, thereby preventing a marked insulin surge. Restricting exercise to brief walks on a leash might also help to reduce clinical hypoglycemia. Diazoxide is the preferred drug for treatment of INS-induced hypoglycemia. Diazoxide raises blood glucose concentrations mainly through direct inhibition of pancreatic insulin release, but also through stimulation of hepatic gluconeogenesis and glycogenolysis and inhibition of glucose uptake by tissues. Possible side effects of diazoxide treatment are anorexia, vomiting and ptyalismus. An alternative to diazoxide therapy is glucocorticoid therapy. Glucocorticoids, such as prednisolone, antagonize the effects of insulin at the cellular level and increase...
gluconeogenesis. In addition to the commonly used drugs described above, treatment with somatostatin (analogs) and cytotoxic treatment with streptozocin have been described. Depending on the pancreatic localization, INS can be removed by local enucleation or partial pancreatectomy. Partial pancreatectomy is the preferred method, because it results in longer survival times than local enucleation. Therefore, local enucleation should only be considered if the INS is located in the body of the pancreas. Partial pancreatectomy is commonly performed using either the suture-fracture technique, the dissection-ligation technique or using the LigaSure Vessel Sealing System. LigaSure pancreatectomy is fast, caused no intraoperative complications and annihilates the use of suture materials or clips. The presence of metastatic disease is evaluated in 2 ways: (1) gross inspection of common target organs including lymph nodes and liver, and (2) on the basis of the blood glucose concentrations after the glucose infusion has stopped. All macroscopically enlarged lymph nodes should be excised and submitted for histologic examination. In case of liver metastases, our approach is aggressive: a tumor debulking approach is warranted to decrease tumor mass and increases the effects of medical therapy after surgery. Canine INS has a reserved prognosis, because metastasis, tumor regrowth and return of clinical signs are almost inevitable.

References