CEREBROVASCULAR DISEASE OF DOGS & CATS

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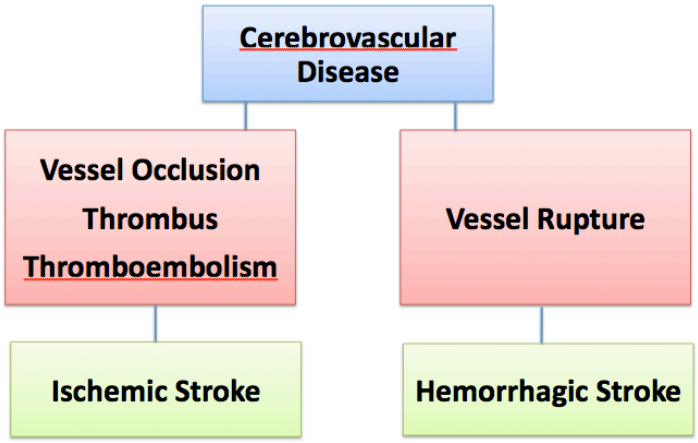
- **Key Points**
- The term "cerebrovascular disease" is defined as any abnormality of the brain resulting from a pathologic process compromising its blood supply
- Pathologic processes of the blood vessel include occlusion of the lumen by a thrombus or embolus, rupture of a blood vessel wall, lesion or altered permeability of the vessel wall, and increased viscosity or other changes in the quality of the blood
- Cerebrovascular accident (CVA), also known as stroke, is the most common clinical presentation of cerebrovascular disease, defined as a sudden onset of nonconvulsive and nonprogressive focal brain signs secondary to cerebrovascular disease
- By convention, these signs must remain for more than 24 hours to qualify for the diagnosis of CVA, which is usually associated with permanent damage to the brain
- If the clinical signs resolve within 24 hours, the episode is called a transient ischemic attack (TIA)

Causes and Pathophysiology

From a pathologic point of view, the lesions affecting the cerebral blood vessels are divided into 2 broad categories;

1. Ischemic stroke and
2. Hemorrhagic stroke.

- Ischemic strokes result from occlusion of a cerebral blood vessel by a thrombus or embolism, depriving the brain of oxygen and glucose
- Hemorrhagic strokes result from rupture of a blood vessel wall within the brain parenchyma or subarachnoid space, causing bleeding into or around the brain



Ischemic Strokes

Ischemic strokes have been reported infrequently in the veterinary medical literature when compared with the human medical literature.

Most reports have been based on postmortem results in dogs that died or were euthanized as a result of the severity of the ischemic stroke or the suspected underlying cause of the stroke. This limitation may affect the prevalence and type of underlying causes, as it is likely that only the most severely affected dogs, or dogs in which infarction occurred secondarily to a disease with a poor prognosis, would die or be euthanized. Suspected underlying causes identified in histopathologically confirmed cases include: septic thromboemboli associated with bacterial endocarditis or other sources of infection; atherosclerosis associated with primary hypothyroidism and Miniature Schnauzers with hyperlipoproteinemia; aberrant parasite migration (*Cuterebra*) or parasitic emboli (*Dirofilaria immitis*); embolic metastatic tumor cells; intravascular lymphoma; fibrocartilaginous embolism; and aortic or cardiac thromboembolism.

In a study of magnetic resonance imaging (MRI) of dogs with brain infarct, a concurrent medical condition was detected in just over 50% of dogs, most commonly hyperadrenocorticism, chronic kidney disease, hypothyroidism, and hypertension. The most commonly suspected causes of hypertension were chronic kidney disease and hyperadrenocorticism. In human patients, infarcts of unknown cause are referred to as cryptogenic infarcts. No age, sex, or breed predisposition was identified in that study, although Cavalier King Charles Spaniels (CKCS) and Greyhounds were overrepresented.

Reports of ischemic strokes in cats are scarce. The term feline ischemic encephalopathy has been used to describe cases of peracute onset of clinical signs consistent with a unilateral cerebral or brainstem problem caused by ischemia. Although the cause remains unknown in most cases, some of them have been linked to *Cuterebra* migration. It is believed that the migrating parasite or the host response leads to vasospasm in the cerebral vasculature, typically the middle cerebral artery.

The pathophysiology of ischemic stroke is based on the principle that with limited energy stores, the brain relies on a constant supply of glucose and oxygen to maintain ionic pump function. When perfusion pressure falls to critical levels, ischemia develops, progressing to infarction if it persists long enough or is severe enough. An infarct is an area of compromised brain parenchyma caused by a focal occlusion of one or more blood vessels. An infarct may be due either to vascular obstruction that develops within the occluded vessels (thrombosis) or to obstructive material that originates from another vascular bed and travels to the brain (thromboembolism). Infarcts can be a consequence of small vessel disease (ie, superficial or deep perforating artery) that gives rise to a lacunar infarct, or large vessel disease (ie, a major artery of the brain or its main branches) that gives rise to a territorial infarct. Two distinct regions can be distinguished, the core where ischemia is severe and infarction develops rapidly, and the surrounding penumbra containing a more moderate decrease of cerebral blood flow (CBF) that allows longer duration of ischemic stress to be tolerated. The relative volume of these 2 regions changes as the infarct evolves. The factors causing the evolution of the penumbra to irreversible injury are multiple and complex, and include the degree of blood flow

reduction, the region of the brain involved, and the individual patient. In the penumbra, neurons are still viable but at risk of becoming irreversibly injured. Tissue within the penumbra has the potential for recovery and therefore is the target for therapy in acute ischemic stroke. At the cellular level, the ischemic neuron becomes depolarized as adenosine triphosphate is depleted and the Na^+/K^+ adenosine triphosphate pump and other ionic membrane pumps fail, leading to loss of fluid-electrolyte homeostasis. This process results in loss of ionic gradients and a net translocation of water from the extracellular to the intracellular compartment, causing the cell to swell (cytotoxic edema). Over time the ischemic cascade progresses, resulting in cell lysis, increased macrophage activity, and disruption of the blood-brain barrier, leading to vasogenic edema. Vasogenic edema typically takes 4 to 6 hours to develop once blood flow decreases to ischemic levels, and may continue to progress for 24 to 48 hours. Because neurons have the highest demand for oxygen, neuronal function is first affected; this is followed, in declining order of vulnerability, by the function of oligodendrocytes, astrocytes, mesodermal microglia, and fibrovascular elements. If sufficient perfusion is not reestablished, severe ischemia results in an area of dead tissue described as an infarct. Ischemia is thus a continuum between normal cellular function and cell death.

Hemorrhagic Strokes

In contrast to the high incidence in man, intracerebral hemorrhage resulting from spontaneous rupture of vessels is considered rare in dogs. Secondary hemorrhage has been reported in dogs in association with rupture of congenital vascular abnormalities, primary and secondary brain tumors, intravascular lymphoma (malignant angioendotheliomatosis), cerebral amyloid angiopathy and inflammatory disease of the arteries and veins (necrotizing vasculitis), brain infarction (hemorrhagic infarction), and impaired coagulation (extracranial diseases predisposing for disseminated intravascular coagulation such as neoplasia, von Willebrand disease, or *Angiostrongylus vasorum*). Nontraumatic subdural or subarachnoid hemorrhage has been reported in dogs but remains very rare when compared with its occurrence in man, where aneurysmal rupture is the most common underlying cause.

In hemorrhagic stroke, blood leaks from the vessel directly into the brain, forming a hematoma within the brain parenchyma, or into the subarachnoid space. The mass of clotted blood causes physical disruption of the tissue and pressure on the surrounding brain . This process alters intracranial volume/pressure relationships, and can lead to increased intracranial pressure (ICP) and decreased CBF. Initially, ICP may remain normal due to a system of compensation. Within the closed space of the skull are 3 noncompressable constituents, brain tissue, blood, and cerebrospinal fluid (CSF). A change in the volume of one constituent will be balanced by a compensatory change in another. This principle is called the Monroe-Kellie doctrine. As the hematoma continues to expand, this compensatory system becomes exhausted and ICP starts to increase; this can be clinically associated with herniation. Due to mechanical autoregulation, CBF remains constant even though the cerebral perfusion pressure (CPP) may vary between 40 and 120 mm Hg. The normal autoregulation of CBF may be impaired following cerebrovascular accidents, causing blood flow to damaged regions to become directly dependent on systemic blood pressure. Such animals may be unable to compensate for reductions in mean arterial blood pressure (MABP), causing decreased CPP in the presence of increased ICP. This anomaly emphasizes the importance of maintaining systemic blood pressure. In these circumstances,

systemic hypotension can result in inadequate perfusion of the brain, which leads to cerebral ischemia and secondary neuronal injury.

Clinical Signs

In ischemic or hemorrhagic stroke, the denominative feature is the temporal profile of neurologic events. It is the abruptness with which the neurologic deficits develop that is highly suggestive of the disorder as being vascular. This event is then followed by a plateau and then resolution of the neurologic deficit in all except the fatal strokes. Worsening edema can result in progression of neurologic signs for 24 to 72 hours. Intracranial hemorrhage can be an exception and cause rapid progressive onset over a very short period of time. Clinical signs usually improve after 24 to 72 hours due to a decrease in size of the hematoma and edema.

Neurologic deficits usually refer to a focal anatomic diagnosis and depend on the neurolocalization of the vascular insult (telencephalon, thalamus, midbrain, pons, medulla, cerebellum). Infarction of an individual brain region is associated with specific clinical signs that reflect the loss of function of that specific region. In its mildest form, the impaired regional CBF causes a TIA. The cause of TIA in humans is usually small emboli from the heart or atherosclerotic plaques in the carotid or vertebrobasilar arteries. Similar paroxysmal events have been reported in dogs with suspected or histologically proven infarction, but the underlying cause remains undetermined. With hemorrhagic stroke, the clinical picture is different, as the hemorrhage usually involves the territory of more than one artery and pressure effects cause secondary signs. Neurologic signs are largely related to raised ICP, which gives rise to nonspecific signs of forebrain, brainstem, or cerebellar disturbance.

Diagnosis

Initial evaluation of animals with suspected stroke should focus on the differential diagnosis, including traumatic, metabolic, neoplastic, inflammatory/infectious, and toxic encephalopathies. Fundus examination should be considered in all animals and may reveal tortuous vessels (suggestive of systemic hypertension), hemorrhage (suggestive of coagulopathy or systemic hypertension), or papilledema (suggestive of elevated ICP). Imaging studies of the brain (computed tomography, conventional and functional MRI) are necessary to confirm stroke, define the vascular territory involved, determine the extent of the lesion, and distinguish between ischemic and hemorrhagic stroke. Imaging studies are also necessary to rule out other causes such as tumor, trauma, and encephalitis. Once stroke is confirmed, diagnostic tests focus on identifying an underlying cause.

Ancillary diagnostic tests in cases of ischemic stroke

- – Serial blood pressure measurements
- – Complete blood count
- – Serum biochemistry profile
- – Urinalysis
- – Urine protein/creatinine ratio

– Serum antithrombin III activity
– D-dimers
– Endocrine testing for hyperadrenocorticism, thyroid diseases, and pheochromocytoma
– Thoracic radiographs
– Abdominal ultrasound
– Echocardiography and electrocardiography

Ancillary diagnostic tests in cases of hemorrhagic stroke

– Serial blood pressure measurements
– Complete blood count
– Serum biochemistry profile
– Buccal mucosa bleeding time
– Prothrombin time (PT)
– Activated partial thromboplastin time (APTT)
– Thoracic radiographs
– Abdominal ultrasound

Reference

Garosi LS: Cerebrovascular Disease in Dogs and Cats. Veterinary Clinics of North America: Small Animal Practice 40(1):75-79, 2010.