Cerebral Infarction

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Profile

Definition

- *Cerebrovascular disease* refers to a group of disorders that result from a pathological process that compromises blood supply to the brain.
  - Such disorders may be either ischemic or hemorrhagic.
- Infarction is a local tissue injury or necrosis from reduced or absent blood flow to a specific part of the body, including the brain.
- Cerebral infarction (cerebral infarct, cerebrovascular accident [CVA], or stroke) is usually a *focal ischemic* event with an acute onset of asymmetric clinical signs that are progressive for a short time.
- *Global brain ischemia* can also occur (eg, anesthetic accidents, cardiopulmonary arrest).
- By definition, clinical signs must be present for at least 24 hours to be considered a stroke.[1,2]
- Transient ischemic attack (TIA) is the term used to describe a cerebrovascular disorder in which clinical signs resolve within 24 hours following transient ischemia.

Pathophysiology

- There is little energy reserve in the brain, so it is dependent on continuous delivery of oxygen and glucose for energy; it is capable of only aerobic metabolism.[1]
- The brain receives 20% of cardiac output and accounts for 15% of oxygen consumption, despite comprising only 2% of body weight.[1]
- Infarcts can be described based on their underlying pathophysiology or location and size.

Underlying Pathophysiology[2,3]

- *Ischemic infarct* is secondary to lack of oxygen delivery caused by blood vessel obstruction; this is the most common form of cerebral infarct in dogs and cats.
- *Hemorrhagic infarct* is secondary to ruptured blood vessels leading to hemorrhage within the brain parenchyma.

Location & Size[1,3]

- *Territorial infarct* is a large area of tissue damage secondary to obstruction of one of the major arteries to the brain (eg, middle cerebral artery, rostral cerebellar artery).
- *Lacunar infarct* is a smaller area of tissue damage from obstruction of small superficial or deep penetrating arteries.

Cerebrovascular disease **refers to a group of disorders that result from a pathological process that compromises blood supply to the brain.**

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Predisposing Conditions for Cerebral Infarction

- Aberrant parasite migration (eg, *Cuterebra* spp, *Dirofilaria immitis*)
- *Angiostrongylus vasorum* infection
- Atherosclerosis
- Cardiac disease
- Coagulopathy
- Chronic kidney disease
- Extension of CNS infection
- Hyperadrenocorticism
- Hyperlipidemia
- Hypertension
- Hypothyroidism
- Increased blood viscosity (eg, polycythemia, multiple myeloma)
- Intravascular neoplasia (eg, lymphoma, hemangiosarcoma)
- Liver disease
- Protein-losing nephropathy
- Sepsis and bacterial thromboembolism
- Vasculitis

Table 1. Ancillary Diagnostics

Ischemic infarction	*Hemorrhagic infarction*
Urine protein:creatinine ratio if proteinuria	Rickettsial disease testing
Endocrine testing for hyperadrenocorticism (eg, ACTH stimulation test, dexamethasone suppression testing)	Clotting studies: buccal mucosal bleeding time, prothrombin time (PT), activated partial thromboplastin time (APTT)
Serum antithrombin III activity	von Willebrand factor analysis
D-dimer tests	Testing for *Angiostrongylus vasorum* in endemic regions
Echocardiography and electrocardiography if underlying cardiac condition	

Signalment

- Infarction can occur at any age but is typically diagnosed in middle-aged to geriatric dogs and cats.[4-6]
- No apparent gender predisposition.
- They can occur in all breeds of dogs and cats, but the following breeds may be at increased risk[6-10]:
  - Greyhounds: Especially cerebellar infarcts; these are often idiopathic but may be hypertension-related.
  - Cavalier King Charles spaniels: Possibly related to local alterations in intracranial pressure secondary to Chiari-like malformation.
  - Miniature schnauzers: Possibly related to hyperlipidemia.
  - Brachycephalic breeds: Increased risk for global ischemia, especially with ketamine anesthetic protocols.

Risk Factors

- The three most common risk factors for cerebral infarction are hypertension, hypercoagulability, and hyperviscosity.

Predisposing Conditions[2,4,6,11]

- The most common predisposing causes are idiopathic hypertension, chronic kidney disease, and hyperadrenocorticism.
- A predisposing condition is identified in just over half of dogs with MRI evidence of infarction.
- See **Predisposing Conditions for Cerebral Infarction**.

History

- Patients are usually presented for evaluation following peracute to acute onset of neurologic signs that are non-progressive after 24 hours.
  - Rarely, progression may occur at 48-72 hours because of secondary cerebral edema.[1,2]
- Common clinical signs noted by owners include vestibular dysfunction, seizures, altered mental status, paresis, or ataxia.

Physical Examination

- General examination may be normal or demonstrate changes consistent with a predisposing condition (eg, cranial abdominal organomegaly, thin hair coat).
- Retinal fundic examination is recommended.
  - Hypertension may cause enlarged or tortuous retinal vessels.
  - Papilledema may be present if increased intracranial pressure.
  - Concurrent chorioretinitis or infil-

DWI = diffusion weighted images

trative disease (eg, lymphoma) further suggests presence of a concurrent, predisposing condition.

Neurologic Examination

- As with all neurologic disorders, neurologic signs reflect lesion location and extent rather than cause.
- Common signs based on lesion location include:
  - Cerebrum: Seizures, mental obtundation, circling, pacing, inappropriate elimination
  - Thalamus: Signs of cerebral disease as above or vestibular dysfunction (possibly from damaged thalamic relay centers associated with cerebellar and vestibular nuclei; damage to the medial longitudinal fasciculus; input of vestibular information to the thalamus; or diaschisis, a sudden change in function in one area of the brain from damage in a distant location).
  - Brainstem: Altered mental status, cranial nerve deficits, vestibular dysfunction, paresis, ataxia.
  - Cerebellum: Paradoxical central vestibular dysfunction, hypermetria, cerebellar (intention) tremors, truncal sway/ataxia.

Dx Diagnosis

Definitive Diagnosis

- Definitive diagnosis requires histopathology at necropsy.
  - CT- or MRI-guided stereotactic biopsy may not provide a definitive diagnosis of infarction but may help rule out other possible causes (eg, neoplasia, encephalitis).
- A presumptive diagnosis can be made via advanced imaging and exclusion of other potential causes.

Differential Diagnoses

- Intracranial neoplasia
- Immune-mediated, non-infectious encephalitis (eg, granulomatous meningoencephalomyelitis, necrotizing encephalitis)
- Infectious encephalitis
- Traumatic brain injury

Laboratory Findings

- Minimum database includes CBC, serum chemistry panel, thyroid hormone analysis, and urinalysis.
- Serial systolic blood pressure measurements should be obtained to rule out systemic hypertension.
- Thoracic radiographs and abdominal ultrasound are recommended to screen for neoplasia and predisposing conditions.
- Ancillary diagnostics should be performed based on the type of infarction present (**Table 1**, previous page).

Imaging

- MRI is the advanced imaging modality of choice given its superior soft tissue resolution.
  - The classic MRI characteristic of an ischemic stroke (**Figure 1**, next page) is an intra-axial lesion (often wedge-shaped) that is hyperintense (bright) on T2-weighted and fluid attenuation inversion recovery (FLAIR) images, iso- to hypointense (dark) on pre-contrast T1-weighted images, and minimal to no contrast enhancement.
  - Diffusion weighted imaging (DWI; **Figure 2**, next page) is the sequence of choice for acute ischemic infarction.
    - DWI detects lack of normal Brownian motion of molecules, particularly lack of intercellular water movement from cell swelling associated with cytotoxic edema.
    - An acute infarction appears as a hyperintense region.
  - The MRI appearance of hemorrhagic infarction (**Figure 3**, next page) varies greatly as blood cells and hemoglobin degrade (**Table 2**).

Table 2. MRI Characteristics of Hemorrhage

Stage	*Time frame*	*Hemoglobin state*	*T2-weighted*	*T1-weighted*
Peracute	<24 hrs	Oxyhemoglobin	Hyperintense	Isointense
Acute	1-3 days	Deoxyhemoglobin	Hypointense	Isointense
Early subacute	3-7 days	Intracellular methemoglobin	Hypointense	Hyperintense
Late subacute	>7 days	Extracellular methemoglobin	Hyperintense	Hyperintense
Chronic	>14 days	Hemosiderin	Hypointense	Iso- to hypointense

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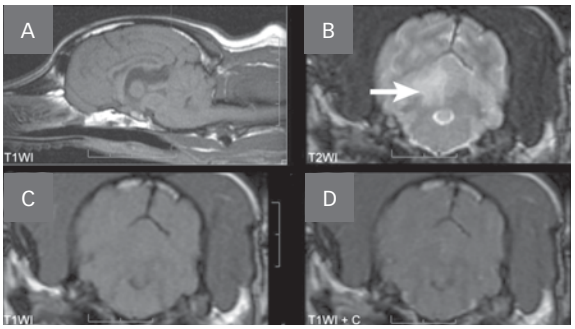
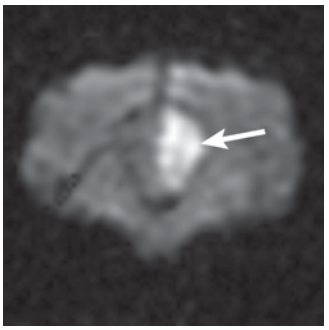
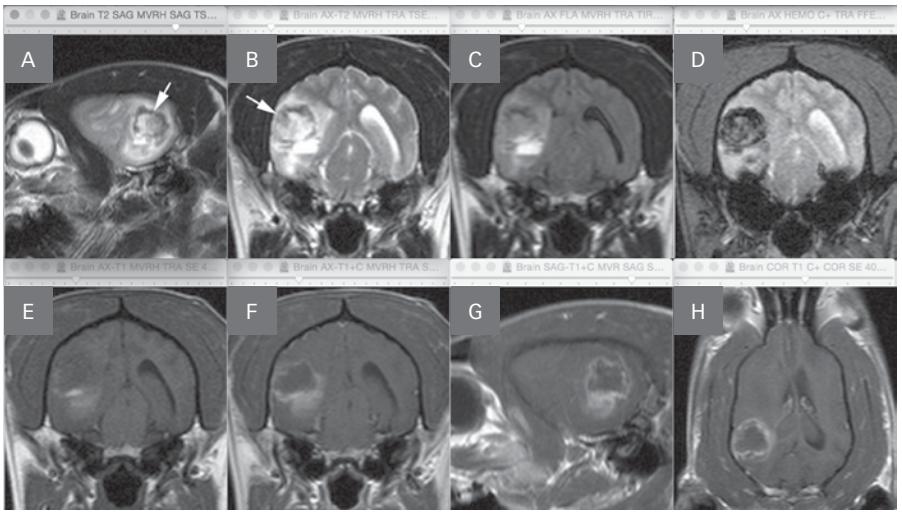


1 **MRI images of a dog with a right cerebellar infarct (A). Note the wedge-shaped intra-axial lesion in the right dorsal cerebellar gray matter (arrow) that is hyperintense on T2-weighted images (B), isointense on T1-weighted images (C), and does not contrast enhance (D).**



2 **DWI obtained from a dog showing a wedge-shaped, markedly hypertintense signal in the left dorsal cerebellar gray matter consistent with a left cerebellar infarct (arrow). DWI is the MRI sequence of choice for peracute to acute infarction.**



3 **MRI images from a dog with a presumed hemorrhagic infarct (arrows) based on improved clinical signs and reduction in size on follow-up MRI imaging without definitive treatment. There is a large, intra-axial lesion in the right parietal & occipital lobes. Images (A) and (G) are parasagittal T2-weighted and T1-weighted images, respectively. Images (B) through (F) are transverse images at the left of the midbrain. Image (H) is a dorsal view. The lesion is heterogeneous and primarily hyperintense on T2-weighted (A, B) and FLAIR (C) images; hypointense on T2*GRE (D) images consistent with hemorrhage; hypointense with a rim of hyperintensity on T1-weighted images (E); and has moderate-to-marked peripheral rim contrast enhancement (F-H).**

- Hemorrhagic infarcts can be difficult to distinguish from hemorrhagic brain tumors (eg, glioma, hemangiosarcoma).
- The T2*-gradient echo (T2*GRE) sequence is best for identifying hemorrhage as it is hypointense on this sequence.
- T2*GRE is also hypointense for mineralization, air, iron, melanin, and foreign bodies.

Tx Treatment

Inpatient or Outpatient

- Patients with mild signs may be treated on an outpatient basis.
- Non-ambulatory patients with moderate to severe clinical signs, especially larger-breed dogs, may need to be hospitalized until they are able to walk with minimal to no assistance.

Acute Medical Treatment

- In general, there is no specific treatment for cerebral infarction.
- So-called *clot busters* or thrombolytic agents (eg, tissue plasminogen activator [tPA], streptokinase) are frequently used in human medicine.
  - These medications are infrequently used in veterinary medicine because blood clots are rarely a cause of infarction in dogs and cats, thrombolytic agents need to be given within 6 hours of infarction, and expense or limited availability preclude their use.
- Mannitol (0.5-1.0 g/kg IV over 10-15 minutes) or hypertonic saline 7.5% (3-5 mL/kg IV over 10-15 minutes) may be needed to reduce brain swelling.
  - There is a theoretical risk for exacerbating hemorrhage or cerebral edema if mannitol is given to patients with intracranial hemorrhage, but benefits likely outweigh risks.
- Hypertension should be treated to prevent ongoing damage.
  - Initial treatment recommendations include enalapril (dogs, 0.5 mg/kg PO q12h) or amlodipine (cats, 0.625-1.25 mg per cat PO daily).
- Oxygen support is recommended in moderate to severe cases, especially if hypoventilation is present.
- Nursing care for recumbent patients is critical and includes frequent turning and thick bedding to prevent pressure

sores, urinary catheterization if indicated, and physical rehabilitation (at a minimum, passive range of motion and massage).

Chronic Medical Treatment

- Underlying predisposing conditions should be treated as indicated to reduce the risk for future infarction.
- Antithrombotics may be considered if a thromboembolic disorder is proven, but their use is controversial and not proven to be beneficial.
  - Options include clopidogrel (dogs, 1 mg/kg PO q24h; cats, 18.75 mg per cat PO q24h) or aspirin (dogs, 0.5-1.0 mg/kg/q24h; cats, 40 mg [1/2 baby aspirin tab] PO q48-72h

Nutritional Aspects

- There are no specific nutritional recommendations for infarction, but diets higher in essential fatty acids and omega-3 may be helpful.[12]
- Diet recommendations should also be based on predisposing conditions, such as a low-protein diet in patients with kidney disease.

Activity

- There are no activity restrictions for this condition.
- Physical rehabilitation is highly recommended to improve recovery and shorten duration of signs.

Client Education

- Clients should be taught how to provide nursing care for recumbent animals, as well as how to treat underlying predisposing conditions.

Follow-up

Patient Monitoring

- Patients should be monitored for signs of progression that might be consistent with a diagnosis other than stroke.
  - If signs are progressive, further examination is required as that would suggest the patient *did not* have a stroke.
- Clients should be instructed to observe for signs of recumbency-associated aspiration pneumonia (eg, coughing, tachypnea, dyspnea).

Complications

- The most common complication is recumbency-associated aspiration pneumonia.
- Other complications may be observed depending on concurrent predisposing conditions.

In General

Relative Cost

- Diagnostic workup and acute treatment: $$$$-$$$$$
- Chronic treatment and follow-up: $$-$$$

Cost Key
$ = up to $100
$$ = $101-$250
$$$ = $251-$500
$$$$ = $501-$1000
$$$$$ = more than $1000

Prognosis

- In general, the prognosis for recovery is good to excellent for patients with focal infarctions that have limited initial clinical abnormalities, if given enough time and supportive care.
- Some patients have residual clinical signs, but quality of life is acceptable for most patients.
- The prognosis for global brain ischemia is guarded to fair. ■ cb

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Suggested Reading

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