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Musculoskeletal and Neurologic Diseases

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Ferrets can manifest with neurologic signs as a result of various conditions that may be of nervous or muscular origin; however, suggestive signs can also originate from weakness, cardiac conditions, or orthopedic abnormalities. Therefore, before neurologic evaluation, conduct a thorough general physical examination. In cases of altered mentation, check for signs of shock, such as tachycardia, delayed capillary refill time, and pale mucous membranes. Perform laboratory evaluations (e.g., a complete blood count, plasma biochemical analysis, etc.) as part of the complete physical assessment. In ferrets with gait abnormalities, perform a complete orthopedic evaluation. If results of the orthopedic and laboratory tests are normal, perform a neurologic examination to identify functional deficits.

NEUROLOGIC EXAMINATION

Neurologic examination of ferrets follows the same principles as for dogs and cats.⁵¹ First, assess the level of consciousness, posture, and gait. Normal ferrets are hyperactive and have a characteristic hunchback posture while taking small steps. Cranial nerve examination is also performed in the same way as in dogs

and cats. Ferrets normally have a keen sense of smell, but olfactory assessment is rarely performed. A ferret's vision is adapted to a crepuscular lifestyle and is presumed to be inferior to dogs and cats.²⁸ Ferrets generally do not have a menace response; therefore, vision is difficult to assess. Albino ferrets reportedly have a poorer ability to detect motion by sight compared with other ferrets.^{23,38} Assess pupillary size as well as physiologic nystagmus during head movement. Keep in mind that ophthalmic examination can be difficult to perform in ferrets because of the reduced size of the globe, the relatively large lens, and the darkly pigmented iris.

Jaw tone is easily assessed in ferrets. To assess facial sensitivity and response, begin by gently placing the tip of a cotton-tipped applicator on the corneal surface to elicit the corneal reflex. Test the palpebral reflex by touching the medial or lateral canthus, and trigger nasal stimulation and facial sensitivity by touching a naris with a pointed instrument.

Hearing is difficult to evaluate in ferrets. The owner may report a lack of response to vocal stimuli or difficulty in training. Congenital deafness appears to be a problem in certain ferrets. In an epidemiologic study of 152 ferrets,

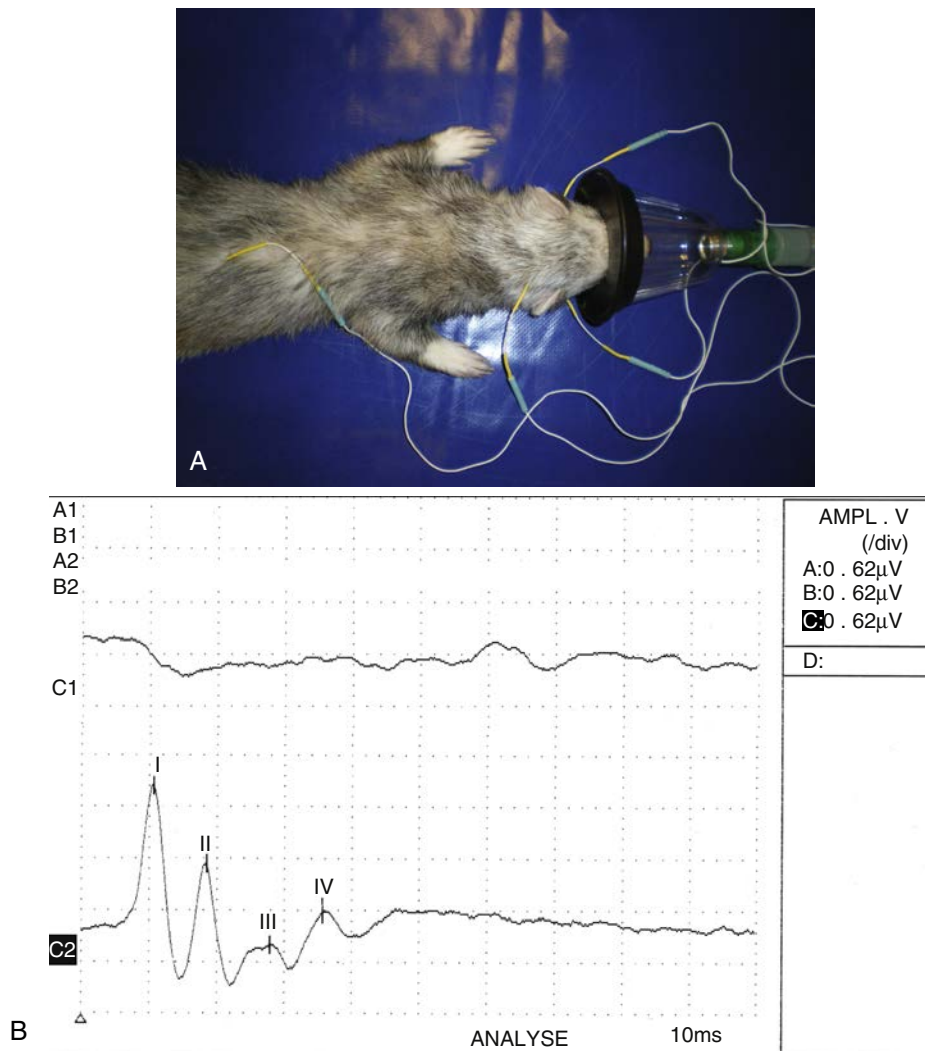


Fig. 10.1 (A) Setup used for brainstem auditory-evoked response (BAER) measurement in a ferret. (B) BAER recording in a unilaterally deaf ferret. The lower curve (C2) represents the normal hearing ear and includes peaks I, II, III, and IV. The upper curve (C1) represents the deaf ear with absence of the expected peaks.

the high prevalence of deafness (29%) was strictly associated with coat color patterns, specifically white markings and premature graying.⁶⁷ All panda, American panda, and blaze ferrets were deaf.⁶⁷ It is important for breeders to have a keen awareness and understanding of this defect to reduce its prevalence. Brainstem auditory evoked response (BAER) is the only reliable method for clinical evaluation of hearing in ferrets (Fig. 10.1).⁶⁷ The procedure can be performed easily in anesthetized ferrets as young as 8 weeks of age. A reliable routine protocol for BAER in ferrets has been established.⁶⁸

Perform postural tests to assess proprioception and motor nerves. In very active animals, performing hopping and wheel barrowing may be easier than proprioceptive placing. Evaluate the presence of voluntary movement. Tests of spinal reflexes, which include withdrawal in all four limbs, are easy to perform and reliable. However, the patellar reflex is difficult to assess, primarily because the patellar ligament is reduced in ferrets. If voluntary movement is absent, assess nociception by using a hemostat.

ABNORMAL NEUROLOGIC SIGNS

Paresis

Pelvic limbs paresis, or paraparesis, is a common presentation in ferrets and has several possible causes (Table 10.1). Because of the elongated body of ferrets, generalized weakness is often more pronounced in the rear legs. It is important to rule out hypoglycemia, orthopedic conditions, abdominal pain (e.g., from foreign body ingestion, cystitis, or prostatitis), and organomegaly (e.g., splenomegaly or lymphadenopathy) as possible causes.

Pelvic limb paresis can involve upper motor neuron (UMN) or lower motor neuron (LMN) deficits. Upper motor neuron deficits involving both pelvic limbs (with normal thoracic limbs) reflect a T3-L3 spinal cord lesion, and differential diagnosis includes a focal or diffuse, intramedullary or extramedullary lesion in this segment of the spinal cord. Further diagnostic testing involves imaging and analysis of cerebrospinal fluid (CSF). Subsequent to survey radiography of the vertebral column, computed tomography (CT) can be performed to enhance

TABLE 10.1 Pelvic Limb Paresis: Differential Diagnosis in Ferrets

Classification	Examples
Immune-mediated	<ul style="list-style-type: none"> Disseminated myofasciitis Myasthenia gravis
Infectious	<ul style="list-style-type: none"> Toxoplasmosis Sarcocystosis
Toxicity	<ul style="list-style-type: none"> <i>Clostridium botulinum</i> endotoxin
Spinal defects	<ul style="list-style-type: none"> Congenital (spina bifida, vertebral defects) Acquired (trauma, luxation)
Metabolic	<ul style="list-style-type: none"> Hypoglycemia
Neoplasia	<ul style="list-style-type: none"> Chordoma/chondrosarcoma Lymphoma Fibrosarcoma Histiocytic sarcoma Plasmacytoma Teratoma
Degenerative	<ul style="list-style-type: none"> Intervertebral disk disease

three-dimensional visualization. Myelography or myelo-CT can be performed to identify spinal cord compression. The spinal cord can be delineated, and external compression and focal intramedullary swelling can be differentiated by injecting contrast medium (e.g., iohexol at 0.25 to 0.5 mL/kg) with a 25-gauge spinal needle into the subarachnoid space. When the spinal needle is inserted, a CSF sample can also be obtained for cytologic analysis and further testing (e.g., polymerase chain reaction [PCR]). Sites for CSF tap and myelography are the atlantooccipital and lumbar (L5-L6) regions (Fig. 10.2).

Lower motor neuron deficits of the pelvic limbs can reflect a lesion in the spinal cord at the level of L4-S2 or a neuromuscular disorder (e.g., a neuropathy, junctionopathy, or myopathy). Perform a complete systemic evaluation, including assessing results of routine blood tests, before considering primary neurologic disease. Ferrets suffering from systemic disease, such as hypoglycemia, may appear to have posterior paresis. If the lesion is suspected to involve the vertebral column, use the diagnostic approach suggested for UMN deficits. However, if an abnormality involving the peripheral nerves or neuromuscular junctions is suspected, perform electromyographic and nerve conduction velocity tests (Fig. 10.3). Normal values have been published in ferrets.⁵



Fig. 10.2 (A) Cerebrospinal tap from the cisterna magna in a ferret. With the ferret in lateral recumbency at the edge of the table, the head is flexed so that the point of the nose is at 90 degrees to the long axis of the body. The wings of the atlas and the point of the occipital condyle are used as landmarks. (B) Lumbar cerebrospinal fluid (CSF) collection at L5-6. Only a few drops of CSF can be collected; therefore, to maximize the sample, the fluid can be collected directly into a microtainer (C) or hematocrit tube (D).



Fig. 10.3 Electromyographic and electroneurographic study in a ferret. The figure demonstrates measurement in the thoracic limb only; however, both thoracic and pelvic limbs are evaluated. The technique is described by Bianchi et al.⁵

Tetraparesis (i.e., paresis involving all four limbs) can reflect a C1-T2 abnormality or an intracranial or multifocal disorder. Spinal lesions cranial to C5 often manifest with UMN deficits in all four limbs, whereas a C6-T2 lesion often results in LMN deficits in the thoracic limbs and UMN deficits in the pelvic limbs; LMN deficits in all four limbs reflects a neuromuscular disorder.

Ataxia

Ataxia is incoordination; it can be characterized as either cerebellar, vestibular, or proprioceptive in origin. Cerebellar ataxia (e.g., hypermetria, intention tremor, broad-based stance) is caused by a lesion in the cerebellum. Because the cerebellum does not initiate motor activity but rather coordinates it, affected patients will have intact strength but will demonstrate abnormal rate, range, or force of movement. Paresis is not present with cerebellar dysfunction. Vestibular ataxia (i.e., peripheral or central vestibular disease) occurs when the vestibular system (i.e., inner ear, vestibular nerve, and vestibular nuclei) is damaged or diseased (e.g., otitis media, tumor). The vestibular system refines and coordinates motor activity by controlling muscles used to maintain head position, eye movement, and equilibrium. Dysfunction results in loss of balance; animals often list or fall to one side and may have a head tilt. Proprioceptive ataxia is caused by spinal disease, which will result in proprioceptive deficits that can be localized to the affected region of the spinal column. In the differential diagnosis, consider trauma, intervertebral disk disease, and tumors arising within or compressing the spinal cord or nerves.^{42,62} In the diagnostic workup, a CT scan will provide important information about bone abnormalities, whereas magnetic resonance imaging (MRI) provides better imaging of soft tissue abnormalities of the spinal cord and brain (Fig. 10.4).

Seizures

Seizures in ferrets are most commonly caused by hypoglycemia secondary to insulinoma, particularly in middle-aged and older ferrets. The other possible causes are an intracranial lesion, another metabolic abnormality, or an idiopathic condition. The anamnesis

must be reviewed critically when the ferret is not presented in status. Many presentations, such as gastritis, may mimic tremors and salivation, which may be mistaken for neurologic signs.

In any seizing ferret, direct the initial treatment toward arresting seizure activity. Check the blood glucose concentration immediately in any ferret presenting with seizures, ataxia, or other neurologic signs. If the glucose level is lower than 60 mg/dL, administer an intravenous (IV) bolus of 50% dextrose solution (diluted 1:1 in crystalloid fluid) at a dose of 2–5 mL/kg, or titrate to effect.¹⁸ Begin a dextrose drip infusion adequate to maintain normoglycemia while performing further diagnostic testing. Some ferrets require as much as 10% dextrose added to IV fluids to achieve normoglycemia. Administer prednisone or prednisolone to hypoglycemic patients to enhance hepatic gluconeogenesis and inhibit glycogenolysis. If an insulinoma is suspected, consider initiating additional treatment, such as diazoxide.

If seizures persist and the blood glucose concentration is normal (or has been restored to normal), begin aggressive seizure management, extrapolating from treatment protocols developed for traditional small animals.⁶⁹ Administer diazepam (0.5–1.0 mg/kg IV) or midazolam (0.25–0.5 mg/kg IV); if venous access is not readily available, administer diazepam or midazolam intramuscularly, intranasally (for more rapid absorption), or rectally. Double the dose for rectal or nasal administration. Repeat up to three times to arrest seizure activity. If generalized or focal seizures persist, begin a constant-rate infusion (CRI) of midazolam (0.1–0.3 mg/kg per hour) or, if not accessible, use diazepam (0.1–1.0 mg/kg per hour); however, diazepam molecules tend to adsorb to plastic tubing. At the same time, to prevent seizure reoccurrence, initiate phenobarbital by bolus; use 3 mg/kg slow IV up to a total dose of 18 to 24 mg/kg over the first 24 hours, then 3 mg/kg every 12 hours. Phenobarbital and diazepam can be administered concurrently. Levetiracetam (20 mg/kg IV) can also be considered, using a high initial dose (60 mg/kg once) to provide rapid seizure control.

Use of propofol is controversial and should be considered only as a last resort in an attempt to control seizure activity.⁵³ Administer in aliquots of 2 mg/kg to effect, then 6 mg/kg per hour via CRI to effect. If increased intracranial pressure is suspected (e.g., as evidenced by stupor, anisocoria, bradycardia in the presence of systemic hypertension), use mannitol (0.5–1.0 g/kg IV over 20 minutes) or hypertonic saline solution (NaCl 7.5% dosed at 2–4 mL/kg over 5–10 minutes). Dexamethasone can be used in case of meningoencephalitis (0.2 mg/kg) or in case of vasogenic edema (e.g., in the presence of a brain tumor).

When no seizures have occurred for 6 hours, taper the diazepam or midazolam infusion slowly. Once seizures are controlled, use oral phenobarbital (1–2 mg/kg orally [PO] every 12 hours or levetiracetam (10 mg/kg PO three times daily), if necessary, for long-term seizure management. Potassium bromide can also be used for seizure control; it is administered at 70–80 mg/kg PO per day if used alone or at 22–30 mg/kg per day in combination with phenobarbital. Check blood levels of phenobarbital within 2 to 3 weeks after starting therapy; however, potassium bromide levels may not reach steady state for 60–90 days. Adjust dosages based on blood levels and clinical signs. To date, no pharmacokinetic study results are available

TABLE 10.2 Seizures: Differential Diagnosis in Ferrets

Classification	Classification
Immune-mediated	<ul style="list-style-type: none"> • Meningoencephalitis • Eosinophilic syndrome
Infectious	<ul style="list-style-type: none"> • Viral <ul style="list-style-type: none"> • Aleutian disease • Coronavirus • Distemper • Rabies • Parasitic <ul style="list-style-type: none"> • Toxoplasmosis • Sarcocystosis • Bacterial <ul style="list-style-type: none"> • <i>Streptococcus zooepidemicus</i> • Fungal <ul style="list-style-type: none"> • Cryptococcosis • Blastomycosis
Toxicity	<ul style="list-style-type: none"> • Ibuprofen • Permethrin • Organophosphate • <i>Clostridium botulinum</i> endotoxin
Trauma	<ul style="list-style-type: none"> • Traumatic brain injury
Congenital	<ul style="list-style-type: none"> • Skull / brain defect
Metabolic	<ul style="list-style-type: none"> • Hypoglycemia • Hypocalcemia
Idiopathic	<ul style="list-style-type: none"> • Idiopathic epilepsy
Neoplasia	<ul style="list-style-type: none"> • Osteoma • Granular cell tumor • Lymphoma
Degenerative	<ul style="list-style-type: none"> • Neuronal vacuolation

in ferrets for the use of phenobarbital, gabapentin, zonisamide, imepitoin, or levetiracetam. Investigate any underlying disease stimulating the seizure activity after the patient is stable (see Table 10.2 for differential diagnosis). A full complete blood count and plasma biochemical panel, including electrolytes, is recommended. Magnetic resonance imaging has better resolution than a CT scan for brain evaluation in exploring structural changes. Administer a contrast agent IV to enhance brain lesions. Whenever meningoencephalitis is suspected, attempt to collect a CSF sample.

SPINAL DISORDERS

Spinal Defects

Spinal defects can be either congenital or acquired. The most common congenital vertebral lesion in ferrets is a transitional vertebra.⁷⁰ Block and wedge vertebrae are also found (Fig. 10.5).⁷⁰ Spina bifida was described in one stillborn ferret.²⁷ Congenital vertebral lesions are not always clinical but may predispose to intervertebral disk herniation.⁴⁹ One case in a 3-month-old ferret involved congenital occipitoatlantoaxial malformation that caused severe neurologic signs, including nonambulatory tetraparesis and head tilt.¹⁰ Acquired spinal deformities include trauma and luxations. Because of

the increasing popularity of raw-meat diets, ferret kits can be affected by nutritional secondary hyperparathyroidism, which can result in the spontaneous fracture of long bones and severe spinal deformities (Fig. 10.6). Metabolic bone disease was also reported in association with a congenital vitamin D deficiency in a young ferret.⁷⁵

Intervertebral Disk Disease

There are several reports of intervertebral disk disease (IVD) in ferrets.^{21,49,55,63,77} The most commonly affected site is L2-L3.^{49,55,77} Clinical signs are similar to those seen in other mammals with IVD and may range in severity from mild postural deficits to complete paralysis. Predisposing factors, such as vertebral abnormalities or spondylosis, are sometimes reported.^{55,63} In two cases, ferrets with prolapse or herniation of an intervertebral disk presented with paresis or paralysis accompanied by postural reaction deficits caudal to the lesion.^{49,77} The ferrets affected ranged in age from 7 months to 6 years. Diagnosis of IVD is usually made with myelography, alone or in combination with CT (Fig. 10.7).

Surgical decompression is the treatment of choice for IVD. In two of the ferrets reported, hemilaminectomy was performed successfully and resulted in ambulatory recovery within 1 and 2 months after surgery, respectively.^{49,55} One case was successfully managed medically with physiotherapy and hydrotherapy.⁷⁷ For ferrets with paresis or paralysis, begin passive range-of-motion exercises with the affected limbs three to four times daily to prevent contracture. Gently massage muscles to enhance blood flow. Implement active exercise as early as possible to preserve muscle tone and stimulate neural return.³ Use guidelines for prognosis in IVD in companion animals based on the presence or absence of nociception and the duration of clinical signs.

Spinal Neoplasia

Chordomas and Chondrosarcomas

Chordomas are tumors that arise from remnants of notochord.²⁰ In ferrets, these tumors develop most commonly at the tip of the tail, but they have also been described in the cervical and thoracic regions (Figs. 10.4 and 10.8).^{1,13,14,22,35,71,83} Ferrets with cervical or thoracic chordoma can present with posterior paresis and ataxia localized to the area of the lesion (Fig. 10.8).^{71,83} In such cases, perform spinal radiography and myelography to identify a site for surgical approach.

Depending on the location, chordomas may be amenable to surgical resection; however, the one reported case of recurrence and metastasis of a chordoma in a ferret was that of a cervical chordoma that had been surgically excised.⁸³ Another ferret that was euthanized after presentation with a large cervical mass and a 1-week history of abnormal ambulation was diagnosed postmortem with a cervical chordoma that had metastasized to the lung.²² In the case of a ferret with a thoracic chordoma, clinical signs persisted in spite of decompressive surgery.⁷¹

In the tail, chordomas appear as lobulated, firm, nonencapsulated, ulcerated masses at or near the last caudal vertebra. Microscopically, these tumors consist of lobules of

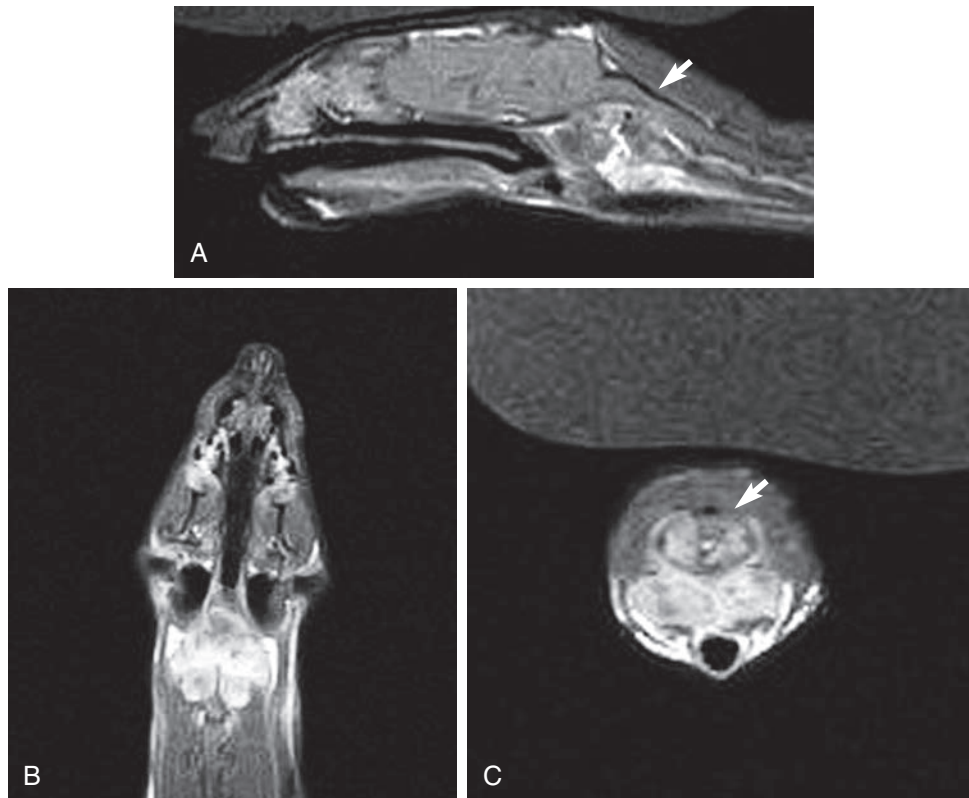


Fig. 10.4 (A–C) MRI of a ferret exhibiting ataxia with a cervical chordoma of C2-3. The spinal cord is compressed ventrally by the mass (*arrow, A*), which also caused lysis of the vertebral body (*arrow, C*) and extended into the base of the skull.

physaliphorous cells with areas of well-differentiated bone or cartilage throughout.^{14,36,83}

Chondrosarcoma of the tail has also been described in ferrets.³⁵ Clinical and morphologic descriptions are almost identical to those of chordoma. Differentiation must be made on the basis of immunohistochemical staining, with positive uptake of low-molecular-weight cytokeratin occurring in chordoma but not in chondrosarcoma.^{14,35} In ferrets with any distal tail mass, amputate several vertebrae proximal to the lesion. In cases of chordoma and chondrosarcoma, this is considered curative. Recurrence has not been reported.

Other Neoplasia

Invasion of the vertebral body and subsequent spinal compression have also been reported with lymphoma, fibrosarcoma, and histiocytic sarcoma (Fig. 10.9).^{34,61,81} A fibrosarcoma originating at T15-L2 metastasized to the lungs.⁶¹ A case of plasmacytoma eventually resulted in a fracture of the cranial articular vertebral process and spinal compression.⁴⁷ Treatment with surgical decompression and prednisone resulted in adequate mobility.⁴⁷ One case of adrenal neuroblastoma and one case of adrenal carcinoma in ferrets were reported to invade the vertebrae.^{37,54} Two cases of intramedullary neoplasia have been reported in ferrets: one case was a lymphosarcoma and the other a lumbosacral teratoma.^{39,42} Both carried a poor prognosis.

INTRACRANIAL DISORDERS

Neoplasia

In ferrets, osteomas of the skull can arise from the zygomatic arch, parietal bone, or occipital bone (Fig. 10.10).⁴⁰ There is also a report of a multilobular osteoma originating from the neck and extending from the base of the skull to C5, causing extradural compression of the spinal cord.³² Although these are benign neoplasms, clinical signs are related to physical displacement or compression of normal structures. Diagnosis is made via radiography. Biopsy may be difficult without surgical removal of the mass because of the extreme density of the tumor. Histopathologic evaluation usually reveals compact lamellar bone, bony trabeculae, and mild to moderate osteoblastic and hematologic activity.⁴⁰ Surgical removal is the treatment of choice and is usually curative if excision is complete.

A primary granular cell tumor (sometimes called a *myoblastoma*) was reported in the cerebrum of a ferret. Presenting signs included progressive head tilt, ataxia, and circling followed by refractory seizures.⁷⁶

Neuronal Vacuolation

Neuronal vacuolation was reported in one ferret that presented with rapidly progressive convulsions and incoordination.³⁰ Characteristic lesions were identified on histologic examination of tissue samples collected during postmortem examination.

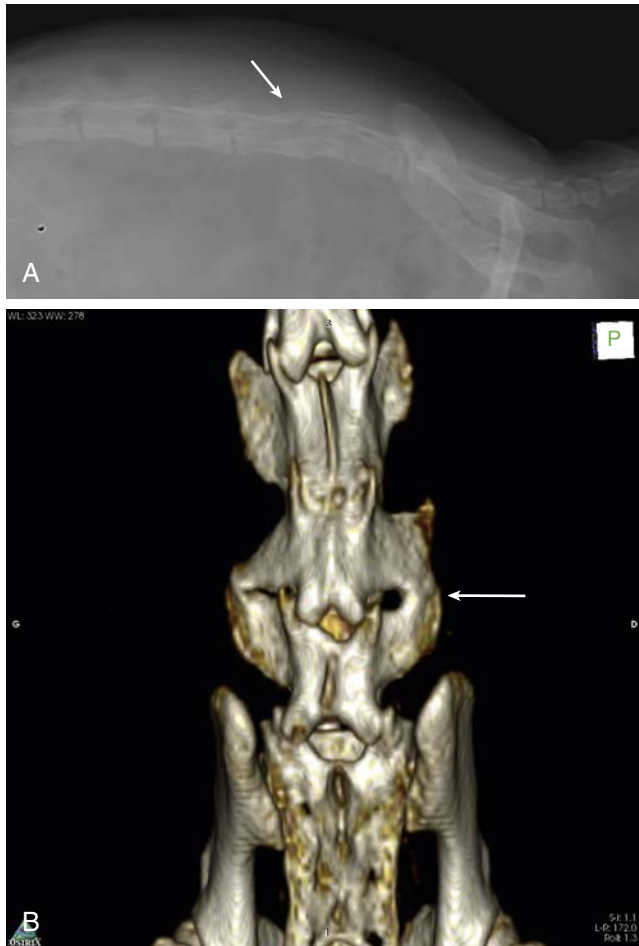


Fig. 10.5 Radiograph (A) and CT scan 3D reconstruction (B) of a bloc vertebra (*arrow*) between L4 and L5 causing hindlimb paresis in a ferret.

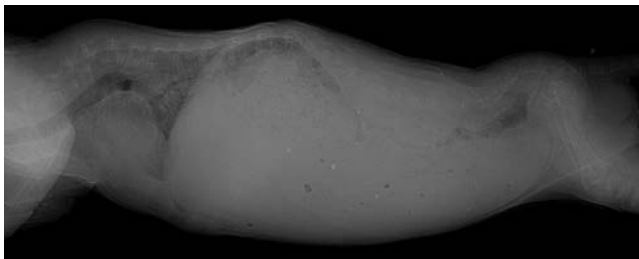


Fig. 10.6 Radiograph of a paretic ferret kit affected with metabolic bone disease from nutritional secondary hyperparathyroidism. Note the severe loss of bone density throughout, as well as vertebral deformities.

METABOLIC DISEASE

Hypoglycemia

Hypoglycemia is one of the main causes of neurologic signs in ferrets, with insulinoma being the most common cause. However, hypoglycemia potentially can be caused by various other diseases, including other forms of neoplasia, sepsis, starvation, hepatic disorders, or polycythemia vera. Notably, in a case series of lymphoma in ferrets, 4 out of 22 individuals exhibited low glucose levels.¹⁶ Four of nine ferrets affected with megaesophagus were hypoglycemic, presumably secondary to starvation and chronic regurgitation.⁶

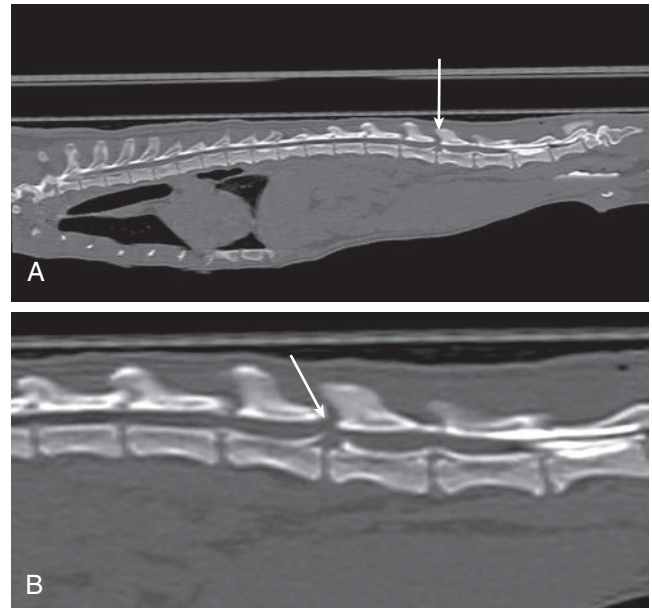


Fig. 10.7 (A) A contrast myelo-CT scan demonstrating an intramedullary compression secondary to intervertebral disk prolapse at L2-L3. (B,) Closeup of disk prolapse (*arrow*).

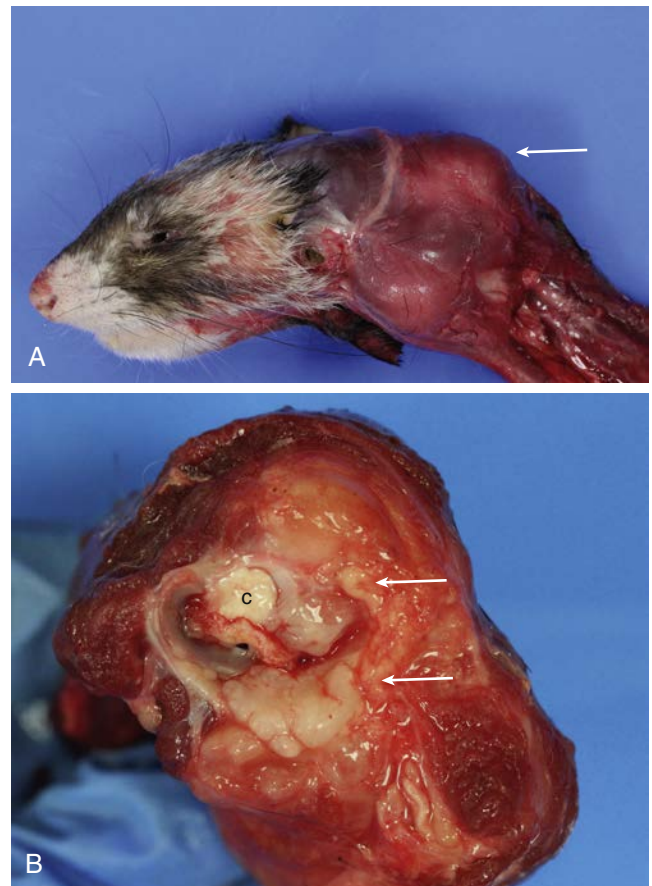


Fig. 10.8 (A) Ferret with a chordoma within the muscle of the neck, caudal to the skull (*arrow*). (B) Cross-section of the skull showing the chordoma infiltrating the epaxial muscles, cervical vertebra (*arrows*), and vertebral canal and impinging on the spinal cord (*c*). Photo courtesy K. Quesenberry.

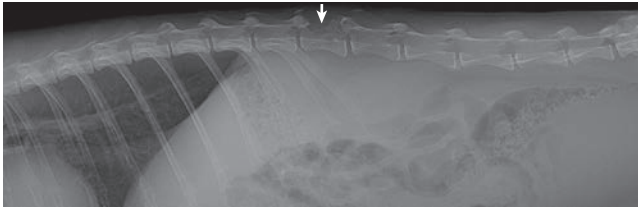


Fig. 10.9 Vertebral tumor affecting L1. Note the osteolysis of the vertebral process (arrow).



Fig. 10.10 Osteoma of the zygomatic arch in a ferret. Osteomas usually cause neurologic signs when located on a cervical vertebra or on the parietal bone.

Hypocalcemia

Primary hypoparathyroidism has been described as a cause of hypocalcemia in ferrets.^{11,52} Lethargy was reported consistently, in addition to intermittent seizures in one case. Diagnosis of primary hypoparathyroidism is supported by low total and ionized calcium levels, high phosphorus levels, and concurrent low parathyroid hormone (PTH) levels without renal impairment. Because PTH levels can vary throughout the day, it has been recommended in human medicine to collect samples at midmorning.⁵²

Treatment of primary hypoparathyroidism is based on administration of calcium gluconate during the hypocalcemic episode followed by maintenance treatment with calcium carbonate (25–50 mg/kg PO every 12 hours) and dihydrotachysterol (6.6 µg/kg every 12 hours to 24 µg/kg every 5 days). A phosphate binder, such as aluminum hydroxide, may be used to reduce high plasma phosphorus levels. Survival of 21–24 months was reported in response to daily supplementation.^{11,52}

Another condition called pseudohypoparathyroidism has been described in a ferret.⁸⁴ In this syndrome, plasma PTH levels are very high, but there is a lack of response to the hormone.

Nutritional secondary hyperparathyroidism can affect ferrets fed a meat-only diet that is not adequately supplemented with vitamins and minerals. A common cause in young, primiparous jills late in gestation is toxemia of pregnancy. Long bone fractures and deformities usually precede neurologic signs. In fact, although hypocalcemia, hypophosphatemia, and ketosis may develop, neurologic signs are rare unless hepatic lipidosis is so severe that encephalopathy is present.⁴ The differential diagnosis includes hypomagnesemia, hypoalbuminemia, acute pancreatitis, renal disease, and tumor lysis syndrome.

Toxicosis

There are very few reports of ferrets with neurologic signs secondary to toxin exposure. However, ibuprofen toxicosis can typically cause neurologic signs such as ataxia, tremors, and weakness, as well as renal compromise.⁷³ Doses greater than 200 mg/kg can be lethal.⁷³ *Clostridium botulinum* type A, B, and C endotoxin were reported to cause ataxia and ascending LMN paralysis in ferrets within 12–96 hours after ingestion of contaminated feed.⁷⁸ Anecdotally, permethrin toxicosis can produce neurologic effects in ferrets; however, there are no published case reports to support this assertion.¹⁵

INFECTIOUS DISEASE

Viral Disease

Rabies

Ferrets, as any carnivores, are susceptible to rabies.^{31,59,60} Clinical disease includes ascending paralysis, ataxia, cachexia, bladder atony, fever, hyperactivity, tremors, and paresthesia. Although usually fatal, one ferret experimentally inoculated with a rabies virus of skunk origin survived with paraplegia until being euthanized 180 days post infection.³¹ Rabies should remain in the differential list of any ferret with neurologic disease. Vaccination is strongly recommended—and, in some locales, mandated—to prevent rabies. Note that legislation may vary among states and countries regarding rabies vaccination and surveillance in ferrets (see [Chapter 2](#)).

Canine Distemper

As discussed in more detail in [Chapter 6](#), ferrets are sensitive to infection by canine distemper virus (CDV), with clinical signs generally becoming apparent within 7–10 days after exposure. Neurologic signs appear in the late stage of the disease, usually after respiratory, dermatologic (inconsistent), and digestive signs. In the neurotropic phase, ferrets exhibit hyperexcitability, tremor, seizures, and coma.⁴⁴ The disease mortality rate approaches 100%, usually 12–16 days after infection with a ferret-adapted CDV strain and 21–35 days after infection with a canine CDV strain.⁴³ Diagnosis relies primarily on a thorough anamnesis (e.g., a ferret unvaccinated against CDV) and suggestive clinical signs. In addition, severe leukopenia is often noted one week after infection. Additional supporting clinical data include demonstration of eosinophilic nuclear inclusions on conjunctival scraping or lymphoid tissue samples, and increased protein levels and lymphocyte counts on CSF analysis. Definitive diagnosis is based on positive findings of reverse

transcription PCR testing of peripheral blood, conjunctival scrapings, CSF, or urine. To protect other hospitalized dogs or ferrets, isolate ferrets suspected of CDV. Ferrets should be protected by vaccination against CDV (see [Chapter 2](#)).

Aleutian Disease

Aleutian disease is caused by Aleutian disease virus, a parvovirus that was originally reported in mink but can also infect ferrets (see [Chapter 5](#)). Some infected ferrets may be asymptomatic but remain persistently infected, or the disease may be self-limiting and nonpersistent.⁸² In other ferrets, associated neurologic signs may vary from mild incoordination to posterior ataxia, ascending paresis, persistent tremors, and quadriplegia.⁷⁹ Clinical signs in one outbreak developed as soon as 24 hours or as long as 90 days after exposure.⁷⁹ The most significant biochemical abnormality is hypergammaglobulinemia, with gamma globulin concentrations increased to greater than 20% of the total serum protein concentration. However, not all affected ferrets have high gamma globulin concentrations.⁸² Histopathologic changes involving the brain and spinal cord include perivascular cuffing with lymphocytes and sometimes plasma cells, nonsuppurative meningitis, astrocytosis, mononuclear cell infiltration, and focal malacia.⁸² Tentative diagnosis is based on a positive result of Aleutian disease virus serologic testing, high gamma globulin concentration, and the presence of compatible clinical signs; however, definitive diagnosis relies on demonstration of positive testing by PCR or enzyme-linked immunosorbent assay. Disease in suspected ferrets is confirmed by demonstration of lymphocytic and plasmacytic infiltrates on histologic examination of tissue samples collected at necropsy. The overall incidence of Aleutian disease in ferrets appears to be low; in one serologic study of 446 ferrets, the incidence of seropositive animals was 8.5%.⁸² Treatment consists of supportive care and isolation of suspected animals from unaffected ferrets.

Coronavirus

Systemic coronavirus (see also [Chapter 3](#)), which was first described in ferrets in 2004, has similarities to feline infectious peritonitis.²⁴ Although the disease is predominantly visceral; neurologic lesions may be present, associated with clinical signs such as hind limb paresis, ataxia, and seizures.^{24,66} An initial description of systemic coronavirus in 23 ferrets reported nonsuppurative meningoencephalitis in five animals and one case of pyogranulomatous lesions in the brain.²⁴ Diagnosis can be achieved with PCR or immunohistochemistry applied to biopsy samples. One case was more completely described on a CT scan that revealed contrast-enhancing extraparenchymal lesions.²⁶ Pyogranulomatous lesions were identified and systemic coronavirus infection was confirmed with immunohistochemistry.²⁶ Treatment is typically unsuccessful and relies primarily on controlling signs of inflammation with corticosteroids and supportive care.⁶⁶

Bacterial Disease

Streptococcus equi subspecies *zooepidemicus* has been isolated in a ferret as a cause of pneumonia and meningitis.⁵⁸ The ferret initially presented for head tilt and facial tics. The neurologic status

deteriorated rapidly, and the ferret was euthanized. Histologic findings were consistent with meningoencephalitis, and *S. equi* subspecies *zooepidemicus* was cultured from brain tissue.⁵⁸

Fungal Disease

Various fungal diseases are associated with neurologic manifestations in ferrets. Disseminated cryptococcosis can cause granulomatous meningoencephalitis and exudative chorioretinitis.^{29,74} Blindness, ataxia, and incontinence can be also be present, although lethargy, respiratory signs, and lymph node enlargement are more common.^{17,33,50,74} Diagnosis can be achieved by demonstration of intralesional yeast on fine-needle aspirates of infected lymph nodes and subsequent identification by PCR. In ferrets with granulomatous lesions, MRI studies may reveal a compressive mass in the spinal cord.⁷⁴ Treatment includes antifungal drugs, such as fluconazole (10 mg/kg PO every 24 hours) and itraconazole (15 mg/kg PO every 24 hours). In cases of chorioretinitis, prednisone 0.5 mg/kg every 24 hours may be added.

In one case of blastomycosis in a ferret, granulomatous lesions were present in the meninges and brain; however, clinical signs were predominantly respiratory.⁴⁵ Histoplasmosis has also been described in two ferrets, one of which exhibited seizures.^{19,41} However, most cases of histoplasmosis in ferrets are subclinical.¹⁹

Parasitic Disease

Toxoplasmosis

Ferrets are sensitive to toxoplasmosis (*Toxoplasma gondii*), although the disease is rarely reported and clinical manifestation appears to be rare. Farmed ferrets infected with toxoplasma cysts were reportedly asymptomatic.⁶⁵ In colonies of black-footed ferrets with toxoplasmosis, neurologic manifestations included posterior weakness, disorientation, depression, head tilt, and circling.⁸ Necrotizing nonsuppurative or granulomatous meningoencephalitis was found on postmortem examination.⁸

Toxoplasma may encyst in various tissues, including the brain, liver, muscles, and retina.⁶⁵ Transmission occurs when raw meat with encysted stages is ingested or by contact with cat feces containing oocysts. Serologic or PCR testing of CSF is used for antemortem diagnosis; however, histologic examination is the gold standard for definitive diagnosis. Treatment is sulfadiazine and pyrimethamine or clindamycin.⁶⁵

Sarcocystosis

One ferret infected with *Sarcocystis neurona* was presented for rhinitis and hindlimb paresis.⁷ Disseminated disease was diagnosed on histologic examination of brain tissue. *Sarcocystis* species are known to induce nonsuppurative meningoencephalitis in mink.⁶⁵

VESTIBULAR SYNDROME

Vestibular syndrome can be classified as peripheral or central. Peripheral vestibular syndrome, which involves the inner ear or the vestibular nerve, is primarily explored with



Fig. 10.11 CT scan of a ferret with a head tilt. Note the filling of the right tympanic bulla with radiodense material consistent with otitis media.

TABLE 10.3 Vestibular Syndrome: Differential Diagnosis in Ferrets

Classification	Examples
Inflammatory	<ul style="list-style-type: none"> • Meningoencephalitis
Infectious	<ul style="list-style-type: none"> • Otitis media/interna • <i>Otodectes cynotis</i> • <i>Toxoplasma</i> • <i>Streptococcus zooepidemicus</i>
Toxicity	<ul style="list-style-type: none"> • Ototoxic drugs
Traumatic	<ul style="list-style-type: none"> • Traumatic head injury
Congenital	<ul style="list-style-type: none"> • Congenital vestibular syndrome
Neoplasia	<ul style="list-style-type: none"> • Vestibular papilloma • Granular cell tumor • Cholesteatoma

otoscopy, CT, and/or MRI (Fig. 10.11). Central vestibular syndrome can arise from a brainstem, cerebellar, or thalamic lesion and is most reliably investigated with MRI.

Vestibular syndrome is rarely described in ferrets. The differential diagnosis is presented in Table 10.3. Otitis externa is relatively common in ferret, and infection with *Otodectes cynotis* infection has been implicated.⁴⁶ Complications include otitis media and otitis interna. Systemic antibiotic and anti-inflammatory drugs are needed. Primary otitis interna was diagnosed in a 4-year-old ferret.¹² No cause was identified and the ferret responded favorably to antibiotic and steroid therapy. Congenital vestibular syndrome with asymmetry of the inner ear, identified by MRI, was described in a 2-year-old ferret.⁵⁶ A choroid plexus papilloma originating from the fourth ventricle in a 6-year-old ferret caused head tilt, ataxia, and hemiparesis.⁸⁰ The mass was located by use of contrast-enhanced CT, and the diagnosis was confirmed by histologic examination of tissue samples. Another case involved a cerebral granular cell tumor in a ferret that presented for head tilt.⁷⁶

TABLE 10.4 Disseminated Idiopathic Myofasciitis: Treatment Plan⁶⁸

Drugs	Dosage
Prednisolone	<ul style="list-style-type: none"> • 1 mg/kg every 12 hours for 1 month and then every 24 hours until recovery
Cyclophosphamide	<ul style="list-style-type: none"> • 10 mg/kg SC on day 1 and day 14, then every 4 weeks for 3 months or until DIM is resolved
Chloramphenicol	<ul style="list-style-type: none"> • 50 mg/kg PO every 12 hours for 6–8 weeks

DIM, Disseminated idiopathic myofasciitis; PO, orally; SC, subcutaneously.

MUSCULOSKELETAL DISORDERS

Disseminated Idiopathic Myofasciitis

Disseminated idiopathic myofasciitis, also known as myofasciitis or polymyositis, was first described in 2003.²⁴ This disease affects young ferrets ranging from 5 to 24 months of age.²⁴ The clinical presentation can be very diverse and nonspecific, with signs including lethargy, inappetence, enlarged lymph nodes, a subcutaneous mass effect, green diarrhea, nasal and ocular discharge, coughing, or seizures.²⁵ Myofasciitis is often painful; thus most clinical signs are believed to be a consequence of hyperesthesia.⁷² Dysesthesia has also been described.⁷² Disease is usually acute or subacute in onset, and ferrets frequently present with a high fever (e.g., 104°F–108°F).²⁵ Some individuals may decline rapidly, whereas others remain in poor condition for months and ultimately die.⁷²

Hematologic findings are characterized by anemia and a marked neutrophilia with an occasional left shift. However, creatine kinase levels, which are usually a marker of muscle necrosis, are generally not elevated in affected ferrets. One theory for this unusual finding is that, although muscles are severely inflamed, histopathologic examination shows minimal muscle necrosis.⁷² Diagnostic imaging findings are nonspecific and usually performed to rule out other causes of hyperthermia. Antemortem diagnosis relies primarily on muscle biopsy. Open surgical biopsy samples collected from several sites are usually recommended, focusing especially on atrophied muscle and avoiding sites of previous injections. The vastus lateralis, cranial tibial, and triceps brachii muscles are the most easily accessed sites. Gross lesions can be subtle in acute cases but more obvious in chronic cases. Microscopic lesions are multifocal and include mild to severe suppurative to pyogranulomatous lesions involving the fascia between muscle bundles. A pathognomonic lesion is a circumferential transmural infiltrate in the muscular tunics along the entire length of the esophagus.

Several treatments have been attempted. In three confirmed cases, ferrets recovered after being treated with a combination of prednisolone, cyclophosphamide, and chloramphenicol (Table 10.4).⁷² Supportive care is crucial and includes nutritional management, fluid therapy, pain management, and gastrointestinal protectants. Acupuncture may be beneficial in some cases.⁷²

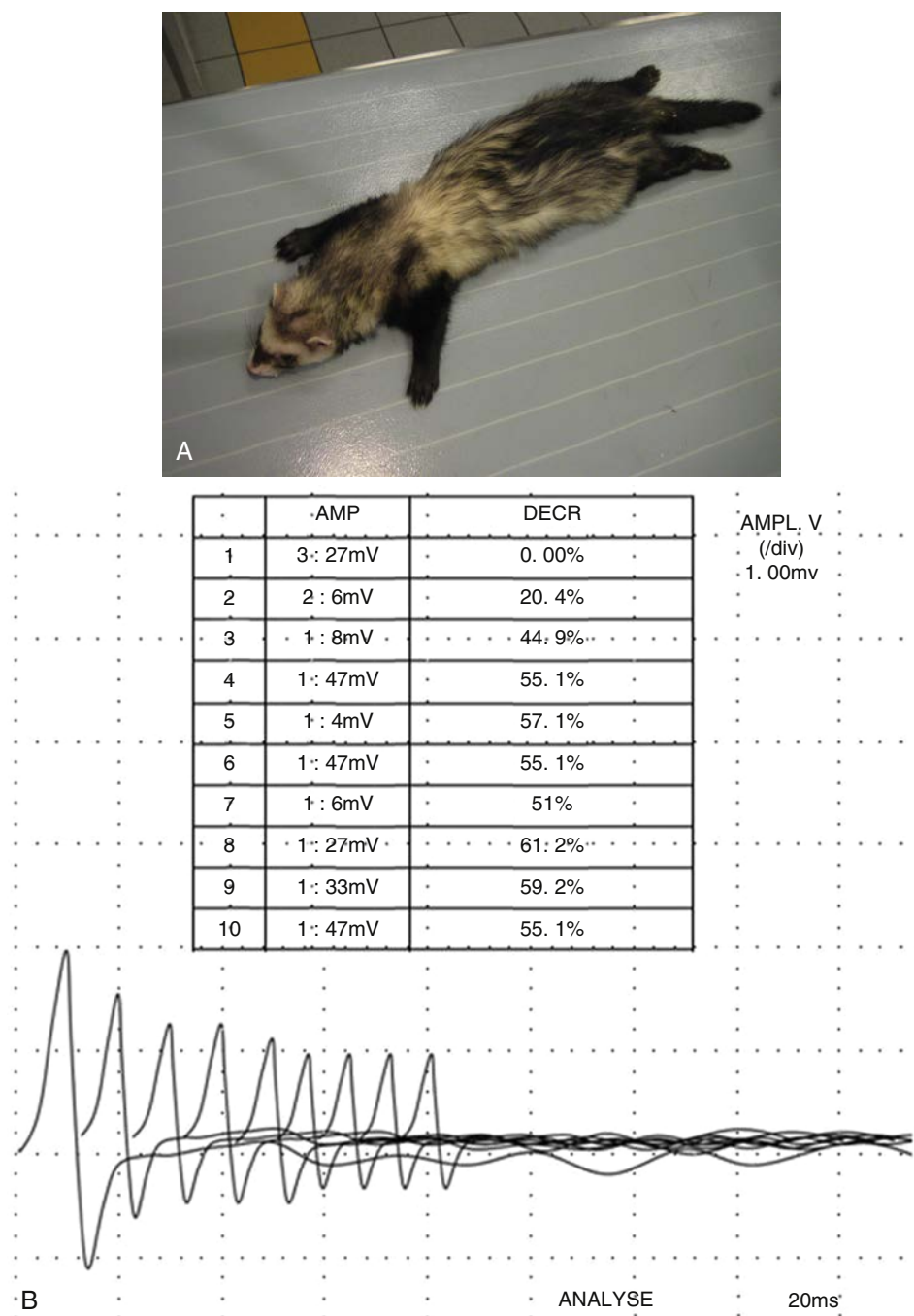


Fig. 10.12 Ferret affected by myasthenia gravis (A). Repetitive nerve stimulation (B) demonstrated a severe decremental response (>50%) of the compound action potential.

The cause of disseminated idiopathic myofasciitis remains unidentified.⁷² Similar lesions were inadvertently induced in ferrets during an experimental vaccine trial, and affected ferrets were known to have received at least one dose of canine distemper vaccine.²⁵ One distemper vaccine (Fervac-D; United Vaccines, Madison, WI) was suspected to induce the disease, especially after the number of cases decreased dramatically subsequent to removal of the product from the market in 2006. However, no clear relationship was established because of considerable variability between vaccination and the onset of disease. Furthermore, additional cases have been identified since

the vaccine was discontinued in the United States, as well as in Europe where the vaccine is not available.^{48,57}

Myasthenia

Myasthenia gravis is characterized by a defect in the neuromuscular junction caused by either an immune-mediated disease (acquired myasthenia) or a congenital defect of the acetylcholine receptor. The literature includes three case reports involving a 7-month-old ferret, a 4.5-year-old ferret, and a 6-year-old ferret, respectively.^{2,9,64} Clinical presentation included generalized weakness and paraparesis that progressed to tetraparesis (Fig. 10.12).

Diagnosis was made by nerve conduction velocity testing, which showed a characteristic decremental response of the compound muscle action potential with repetitive nerve stimulation.^{9,64} In all ferrets, response to cholinesterase inhibitor administration induced a dramatic resolution of the locomotor deficit. Levels of antiacetylcholine receptor antibodies were also elevated in all animals (normal value <0.06 nmol/L based on 5 normal ferrets).^{2,9,64} In one case, resolution of the condition has been associated with a return to baseline antibody titer.⁶⁴

Treatment with pyridostigmine bromide (0.5–1 mg/kg every 8–12 hours) may achieve normal mobility. However, overdosing may mimic signs of myasthenia gravis; therefore regular reassessments are necessary.² Because this condition may have an immunologic component, prednisolone may be beneficial in some cases.² The prognosis is guarded. In reported cases, one ferret died within 1 month and the other was managed for more than 2 years on medical therapy.^{2,9} Finally, one case recovered fully with pyridostigmine and prednisone therapy despite a lack of clinical response within the first 2 months, which suggests that supportive care and patience are crucial during the initial stage of the disease.⁶⁴

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