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AMERICAN COLLEGE OF VETERINARY INTERNAL MEDICINE

What Is Your Neurologic Diagnosis?

A 10-year-old 11.7-kg (25.7-lb) neutered male Patterdale Terrier was referred to a veterinary teaching hospital for evaluation of a 5-day history of sudden-onset progressive lethargy, pyrexia, hyporexia, cervical and left thoracic limb hyperesthesia, stiff thoracic limb gait, and low head carriage. Radiographic findings for the cervical region were unremarkable. Prior to the referral evaluation, the referring veterinarian had treated the dog with enrofloxacin for 3 days, and 2 days before referral, a dose of dexamethasone had been administered. Initially, the dog seemed to respond to this treatment, however on the day of referral the dog's condition deteriorated. On arrival at the hospital, the dog was in lateral recumbency; it could bear weight on all 4 limbs when placed in a standing position but was reluctant to walk. Physical examination revealed rectal temperature of 39.0°C (102.2°F), heart rate of 120 beats/min with strong femoral pulses that were synchronous with the heartbeat, respiratory rate of 24 breaths/min, and bilateral viscous mucoid discharge from the eyes. Hyperesthesia of the neck and both thoracic limbs was evident during manipulation of those regions.

Neurologic examination

Observation

Mental	Alert		Depressed	X	Disoriented		Stupor		Coma		
Posture	Normal		Head tilt		Tremor		Falling				
Gait	Normal		Ataxia		Pelvic limbs		All 4	X	Circling		
Paresis	Pelvic limbs		Tetra	X	Hemi		Mono				
Other	Low head carriage, short-strided thoracic limb gait, and wide-based stance and reduced stride height in the pelvic limbs										

Postural reactions

Key: 4 = Exaggerated, clonus; 3 = Exaggerated; 2 = Normal; 1 = Diminished; 0 = None; NE = Not evaluated.

	Left forelimb	Right forelimb	Left hind limb	Right hind limb
Wheelbarrow	NE	NE		
Hopping	1	2	2	2
Extensor postural thrust			NE	NE
Proprioceptive positioning	2	2	1 (mildly diminished)	1 (mildly diminished)
Hemistand/walk	NE	NE	NE	NE
Placing–tactile	NE	NE		
Placing–visual	NE	NE		

Spinal reflexes

	Left forelimb	Right forelimb	Left hind limb	Right hind limb
Quadriceps			2	2
Extensor carpi	2	NE		
Flexion	1 (markedly diminished)	1 (markedly diminished)	2	2
Crossed extensor	0	0	0	0
Perineal			2	2

Cranial nerves

	L	R
II, VII–Vision menace	2	2
II, III–Pupils resting	2	2
Stim L	2	2
Stim R	2	2
II–Fundus	2	2
III, IV, VI–Strabismus, resting	0	0
III, IV, VI, VIII–Strabismus, position	0	0

	L	R
VIII–Nystagmus, resting	0	0
VIII–Nystagmus, change	2	2
V–Sensation	2	2
VII–Facial mm	2	2
V, VII–Palpebral flex	2	2
IX, X–Gag	2	2
XII–Tongue	2	2

Comments
No response to nasal stimulation

Sensation (Locate and describe any abnormality)

Hyperesthesia	Present bilaterally in the thoracic limbs and axillary and cervical regions	Hyperesthesia was evident during flexion of right and left elbow and shoulder joints and on palpation of the ventral aspect of the cervical region. Range of movement of the neck was markedly reduced.
Superficial pain	NE	Not evaluated because voluntary motor function was present
Cutaneous reflex	2	Bilaterally normal
Deep pain	NE	Not evaluated because voluntary motor function was present

What is the problem? Where is the lesion? What are the most probable causes of this problem? What is your plan to establish a diagnosis? Please turn the page.

Assessment

Anatomic diagnosis

Problem	Rule out location
Decreased mentation and lack of response to nasal stimulation	Lesion within the somatosensory cortex of the forebrain or the ascending reticular activating system within the brainstem, or secondary to systemic disease or marked hyperesthesia in the cervical region and thoracic limbs
Progressive tetraparesis with short-strided gait in the thoracic limbs and reduced stride height in the pelvic limbs	Lower motor neurons or muscles of the thoracic and pelvic limbs or secondary to systemic disease or marked hyperesthesia
Postural deficits in the left thoracic limb; decreased hopping with normal proprioceptive posturing	C1-C5 or C6-T2 spinal cord segments, brachial plexus or peripheral nerves of the left thoracic limb, or secondary to marked hyperesthesia
Bilateral mild postural deficits in pelvic limbs; decreased proprioceptive posturing with normal hopping	C1-C5 or C6-T2 spinal cord segments or secondary to marked hyperesthesia
Markedly reduced withdrawal (flexor) reflexes with normal extensor carpi radialis reflexes in both thoracic limbs	C6-T2 spinal cord segments; brachial plexus; the musculocutaneous, median, and ulnar nerves; or neuromuscular junctions or muscles innervated by the musculocutaneous, median, and ulnar nerves
Low head carriage, markedly reduced range of movement in the cervical region, and hyperesthesia evident during palpation of the neck	Hyperesthesia secondary to inflammation or compression of the cervical spinal cord, meninges, spinal nerve roots, spinal nerves, vertebrae, articular facet joints, intervertebral disks, muscles, or tendons or ligaments

Likely location of 1 lesion

Both brachial plexuses were most likely affected. A lesion of the C6-T2 spinal cord segments was considered less likely because the pelvic limb deficits were not consistent with the degree of dysfunction in the thoracic limbs.

Etiologic diagnosis—On the basis of the sudden onset, progression, and neurolocalization of the dog's clinical signs, the primary differential diagnoses included inflammatory neuropathy or less likely myelopathy (immune-mediated or infectious cause [ie, toxoplasmosis, neosporosis, ehrlichiosis, anaplasmosis, or borreliosis]), neoplasia directly affecting the peripheral nervous system (eg, lymphoma) or within the vertebral column (eg, lymphoma, histiocytic sarcoma, or meningioma), or intervertebral disk disease (Hansen type I disk extrusion). The diagnostic plan included a CBC and serum biochemical profile (to evaluate for evidence of systemic involvement), MRI of the cervical portion of the vertebral column and both brachial plexuses (to evaluate for evidence of involvement of C6-T2 spinal cord segments, spinal nerve roots, spinal nerves, brachial plexuses, or peripheral nerves of the thoracic limbs), cross-sectional CT of the thorax (to evaluate for evidence of primary or metastatic neoplasia), and abdominal ultrasonography (to evaluate for evidence of primary or metastatic neoplasia). Infectious disease testing included serologic assessment for antibodies against *Toxoplasma* spp, *Neospora* spp, *Borrelia burgdorferi, Ehrlichia canis*, and *Anaplasma phagocytophilum* and microbial culture of blood and urine samples. Collection and analysis of a CSF sample was to be considered in light of the results of the initial diagnostic investigations.

Diagnostic test findings—The CBC revealed markedly high WBC count (33.0 × 10^9 cells/L; reference interval, 6 × 10^9 to 15 × 10^9 cells/L), predominately neutrophilia (30.7 × 10^9 cells/L; reference interval, 3.6 × 10^9 to 13 × 10^9 cells/L). The PCV was mildly low (35.7%; reference interval, 39% to 55%). The serum biochemical profile revealed marked hypoalbuminemia (16.5 g/L; reference interval, 26 to 35 g/L). Further investigations of the hypoalbuminemia involved a bile acids stimulation test (preprandial and postprandial bile acids concentration, 10.1 µmol/L and 10.0 µmol/L, respectively; reference interval, 0 to 10.5 µmol/L) and assessment of the urine protein-to-creatinine concentration ratio (0.79; values > 0.5 are indicative of proteinuria). The dog was anesthetized and with a 1.5-T MRI unit,[a] sagittal and transverse T1-weighted with and without fat saturation, sagittal and transverse T2-weighted, and dorsal and transverse T2-weighted STIR sequences of the cervical portion of the vertebral column, shoulders, and brachial plexuses were obtained. Following IV administration of a gadolinium-based contrast medium, T1-weighted images with and without fat saturation were obtained. Magnetic resonance imaging revealed bilateral thickenings of the brachial plexuses that extended to the associated peripheral nerves and were more pronounced on the left than the right. These lesions had high T2-weighted and STIR signals and were isointense on T1-weighted images and heterogeneously contrast enhancing on T1-weighted fat saturation images. Markedly high T2-weighted and STIR signals infiltrated the ventral thoracic soft tissues and the thoracic walls and axillary regions bilaterally, including the right and left superficial and deep

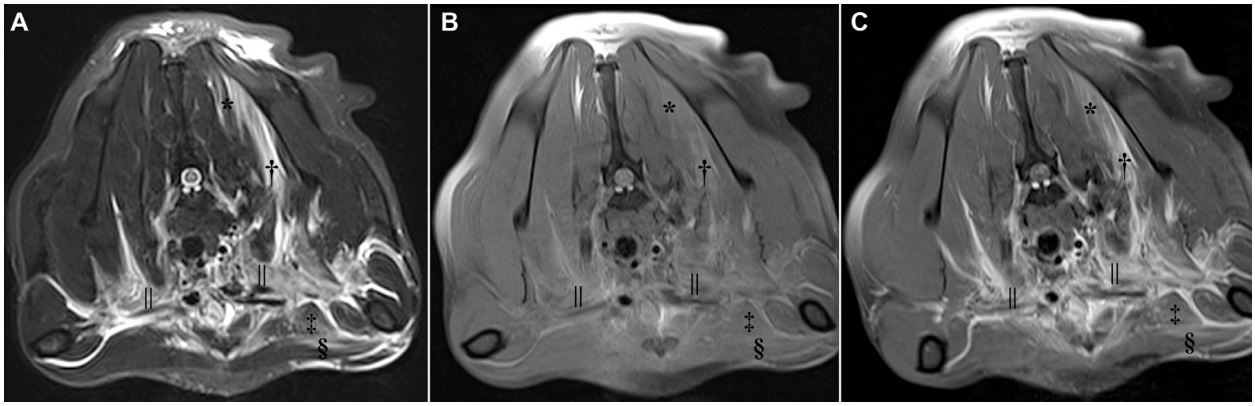

Figure 1—Transverse T2-weighted STIR (A), T1-weighted fat saturation (B), and T1-weighted post-gadolinium fat saturation (C) MRI images obtained at the level of the C7-T1 vertebrae in a dog that was evaluated for a 5-day history of sudden-onset progressive lethargy, pyrexia, hyporexia, cervical and left thoracic limb hyperesthesia, stiff thoracic limb gait, and low head carriage. Notice the marked STIR hyperintensity with homogeneous contrast enhancement of the left serratus ventralis muscle (asterisk), left subscapularis muscle (dagger), left deep pectoral muscle (double dagger), left superficial pectoral muscle (section mark), and both brachial plexuses (parallel mark).

pectoral muscles and the left serratus ventralis, teres major, latissimus dorsi, and subscapularis muscles **(Figure 1)**. These tissues were hyperintense and homogeneously contrast enhancing on T1-weighted fat saturation images. Bilateral axillary and left superficial cervical lymphadenomegaly was also present. An ultrasound-guided fine-needle aspirate specimen was obtained from the left axillary lymph node. Cytologic examination of the specimen yielded inconclusive findings. The population of lymphocytes in the specimen had mild signs of reactivity and focally moderate numbers of neutrophils were present, which could have been blood derived; however, the possibility of concurrent neutrophilic lymphadenitis could not be excluded. A CSF sample was not collected because the lesions were not associated with the CNS. A CT scan (following contrast medium administration) of the dog's thorax was performed with a helical CT scanner unit.[b] Settings used in image acquisitions were as follows: interval, 2 mm; thickness, 2 mm; 100 kV; and 170 mA. Thoracic CT revealed areas of increased attenuation within the right and left lung fields and lymphadenomegaly of the cranial mediastinal, sternal, tracheobronchial, prescapular (bilateral), axillary (bilateral), and hepatic lymph nodes. The soft tissues of the cervical region between C1 and C5 had areas of increased attenuation extending from the ventral to dorsal regions. There were similar changes within the left ventral thoracic soft tissues at the level of the C7-T4 vertebrae. Abdominal ultrasonography revealed that the liver was mildly enlarged and homogeneously hyperechoic with a single hypoechoic nodule (20 mm in diameter) within the left lateral liver lobe. An ultrasound-guided fine-needle aspirate specimen of this lesion was collected. Cytologic examination of the specimen revealed hepatocytes containing discrete lipid vacuoles and low to moderate numbers of blood-derived neutrophils. Blood samples were obtained from 3 peripheral veins for bacterial culture; cultures yielded no bacterial growth. A urine sample was collected via cystocentesis for bacterial culture, which also yielded no growth. Results of serologic testing for *Dirofilaria immitis* antigen and antibodies against *Borrelia burgdorferi, Ehrlichia canis*, *Anaplasma phagocytophilum*, *Toxoplasma* spp, and *Neospora* spp were negative.

On the basis of the dog's MRI findings, inflammatory neuritis bilaterally affecting the brachial plexuses and peripheral nerves of the thoracic limbs with associated myositis and edema of the cervical and thoracic subcutaneous tissues was considered the primary differential diagnosis. Given that the infectious disease test results were all negative, the disease process was considered likely to be of immune-mediated origin. Histologic examination findings for the hepatic nodule were consistent with nodular hyperplasia, and the lymphadenomegaly was considered most likely reactive. The CT findings for both lung fields were considered associated with recumbency-related atelectasis. Neoplasia was considered less likely because of the sudden onset of the clinical signs, the absence of metastatic lesions on diagnostic images, and the lack of detectable neoplastic cells in fine-needle aspirate specimens of a lymph node and the hepatic nodule.

The dog was treated IV with amoxicillin–clavulanic acid (20 mg/kg [9.1 mg/lb], q 8 h) and an anti-inflammatory dosage of dexamethasone (0.15 mg/kg/d [0.07 mg/lb/d]) while results of serologic testing and blood and urine cultures were pending. At first, multimodal analgesia was required to control the marked hyperesthesia and the dog received continuous rate IV infusions of fentanyl and lidocaine and twice daily IV injections of paracetamol (acetaminophen). After 48 hours of IV treatment with amoxicillin–clavulanic acid and dexamethasone, the dog was transitioned to orally administered medications (amoxicillin–clavulanic acid, 20 mg/kg, PO, q 12 h and prednisolone, 1 mg/kg/d [0.45 mg/lb/d], PO, q 24 h). The dog was discharged from the

hospital 5 days following admission; at that time, it was bright and alert with no evidence of hyperesthesia during cervical or thoracic limb manipulation and had a normal gait and normal withdrawal reflexes and proprioception in all 4 limbs. The analgesia plan was that the dog would receive paracetamol (10 mg/kg [4.5 mg/lb]) orally twice daily, which was discontinued after 10 days. Antimicrobial treatment was discontinued following receipt of the negative infectious disease test results. Oral treatment with prednisolone was continued at a tapered dosage (1 mg/kg/d for 8 weeks, followed by 0.6 mg/kg/d [0.27 mg/lb/d] for 4 weeks, 0.4 mg/kg/d [0.18 mg/lb/d] for 4 weeks, 0.2 mg/kg/d [0.09 mg/lb/d] for 4 weeks, and finally 0.2 mg/kg every other day for 4 weeks). Ten months after the onset of clinical signs and 4 months after completion of the tapered course of prednisolone, the owner and referring veterinary surgeon indicated that the dog appeared clinically normal and had had no signs of recurrence of clinical signs.

Comments

Bilateral dysfunction of the brachial plexuses is uncommon in dogs. To our knowledge, there are only 2 previous reports[1,2] of bilateral brachial plexus neuritis in dogs. In 1973, Cummings et al[1] published a case report of sudden-onset thoracic limb paresis in a 9-month-old sexually intact female Great Dane with flaccid paresis of the thoracic limbs and normal demeanor but there was no mention of hyperesthesia. A neurologic examination of that dog revealed multifocal peripheral nerve dysfunction involving the thoracic limbs, femoral nerves, and right facial nerve. The dog had been started on a horse-meat diet 16 days prior to the onset of paresis and had developed generalized urticaria and facial edema 2 days prior to the onset of paresis. Immunologic testing revealed a marked reaction to horse serum, and the dog's disease was suspected to be immune-mediated in origin. Treatment with corticosteroids, tetracycline, and hydrotherapy did not result in an improvement in the dog's condition; the dog developed bilateral wasting of the thoracic limb musculature and was euthanized 49 days following the onset of neurologic signs. Postmortem examination revealed neurogenic atrophy of the thoracic limb musculature and to a lesser extent the axial musculature and advanced Wallerian degeneration within the brachial plexuses, thoracic limb peripheral nerves, and the left hypoglossal nerve.

In 1974, Alexander et al[2] described a case involving an 18-month-old neutered female Doberman Pinscher that had thoracic limb paresis, previous hyperesthesia, an abnormal gait with over-reaching of the thoracic limbs, and muscle atrophy. Results of a neurologic examination suggested a peripheral neuropathy of the thoracic limbs, and segmental degeneration was identified on histologic examination of a biopsy specimen of the cutaneous branch of the radial nerve. No treatment was initiated, and there was a slight improvement in the dog's gait 4 months following the onset of clinical signs.

Both of those case reports commented on similarities of the dogs' condition with those of a condition in humans, which is known as Parsonage-Turner syndrome (PTS) and is also referred to as idiopathic brachial plexopathy or neuralgic amyotrophy. Typically, PTS is associated with peracute onset of unilateral, severe, incapacitating shoulder pain that can extend to the upper arm, forearm, and hand but that is usually self-limiting. Paresis may develop a few days to weeks following the initial onset of clinical signs.[3] Less commonly, asymmetric bilateral involvement develops; such bilateral involvement is evident not only from clinical signs but also results of electromyography or MRI.[4] The paresis is usually progressive, and after 1 month, associated muscle atrophy is often detectable. Various risk factors, most commonly recent viral illness or recent vaccination, have been linked with PTS. It has been postulated, therefore, that PTS is a result of viral infection of the brachial plexus or is an auto-immune response to the viral infection or to viral antigen in vaccines.[3] The most common MRI finding is diffuse, high, T2-weighted signal intensity within the nerves originating from one or both brachial plexuses and the associated muscles. Most commonly, the muscles innervated by the suprascapular nerves are affected with some involvement of the axillary and rare involvement of the subscapular nerves. The MRI findings are thought to be indicative of denervation injury.[4]

Similar to the clinical signs of PTS in humans, the dog of the present report had marked hyperesthesia on manipulation and palpation of the thoracic limbs and axillary and cervical regions. Bilateral brachial plexus involvement was suspected on the basis of neurologic examination findings and was confirmed with MRI. Three days prior to the onset of clinical signs, 2 ticks had been removed from the dog; this may have represented the source of foreign antigenic stimulation. The dog of the present report was treated early in the course of the disease, and therefore, we cannot know whether marked muscle atrophy would have developed or the hyperesthesia would have been self-limiting. However, multimodal analgesia was required to achieve pain control, which did not correlate with treatment requirements for humans with PTS or for the dogs of the previously reported cases.[1,2]

In 2009, Freeman et al[5] published a case report of a 2-year-old neutered female domestic shorthair cat that developed sudden-onset bilateral thoracic limb paresis. Neurologic examination revealed muscle atrophy, paresis, decreased spinal reflexes, hyperesthesia of the thoracic limbs, and reduced jaw muscle tone, all of which were suggestive of multifocal lesions of the brachial plexuses and trigeminal nerves. Abnormal spontaneous electrical activity in the cat's proximal and distal muscle groups in both thoracic limbs, the masseter muscles, and left cranial tibial

muscle was recorded. Abnormal motor nerve conduction with decreased amplitude and velocity in the radial and ulnar nerves was recorded. There was evidence of a conduction block in the left peroneal nerve, and delayed late action potentials across the left brachial plexus were detected. These findings were suggestive of an acute polyneuropathy, predominantly involving the brachial plexuses. On neurologic examination of the dog of the present report, there was no evidence of cranial nerve deficits or diminished spinal reflexes in the pelvic limbs. However, no electrodiagnostic testing was performed to assess more subtle changes in the pelvic limbs. The cat described by Freeman et al[5] initially improved without treatment but relapsed 2 months later with tetraparesis, which also improved without treatment; 13 months later, the owner considered the cat to be normal. Conversely, the condition of the dog of the present report markedly improved following corticosteroid treatment, and there was no evidence of recurrence at 4 months after completion of a 6-month tapering treatment protocol with prednisolone.

For humans with PTS, the long-term prognosis is considered good, and 36%, 75%, and 89% of patients recover full strength in the affected limb or limbs within the first, second, and third years after the onset of clinical signs, respectively. Treatment usually involves analgesia during the initial painful phase and physiotherapy to counteract the muscle atrophy.[6] The use of prednisolone and physiotherapy has been discussed in 1 report,[6] but the authors found there was no evidence that the use of prednisolone affected the course of disease, and patients treated with physiotherapy did not recover more quickly than those not treated with physiotherapy. However, that patient sample was small and individuals were not matched in any manner, so the validity of that statement is questionable. Of the cases reported in the veterinary medical literature, 1 dog's condition slightly improved over a period of 4 months[2] and another dog was euthanized because of progression of clinical signs following treatment with a corticosteroid and tetracycline[1]; for an affected cat, its condition improved without treatment, relapsed, and then improved again, after which the cat was considered normal.[5] The dog of the present report responded well to corticosteroid treatment and did not develop marked muscle atrophy. It is possible that this dog was in a subacute stage of the disease (preceding the onset of thoracic limb paresis or paralysis) when treatment was initiated; therefore, corticosteroid treatment combatted the inflammatory process before a combination of neurogenic atrophy and disuse atrophy was able to develop. As a result, there was no requirement for intensive physical therapy and no protracted recovery period for this dog. Moreover, considering the discrepancies in the onset and clinical signs among all 4 veterinary cases (including that described in the present report), we cannot rule out the possibility that the animals had different diseases, all of which affected the peripheral nerves of the brachial plexuses.

In veterinary and human medicine, the reason that the brachial plexuses are more specifically affected, compared with other peripheral nerves, remains unclear. Lymphocytes obtained from humans with PTS were found to increase their blastogenic activity when cultured with extracts of different brachial plexus nerves and branches but not when cultured with extracts of sacral plexus nerves, suggesting an immune-mediated response to the nerves specific to the brachial plexus.[7]

Footnotes

a. Magnetom Avanto, 1.5 Tesla MRI System, Siemens, Camberley, England.
b. Somatom Definition AS, Siemens, Erlangen, Germany.

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