Clinical cases of neurological disease in foals

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Abstract

Recognizing neurologic disease in neonatal foals is important since many neonatal diseases (e.g., not nursing, lethargy, dysphagia, reduced or lack of muscle tone, weakness, and recumbence) have similar signs. Two most common causes of hospitalization in intensive care units during the neonatal period are sepsis and neonatal maladjustment syndrome. Systemic illness can result in or aggravate neurologic disease. Therefore, it is equally important to perform a complete physical examination and diagnostic blood work in a diseased foal. Metabolic derangements (e.g., hyper- or hyponatremia, hypoglycemia, hyperammonemia, and hyperbilirubinemia) have profound effects on the brain. These derangements, if left untreated, are fatal. Congenital anomalies must be considered as possible causes of disease in the neonatal period. Functional neuroanatomy (with examples of clinical cases) is reviewed.

Keywords: Foal, congenital, encephalopathy, malformation, neonate, neurology

Neuroanatomical localization

Main divisions of the nervous system are brain, spinal cord, and peripheral.[1-3] The brain has 3 functional anatomical areas: cerebrothalamus, brainstem, and cerebellum.[2] Spinal cord consists of spinal cord segments: C1 – C5/6, C6 - T2, T3 - L3, L4 - S2, S-caudal.[1-3] Peripheral system consists of nerve rootlets, roots, ganglia, nerve, and neuromuscular junction.[2,4] This section is illustrated with examples of disease localized to the various regions of the nervous system.

Cerebrothalamus

In cerebrothalamic disease, 1 or more of the following signs might be observed; behavior alterations (compulsive, bizarre, manic, and vocalization [Figure 1]), lack of mare bonding and udder seeking, initiation of movement, central blindness, wide circling ipsilateral to the lesion, seizures, contralateral decreased nociception, and contralateral proprioceptive deficits. Examples of diseases include hypoxic/ischemic encephalopathy, metabolic encephalopathies (ammonia, sodium disorders, hypoglycemia/neuroglycopenia [low glucose concentration in the brain], bilirubin/kernicterus [from neonatal isoerythrolysis, Figure 2]), trauma, neoplasia (rare), hereditary epilepsies (Egyptian Arabian foals), and congenital anomalies/malformations (e.g., lack of corpus callosum).[1-6]

Brainstem

Signs that might be observed include altered state of consciousness or mental status (obtunded, stuporous, comatose), altered sleep, multiple cranial nerve deficits, and proprioceptive deficits.[2] Vestibular nuclei are located in the caudal brainstem; therefore, diseases affecting the caudal brainstem could cause central vestibular disease (i.e., trauma, infection, congenital anomalies).[2]

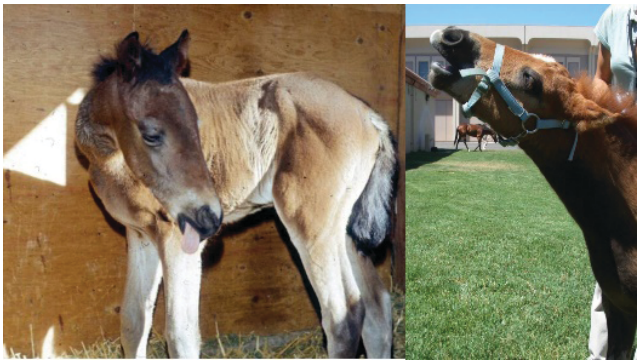

Figure 1. Cerebrothalamic disease characterized by altered behavior; note foal on the left with quiet 'dull' behavior and tongue protruding with lack of retraction. Foal on the right is displaying episodic opisthotonos and vocalization.

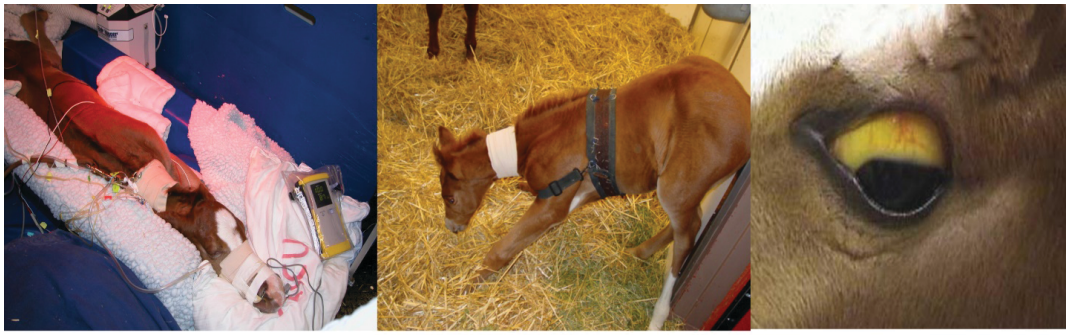

Figure 2. Metabolic encephalopathies. This group of diseases affect the cerebrothalamus and brainstem. Note the altered state of consciousness (foal on left) and behavior (middle); and evidence of icterus (right).

Metabolic encephalopathies, as mentioned previously, also affect the brainstem.[1] Congenital anomalies/malformations can cause brainstem disease.[1-3]

Cerebellum

Cerebellum 'hallmark' signs include intention tremors (tremors upon intended movement); hypermetria of all limbs, but more pronounced in the thoracic limbs; ataxia; with or without menace deficits that may be accompanied by anisocoria.[1-3] Examples of diseases include cerebellar abiotrophy in Arabian horses, cerebellar hypoplasia, Dany-walker syndrome, and congenital cysts.[6] Less commonly, movement disorders could be associated with specific areas affected in the cerebellum.

Spinal cord

Gait deficits (e.g., general proprioceptive ataxia, paresis) and upper motor neuron (UMN) or lower motor neuron (LMN) deficits depending on location within specific spinal cord segments were observed.[1-3,6] With involvement of LMN, weakness is also observed. However, weakness is a very common general sign of various neonatal diseases.[1] Trauma and infection are the most common causes of spinal cord disease in foals.[1,6] Congenital anomalies of the spinal cord and vertebral column can also occur.[1,6] Clinical signs of spinal cord disease (myelopathy) depending on location of disease might involve sensory and/or motor deficits.[1] Sensory deficits include proprioceptive (spinal) ataxia, proprioceptive and postural deficits, and abnormal sensation. Motor deficits include dysmetria, hypermetria or hypometria depending of UMN versus LMN disease. Paresis or paralysis could be from UMN or LMN disease, and weakness from UMN or LMN origin.[1,4] Weakness is profound with LMN disease.[4] In compressive myelopathies, both sensory and motor deficits are observed unlike in specific diseases (e.g., neuroaxonal dystrophy is mainly sensory deficits due to lesion localization to proprioceptive tracts and nuclei within the spinal cord and brainstem). Disease or injury affecting lower motor neurons will be characterized my motor deficits and weakness.[4]

Neuromuscular system

Neuromuscular system has central (lower motor neurons) and peripheral (nerve rootlets, roots, ganglia [sensory], nerves, and neuromuscular junction) components.[4] Neuromuscular disorders can be diffuse or can involve only a single nerve.[4] Diffuse neuromuscular disease induces generalized weakness, difficulty supporting weight, base-narrow stance, paresis or paralysis, muscle fasciculations, and tendency to become recumbent.[4] Segmental reflexes can be decreased or absent in neuromuscular disease.[4] The most common diffuse neuromuscular disease of foals is botulism.[3,4,6] Electrolyte imbalances affect the neuromuscular junction at multiple levels.[4] Focal LMN disease or neuropathy lead to specific signs pertaining to the region affected, such as specific gait deficits and focal muscle atrophy.[4] Foal with botulism and a foal with tetanus are depicted (Figure 3). Foal with botulism displays generalized weakness as noted by low carriage of head and neck and limbs placed under the thorax and abdomen. Signs of botulism result from the interference in the production, packaging, and/or release of acetylcholine vesicles at the presynaptic area of the neuromuscular junction by specific botulinum neurotoxins causing flaccid paresis to paralysis.[4] Foal with tetanus displays generalized rigidity and stiffness, flared nostrils, and a 'camped out' posture. *Clostridium tetani* toxins cause disinhibition of the inhibitory motor interneurons (Renshaw cells) in the spinal cord resulting in spastic paresis to paralysis.[4]

Diagnostic approach

Complete signalment and history are essential first steps in the investigation of any disorder.[1,5,6] Physical and neurological examinations must be performed. Neuroanatomical localization is essential and disorders that might present with clinical signs similar to neuromuscular dysfunction must be ruled out, particularly in the sick neonatal foal that has weakness, inability to rise, apparent decreased muscle tone, among others might be a common presentation for various disorders.[1,5,6] Complete blood work (CBC, chemistry panel, blood gases and pH), and urinalysis are part of base data collection.

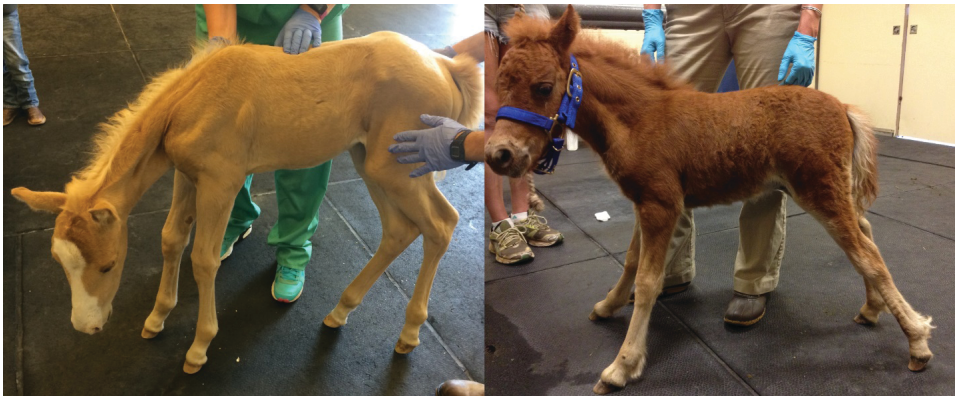

Figure 3. Disease caused by neurotoxins: botulism (left), tetanus (right). Note weakness from flaccid paresis in a foal with botulism as the result of inappropriate production and release of acetylcholine in the presynaptic membrane. Note foal with tetanus that has stiffness and rigidity from rigid paresis as the result of disinhibition of the Renshaw cells in the spinal cord. Also note grimace, flared nostrils, and ears pulled back.

Neuromuscular disorders on which muscle enzymes might be elevated include ionophores and organophosphate toxicity and those associated with tick infestation.[4] Electrolyte analysis should include ionized calcium (Ca^{++}) and magnesium (Mg^{++}), because they are physiologically active ions essential for neuromuscular homeostasis and function.[4] Cerebrospinal fluid (CSF) cytology is usually normal in neuromuscular disorders.[4] Toxicological screening of the diet, water, plants, soil, blood, stomach contents, feces, and body fluids including CSF might add useful information.[4] Consider imaging modalities if applicable (radiography, ultrasonography, scintigraphy, computed tomography and magnetic resonance). Examples of electrodiagnostics include electromyography (EMG), nerve conduction studies, single fiber EMG, and repetitive nerve stimulation (more specific for neuromuscular disorders).[4]

Diseases causing neurologic and neuromuscular disease

Examples of diseases affecting neonatal and older foals are summarized (Table 1). Also, the clinician should be aware that certain type of fluids and drugs might alter function or contribute to neuromuscular dysfunction.[4] Intravenous fluids that might alter the pH and therefore the binding of ionized electrolytes (e.g., calcium, magnesium) to proteins could change neuromuscular and nerve conduction.[4] Some examples of commonly used drugs that could alter neuromuscular function include lidocaine, procaine penicillin, aminoglycosides, tetracyclines, and metronidazole.[4] Complete list of drugs affecting neuromuscular junction is available.[4]

Table 1. Neurologic diseases in foals from Aleman AAEP proceedings 2015 (reprinted with permission)[1]

ANOMALOUS MALFORMATION	DEGENERATIVE	ENCEPHALOPATHY	FAMILIAL HEREDITARY	IATROGENIC	INFECTIOUS	TOXIC	TRAUMA	VASCULAR
Hydrocephalus	Neuroaxonal dystrophy (NAD)	Hypoxic ischemic encephalopathy	Juvenile epilepsy	Salt poisoining (milk replacer)	Meningitis	Polioencephalomalacia	Traumatic brain injury	Aneurysms
Hydranencephaly	Equine degenerative myeloencephalopathy (EDME)	Neonatal encephalopathy (non-hypoxic)	Lavender foal syndrome (*MYO5A*)	Drugs, fluids	Meningoencephalomyelitis	Leukoencephalomalacia	Spinal cord injury	Malformation
Anencephaly		Hepatic encephalopathy	Hydrocephalus Frisian foals *B3GALNT2*		Discospondylitis	Nigropallidal encephalomalacia	Nerve injury	Hematoma
Encephalomeningocele		Bilirrubin encephalopathy	Narcolepsy cataplexy		Osteomyelitis compromising neural structures	Botulism		
Cyclopia		Sodium disorders (hyponatremia, hypernatremia)	Sensorineural deafness (association with *EDNRB*)		Equine protozoal myeloencephalitis	Tetanus		
Cerebellar hypoplasia		Hypoglycemia: Neuroglycopenia	Lethal white foal syndrome (*EDNRB*)		*Halicephalobus gingivalis* meningoencephalomyelitis	Ionophores		
Occipito-atlanto-axial malformation			NAD		Rabies	Moxidectin		
Meningocele			EDME			Organophosphates		
Spina bifida			Cerebellar abiotrophy (Genetic marker)					
Syringohydromyelia			CVM (variants)					
Cervical vertebral malformation (CVM) and variants								
Vertebral column anomalies								

Conflict of interest

None to declare.

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