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Lavender Foal Syndrome (LFS)/Coat Color Dilution Lethal (CCDL)

Lavender Foal Syndrome (LFS), also known as Coat Color Dilution Lethal (CCDL), is a lethal neurological disorder that is caused by a mutation of the MYO5A gene on chromosome 1. Affected foals are born with a diluted coat color that can appear as pale lavender, pale pink, or silver. In addition to the unique color coat, affected foals are unable to stand, and experience episodes of tetany (intermittent muscle spasms, caused by malfunction of the parathyroid glands). During these episodes, the foal will lay on its side in a stiff manner and extend its limbs, neck, and back, and make paddling motions. In addition to this, delivery of affected foals is difficult due to their large size. Not all foals possess the diluted coloration; so many affected foals are often misdiagnosed with neonatal maladjustment syndrome, also known as "dummy foal" (Oke, Stacey). Dummy foals too have an association with difficult delivery. Genetic testing for LFS is available, and allows for easier differentiation between LFS and dummy foals. Despite the inability of affected foals to stand on their own to nurse, they may possess a strong suckle reflex, which enables them to be bottle-fed. There is no treatment for LFS, so affected foals will either die or be euthanized days after birth (Fanelli, H. H).

LFS is considered to be rare. It is also an autosomal recessive trait. Autosomal means that there is no sex linkage, causing both males and females to be affected equally. Recessive means that in order for a foal to be affected, the foal must have two copies of the mutated gene, inheriting one copy from each parent. A horse that has both a copy of the mutated gene and a copy of the normal gene are physically normal but are carriers. These horses have a 50% probability of passing the mutation to their offspring each time they are bred. In recent times, there has been a proposed linkage between LFS and Juvenile Idiopathic Epilepsy (Brooks, Samantha). Despite being associated with horses of Egyptian breeding, LFS has been reported in other bloodline groups. Individuals possess the ability to test their breeding stock to determine if their stock is clear of LFS, is a carrier, or is affected. Therefore, informed choices concerning breeding selections can be made so that another LFS affected foal may never be born (Oke, Stacey).

A study done by Equine Veterinary Education further examined various cases of LFS births in order to make practitioners more aware of the existence of LFS. In Case 4, a female Egyptian Arabian foal was born with assisted delivery. The foal failed to stand after passing through the sternum and exhibited episodes of the characteristic "paddling" associated with LFS. Join rigidity of the forelimbs was also reported. The foal possessed a coat with a slight silver hue. The foal was eventually euthanized, and a post mortem examination was conducted. The examination revealed no lesions in the organs, but large clumps of melanin (pigment responsible for the tanning of skin exposed to sunlight) were found in the hair roots and shafts. In Case 5, another female Egyptian Arabian foal was born unassisted. The foal was unable to stand and displayed episodes of paddling. The foal was euthanized, but was not examined posthumously. Lastly, this foal possessed a coat with a very pale chestnut color. In Case 6 a grey female Egyptian Arabian foal was born using an assisted delivery. The foal possessed a coat with a slight lavender hue. The foal also possessed a strong suckle reflex, however it could not stand. Rigidity in the forelimbs was reported, in addition to intermittent paddling episodes. Additionally, the foal's corneas exhibited ulceration and abrasions over pressure points. Examination of the head and neck revealed a normal skull and cervical vertebrae. The foal was treated for 6 days, but did not show any signs of improvement. The foal was subjected to euthanasia. Posthumous examination of the foal revealed zero lesions in the nervous system and organs. The foal did possess melanin clumps in its hair shafts and follicles. After comparing these cases, it was concluded that the clinical signs of LFS appears to represent a form of tetany caused by the "episodic diffuse release of extensor motor neurons resulting in extensor rigidity and opisthotonus (muscle spasms causing backward arching of the head, neck, and

spine). According to the author, by paddling, the foal may be trying to overcome the tetany in order to properly stand upright on its own. The author provides an alternative explanation for the paddling movements of the foal; being that the paddling episodes could also represent partial seizures due to uncontrolled neuron activity from a prosencephalic (congenital malformation in calves) disorder. Based on the nature of the signs exhibited by the foals, their fully functioning sensory apparatus, and the absence of normal periods between the episodes, the author favors the former interpretation. The author reports that foals that were kept alive with supportive treatments did not show any improvements and were then euthanized. The author then goes on to discuss the proposed relationship of LFS with benign epilepsy of Arabian foals. He states that both conditions occur in Arabian foals of Egyptian breeding. In Case 6, the male parent (stallion) of the filly (young female horse less than four years old), also produced a foal with benign epilepsy when it was bred to a different mare (female horse). In addition to this, Cases 4 and 5 provide a few puzzling factors; the normal foal, half-sibling to the foals in cases 4 and 5, with the dilute chestnut coat, which gradually darkened with age. Whether it was a LFS or an unrelated factor that caused this normal foal, is unknown. The author concludes by saying that LFS appears to be a biochemical lesion (a change that diminishes the fitness of an organism/or leads to a pathological condition) in the central nervous system that is involved in releasing lower motor neurons. (Figure 1, page 3) (Fanelli, H.H).

Additionally, a study published in the PLOS Genetics journal supported the recessive mode of inheritance for LFS. The researchers involved in the publication collected data from six affected foals. They were able to identify a single common ancestor from six to eight generations from the aforesaid six affected foals. The common ancestor was present on both sides of the pedigree in each of the foals. Considering this, this particular stallion may possibly represent a “founder” (loss of genetic variation that occurs when a new population is established by a very small number of individuals from a larger population) among the group, which supports “identity by descent” for the LFS mutation. The average inbreeding (Fi) was 0.0861 for affected foals, compared to 0.0394 for the parents of foals. The pedigree also enabled the researchers to calculate the coancestry coefficient between each living relative and the nearest affected foal in the pedigree. They predicted that the frequency of the LFS allele would be 0.42 among the 30 relatives used for genotyping. (Figure 2, page 4) (Brooks, Samantha).

According to veterinary neurologist, Dr. Alexander de Lahunta, “necropsy studies have found no gross or microscopic abnormality in the central nervous system of these foals. It is therefore suspected that a neurochemical or submicroscopic structural abnormality is the cause of the clinical signs.” (de, Lahunta). A protein called myosin Va, which is coded for by the MYO5A gene, is responsible for the movement and depositing of pigment, therefore affecting hair color. The mutation in the MYO5A gene causes a clumping of pigment particles, therefore causing the hair coat to have a diluted appearance. In addition to its involvement in altering coat color, the MYO5A gene is involved in neuron function. Considering this, the alteration in the normal coding for the MYO5A gene can explain the neurologic aspects involved in LFS (Oke, Stacey).

Recently, Cornell University and the Arabian Horse Foundation conducted a study in 2008 concerning LFS. The study was focused on locating the mutation responsible for LFS and developing a direct DNA test once the mutation was located. In order to do this, the researchers used a technology called single nucleotide polymorphism (SNP). Six samples were obtained from LFS affected foals. After analyzing these samples, the locus (specific location) of interest on chromosome 1 was identified. The genes found at this locus were further sequenced, and a single base deletion in the MYO5A gene was detected. Both the discovery and subsequent mapping of this mutation has been very beneficial for the development of a more advanced LFS test. Multiple labs provide LFS testing, such as the Cornell Animal Health Diagnostic Center (AHDC), VetGen, etc. Pricing for LFS testing varies between $35-$50 per test. (Minnich, Beth).

Figure 1.

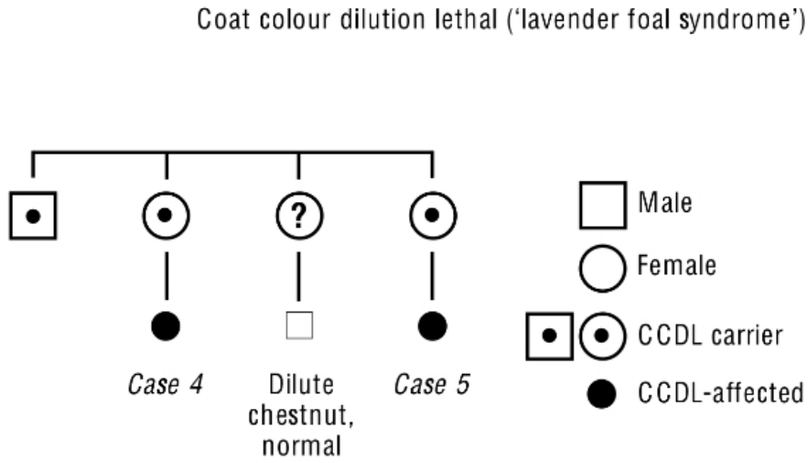


***Fig 6: Pedigree of the foals in* Cases 4 *and* 5.**

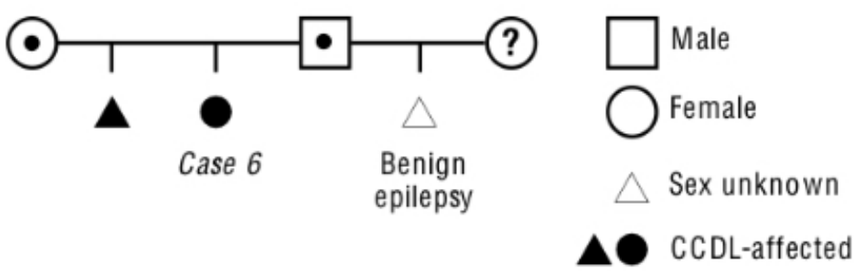
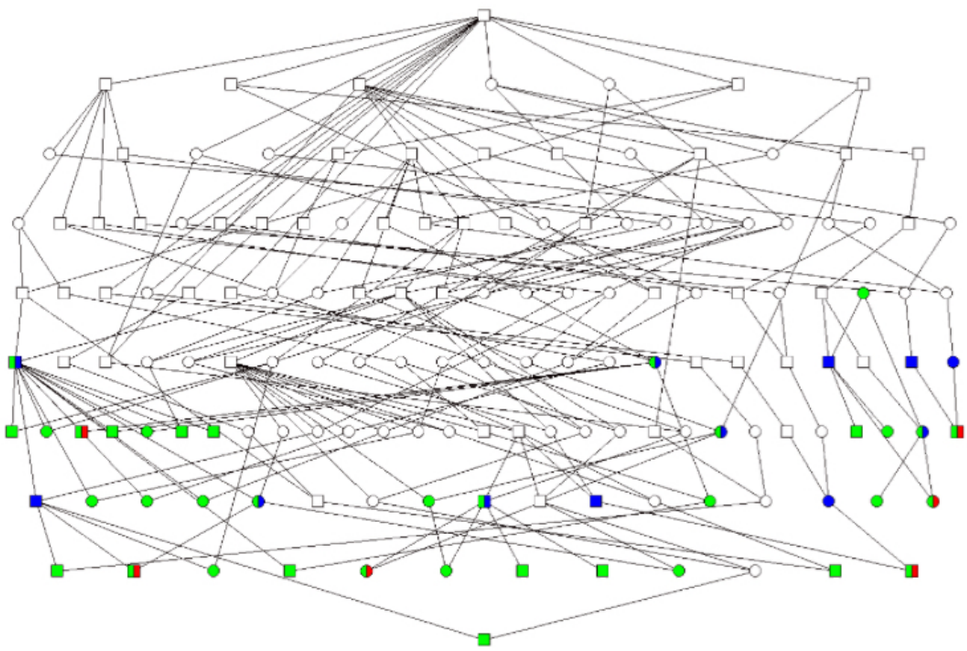


***Fig 5: Pedigree of the foal in* Case 6.**

Figure 2



Pedigree of horses used in this study. Red indicates affected, blue indicates carriers, and green highlights horses chosen for genotyping.

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