Atrophic myopathy in young pigs

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Summary: *A unilateral hind limb atrophic myopathy in 7- to 35-day-old pigs is described in this report. Clinical signs included knuckling of the metatarsal-phalangeal joint, plantigradism, inability to move, and dog-sitting posture. Histologic findings showed a clear muscular atrophy, sciatic nerve inflammation, and hemosiderosis in perisciatic and perimuscular connective tissue. We concluded that excessive iron injections were the cause of this problem.*

Locomotor disturbances resulting in obvious lameness are very common in pigs.[1] Lameness can be caused by mechanical injury, genetic abnormality, malnutrition, and infectious disease. The wide variation in causes of lameness make differential diagnoses of lameness, especially in individual animals, very difficult. Although lameness tends to be a sporadic problem affecting few animals, one may also see lameness outbreaks involving many animals. These tend to be the result of nutritional or infectious problems and usually affect the joints. Although rare, lameness outbreaks can involve muscles rather than the joints. These cases are referred to as myopathy (i.e., the non-inflammatory degeneration of skeletal muscles). About 90% of myopathy cases manifest muscular atrophy (i.e., a decrease in the amount of tissue following normal growth).[2] Atrophy may be seen in all tissues due to a reduced number or reduced size of cells or a combination thereof.[3] Atrophy of muscle is broadly defined as a reduction in size, but in the context of muscle disease, it also means a reduction in muscle fiber diameter or cross-sectional area.[4]

Muscular atrophy may result from a variety of causes, including the following differentials:

- denervation atrophy;
- atrophy following cachexia; and
- disuse atrophy.[5]

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There are some other causes of muscular atrophy in pigs, such as iron-induced atrophy[6,7,8] and some hereditary diseases.[9]

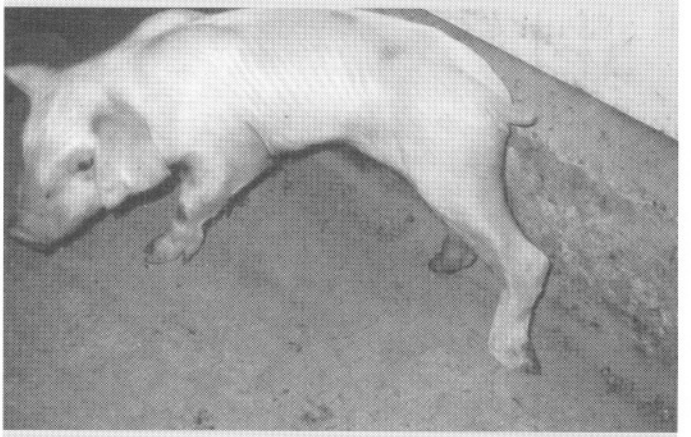
Materials and methods

Herd history and clinical evaluation

A 300-sow farrow-to-finish farm experienced a severe outbreak of locomotor problems in preweaned (< 28-day-old) and nursery (28- to 60-day-old) pigs. This outbreak was seen following previous infections by both *Streptococcus suis* and porcine reproductive and respiratory syndrome virus (PRRSV). *Streptococcus suis* infection occurred in April 1992 with central nervous system (CNS) clinical signs and some lameness, and PRRSV was documented in June 1992 with classic reproductive signs that diminished with time. Locomotor disturbances were first seen in February 1993 in nursery pigs and a week later in preweaned pigs. The outbreak lasted for several months and did not respond to antibiotics or *S. suis* autogenous vaccine.

During that time, 35% of the weaned pigs showed locomotor disfunction that included unilateral hind-limb knuckling of the metatarsal-phalangeal joint (7- to 21-day-old pigs, Figure 1), plantigradism (4- to 6-week-old pigs), inability to move, and dog-sitting posture (6- to 8-week-old pigs). About 30% of affected pigs were euthanized due to severe lameness or died from starvation.

Figure 1



Two-week-old pig showing a unilateral hind limb knuckling of the metatarsal-phalangeal joint. This clinical sign was seen as early as 7 days old.

Four successive groups of pigs were submitted to the Pathology Laboratory at Autonomous University of Barcelona. The first group was comprised of three 21- to 35-day-old pigs, which we euthanized and necropsied using the routine procedure but with special emphasis on CNS structures (brain and spinal cord). Two weeks later, a second group of three pigs (7–15 days old) was necropsied and samples of the hind leg musculature were taken. Three weeks later a third group of four animals (7–40 days old) were necropsied and a fine dissection of all hind leg muscles was performed. Finally, a fourth group of two animals (15 and 25 days old, respectively) was necropsied to perform a dissection of the whole sciatic nerve and hind-leg muscles.

Histopathology

Samples of various tissues were collected at necropsy, fixed by immersion in phosphate-buffered neutral 10% formalin, dehydrated, and stained conventionally with hematoxylin and eosin. These tissues included: brain, spinal cord (cervical, thoracic, and lumbar levels), skeletal muscles of hind limbs (biceps femoris, semitendinosus, semimembranosus, tensor fascia lata, vastum externum, rectum femoris, gastrocnemius, peroneus longi, extensor externum digitum, peroneum anterior, tibialis cranialis, extensor digitum, and interoseum), sciatic nerve, stomach, small intestine, colon, pancreas, liver, kidneys, bladder, lungs, heart, spleen, thymus, and lymph nodes. Samples from the sciatic nerve and skeletal muscles of the hind limbs were stained with Perls' to detect iron (Fe^{3+}) ions.

Immunocytochemistry

Sections of cervical, thoracic, and lumbar spinal cord at different levels, as well as brain piriform lobe from group 1 animals, were used to perform a standard peroxidase-antiperoxidase (PAP) technique in order to detect pseudorabies virus (PRV) using commercial polyclonal antibodies.

Bacteriology

Swabs of the brain's fourth ventricle from animals of groups 1 and 2 were cultured in a standard sheep's-blood agar culture medium in order to detect *Streptococcus suis*.

Results

Gross pathology

Other than the presence of decubitus ulcers, gross lesions were absent. Granulomatous and necrotic cyst tissue appeared sporadically in the biceps femoris of two animals (one from group 2 and the other from group 3). One of the pigs from group 2 was hydrocephalic with no evidence of muscular atrophy of the hind limbs.

Histopathology, immunocytochemistry, and bacteriology

Group 1

A discreet lymphoplasmocytic infiltrate was seen in the medulla oblongata in two of the three animals. One of these showed some perineural and perivascular edema. Immunocytochemistry was performed in these samples against PRV with negative results; bacteriology was also negative.

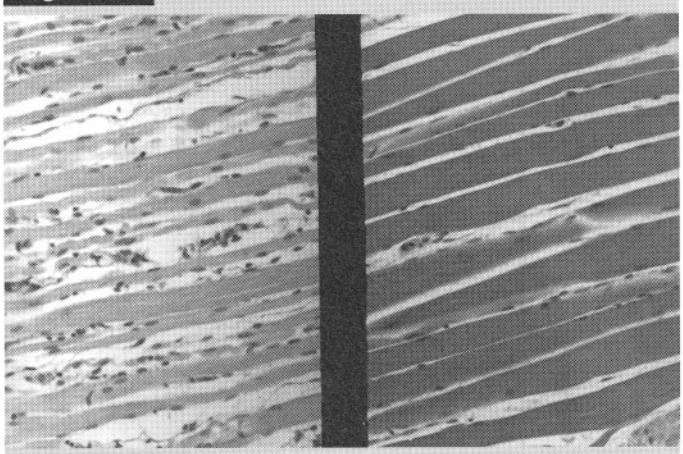
Group 2

Evident size reduction of some muscle fibers of the quadriceps femoris and loss of staining appetance for eosin were seen in two of the three animals (Figure 2). No other microscopic lesions were seen in these animals. Bacteriology was negative.

Group 3

Upon microscopic examination, Zencker's hyaline degeneration of the dorsal hind leg muscles including the semimembranosus and/or semitendinosus was seen in the younger pigs (7–15 days old). In the older pigs (30–40 days old) several muscles of one hind leg had evident atrophy, starting at midleg (at the level of gastrocnemius) in one of them and in the upper portion (at the level of semitendinosus) in the other (Table 1). Hemosiderin deposits were seen in perisciatic and perimuscular connective tissue, which were confirmed with Perls' stain (Figure 3).

Figure 2



Comparison between left and right quadriceps femoris muscle fibers at the same magnification (original magnification ×600). The right one is normal; the left shows a clear atrophy with rupture of muscular fiber and loss of staining capacity.

Group 4

A marked partial or total atrophy was seen microscopically in one hind leg of both animals. The older animal (25 days old) had the most severe lesions. These animals had areas of sciatic perineuritis, neuritis (Figure 4), and Wallerian degeneration (axonal degeneration) of some nervous fibers. Hemosiderin deposits were again seen in perisciatic and perimuscular connective tissue.

Discussion

Following our clinical observations, several differential diagnoses were contemplated, including: splayleg,[10] iron toxicity,[6-8, 11] *Strep-*

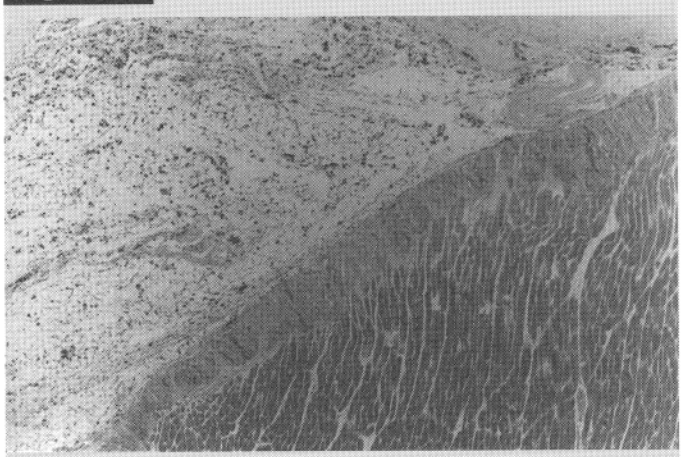
Table 1

Histologic lesions seen in the hind leg muscles in two piglets in group 3.

	Pig 1		Pig 2	
Muscle	**Left hind leg**	**Right hind leg**	**Left hind leg**	**Right hind leg**
M. biceps femoris	NML	NML	NML	NML
M. semitendinosus	NML	NML	NML	part. atrophy
M. semimembranosus	NML	NML	NML	part. atrophy
M. tensor f. lata	NML	NML	NML	NML
M. vastum externum	NML	NML	NML	part. atrophy
M. rectum femorus	NML	NML	NML	NML
M. gastrocnemius	part. atrophy	NML	NML	part. atrophy
M. peroneus longi	tot. atrophy	NML	NML	tot. atrophy
M. extens. e. dig.	tot. atrophy	NML	NML	tot. atrophy
M. peroneum anter.	part. atrophy	NML	NML	tot. atrophy
M. tibialis crani.	tot. atrophy	NML	NML	tot. atrophy
M. extens. digitum	tot. atrophy	NML	NML	tot. atrophy
M. interoseum	tot. atrophy	NML	NML	tot. atrophy
Sciatic nerve	NML	NML	NML; hemosiderosis	NML; hemosiderosis

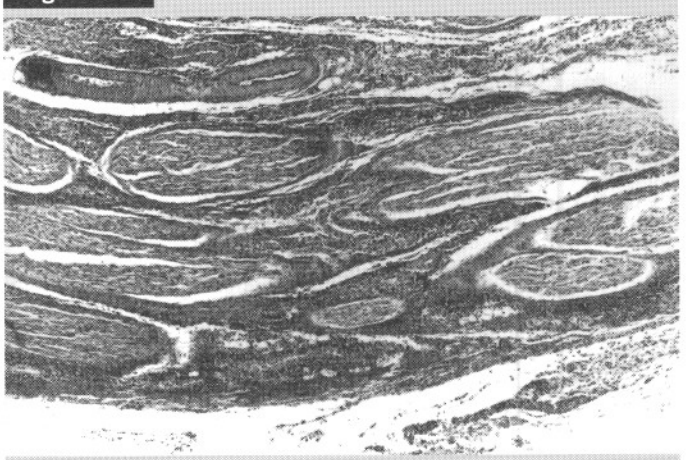
NML: no microscopic lesion; Part.: partial atrophy; Tot.: total atrophy.

Figure 3



Presence of hemosiderin in parimuscular connective tissue. The iron deposits are seen as black deposits in the photograph (original magnification ×300).

Figure 4



Sciatic perineuritis and neuritis in one of the animals of group 4 (original magnification ×600). A lymphoplasmocitary inflammatory infiltration is seen both in nerve fibers and perisciatic connective tissue.

tococcus infection, Teshen-Talfan disease, Pietrain creeper syndrome,[12] traumatism, and hereditary porcine neuronal system degeneration (HPNSD).[9] A definitive diagnosis was not possible based on the history or clinical observations. Histopathology techniques clearly showed that all of the necropsied animals were affected with unilateral skeletal muscle atrophy of the hind limb. This was particularly severe in the 30- to 40-day-old pigs, but could also be histologically observed in 50% of the 10- to 15-day-old necropsied animals. The extent of the lesion varied in each animal independent of the group. In some pigs, only the muscles below the gastrocnemius were affected, whereas in others the whole leg, from the semitendinosus down, showed some degree of atrophy.

Histologic lesions were incompatible with many of the initial differentials. Sciatic perineuritis and neuritis with axonal degeneration strongly suggested that irritation or trauma was responsible for the neural damage. Hemosiderin deposits could also be seen in perisciatic and perimuscular areas. Iron-induced trauma, resulting from iron injections, was the presumptive diagnosis.

A further visit to the farm showed that animals were receiving multiple iron-dextran injections, sometimes as late as 3–4 weeks of age. Also, these injections were being given by an unskilled worker. Because of this, it was not possible to conclude whether the lesions were the result of multiple iron injections or poor injection technique (using too-long needles, injecting in the wrong place, and/or excessive dosage). Following our recommendation,

excessive iron injections (other than at 2–3 days of age) were discontinued, and the injection technique was improved. Now only one iron injection in the first or second day of life is given. No further cases of locomotor disorders have been observed since April 1993, strongly suggesting that iron injections were the cause of this problem.

Several authors[7,8] have suggested that iron injections, especially iron dextrose, may be related to piglet myodegeneration. In fact, Fe^{3+} ions are particularly important in oxidative toxic damage. Fe^{3+} ions can be reduced to Fe^{2+} ions following Fenton's reaction,[13] where free radicals are created. The principal effects of this reactive Fe^{3+} species are on the membranes, lipids, sulphydril protein bridges, and DNA nucleotides. In the present case, since muscular and nerve tissues are very rich in cell membranes and lipids, the lipidic peroxidation caused by free radicals may be responsible for the muscular and sciatic nerve damage. It is probable that repeated injections and poor injection technique, rather than the compound used, were the cause of the problem, since iron-dextran solutions, when properly used, rarely result in obvious problems.

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