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WHITE MUSCLE DISEASE IN A SPANISH PUREBRED HORSE

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SIGNALMENT AND HISTORY

An 11-year-old, neutered male, Spanish Purebred horse was referred to the clinic because of a 72-hour history of dysphagia, hypersalivation, weakness and weight loss. During the last week a poor performance was detected and pigmenturia was seen in the last hours. The horse was treated with two suxibuzone doses (3.3 mg/kg PO) and one single dose of dexamethasone (0.1mg/kg, IV) without good response to the treatment.

PHYSICAL EXAMINATION

On general physical examination, the horse presented a body condition score of 4/9 with mild atrophy of gluteal muscles (figure 1), being otherwise normal. On neurological examination, dysphagia and diminished tone of the tongue was detected. Full exploration of the oral cavity and endoscopic examination of nasal cavity, pharynx and larynx were performed and no abnormalities were found.

INVESTIGATION

Haematology and biochemistry

Complete blood count (ADVIA 120) and serum biochemistry Olympus AU400, fibrinogen by heat precipitation method) were performed and results are listed in tables 1 and 2. Serum colour was unremarkable.

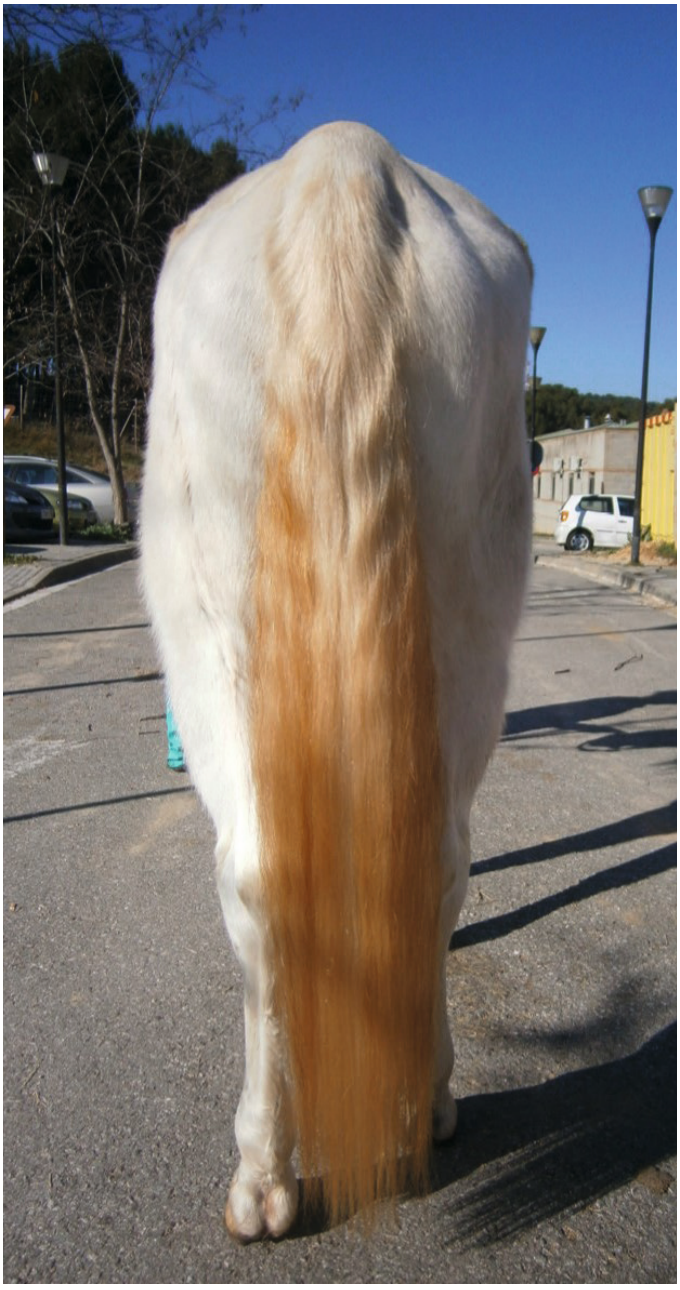

Figure 1: Note the evident muscular atrophy
Source: María Luisa Rodríguez Pozo

Table 1: CBC results

Parameter	Results	Reference intervals	Units
Hematocrit	29	32 – 53	%
RBC	6.36	6.8 – 12.9	$x10^6/\mu L$
Hemoglobina	11.5	11 – 19	g/dL
MCV	46.3	36 – 58	fL
MCH	18.1	10 – 20	pg
MCHC	38.1	31 – 36	g/dL
WBC	5.0	5.4 – 14.3	$x10^3/\mu L$
Segmented neutrophils	3.8	2.3 – 8.6	$x10^3/\mu L$
Band neutrophils	0	0 – 0.1	$x10^3/\mu L$
Lymphocytes	1.1	1.5 – 7.7	$x10^3/\mu L$
Monocyte	0	0 – 1.0	$x10^3/\mu L$
Eosinophils	0.1	0 – 1.0	$x10^3/\mu L$
Basophils	0	0 – 0.2	$x10^3/\mu L$
Platelets	198	100 – 350	$x10^3/\mu L$

Table 2: Serum biochemistry results

Parameter	Results	Reference intervals	Units
Albumin	3.3	2.6 – 3.6	g/dL
Creatinin	1.2	1 – 2	mg/dL
Urea	14	10 – 25	mg/dL
Total bilirrubin	2.9	0.9 – 3	mg/dL
GGT	10	5 – 30	U/L
AST	739	150 – 420	U/L
CK	81.860	60 – 350	U/L
Ionized Calcium	1.33	1.4 – 1.6	mmol/L
Sodium	138	134 – 144	mmol/L
Potassium	3.5	3.5 – 4.5	mmol/L
Fibrinogen	600	200 – 400	mg/dL

Urinalysis

A sample of urine was obtained (figure 2) and urinalysis was performed (table 3). A urine aliquot was centrifuged, and the supernatant was compared to an uncentrifuged aliquot. The supernatant remained equally discoloured and because no red blood cells were detected in the urine sediment, haematuria was ruled out.

Figure 2: Urine sample. Note the dark red-brownish colour.
Source: María Luisa Rodríguez Pozo

Table 3: Urianalysis results

Urinary density	1.025
pH	7.5
Glucose	Negative
Ketone bodies	Negative
Bilirrubin	Negative
Proteins	+
Blood	+++
Leucocytes	Negative
Sediments	Normal

QUESTIONS

1. What is your interpretation of the haematology?
2. Is the biochemistry giving you any hint in order to lead your diagnosis?
3. How is the urinalysis important in this case and how could it help you on your diagnosis?
4. What further test/tests could you do in order to confirm your diagnosis? What is your interpretation of the haematology?

What is your interpretation of the haematology?
Mild normocytic normochromic anaemia likely reflects anaemia of chronic inflammation. Mildly increase in MCHC is likely an artifact. Leukocyte concentration is almost normal. Mild leukopenia due to lymphopenia probably reflects a steroid response (stress).

Is the biochemistry giving you any hint in order to lead your diagnosis?
Mildly increased AST and markedly increased CK serum activity is presumably due to muscle damage. Hyperfibrinogenemia reflects ongoing inflammation

What is the most likely cause of urine discolouration in this case and how can urine help you on your diagnostic?
Because the patient had clear plasma and due to the brownish colour of the urine, **myoglobinuria** rather than hemoglobinuria was considered the most likely pigmenturia.

Based on the clinical history, clinical signs, the increased serum CK and AST activity and the pigmenturia (most likely myoglobinuria) a presumptive diagnosis of **non-exertional rhabdomyolysis** was made.

What further test/tests could you do in order to confirm your diagnosis?
With the clinical suspicion of nutritional myodegeneration, serum and EDTA blood samples were analysed for vitamin D, selenium concentrations and glutathione peroxidase activity determination (table 4). Biopsy and histopathological examination of the muscles would also help to better characterized the muscular lesions.

Table 4. Results of further tests

Parameter	Method	Results	Reference intervals	Units
Vitamina E	Ultra-performance liquid chromatography (UPLC) coupled to photodiode array detection (PDA)	1.7	> 4	µg/mL
Selenium	Inductively coupled plasma mass spectrometry (ICP-MS)	5.4	15 – 20	µg/dL
Glutathione peroxidase	Visible and ultraviolet spectroscopy	1.5		UI/g Hb

Results were consistent with vitamin E and selenium deficiency with markedly decreased antioxidant activity of the glutathione peridoxidase.

Tru-Cut **biopsies** of the gluteal muscle were also obtained (figure 3). Histopathological examination demonstrated fragmentation, hyalinization and generalized loss of muscular striation. Approximately a 25% of muscular fibers were replaced by fibroblasts and a mixed inflammation with macrophages, lymphocytes and plasma cells was present. Masson's trichrome staining revealed mild fibrosis in some areas of the muscle (figure 4).

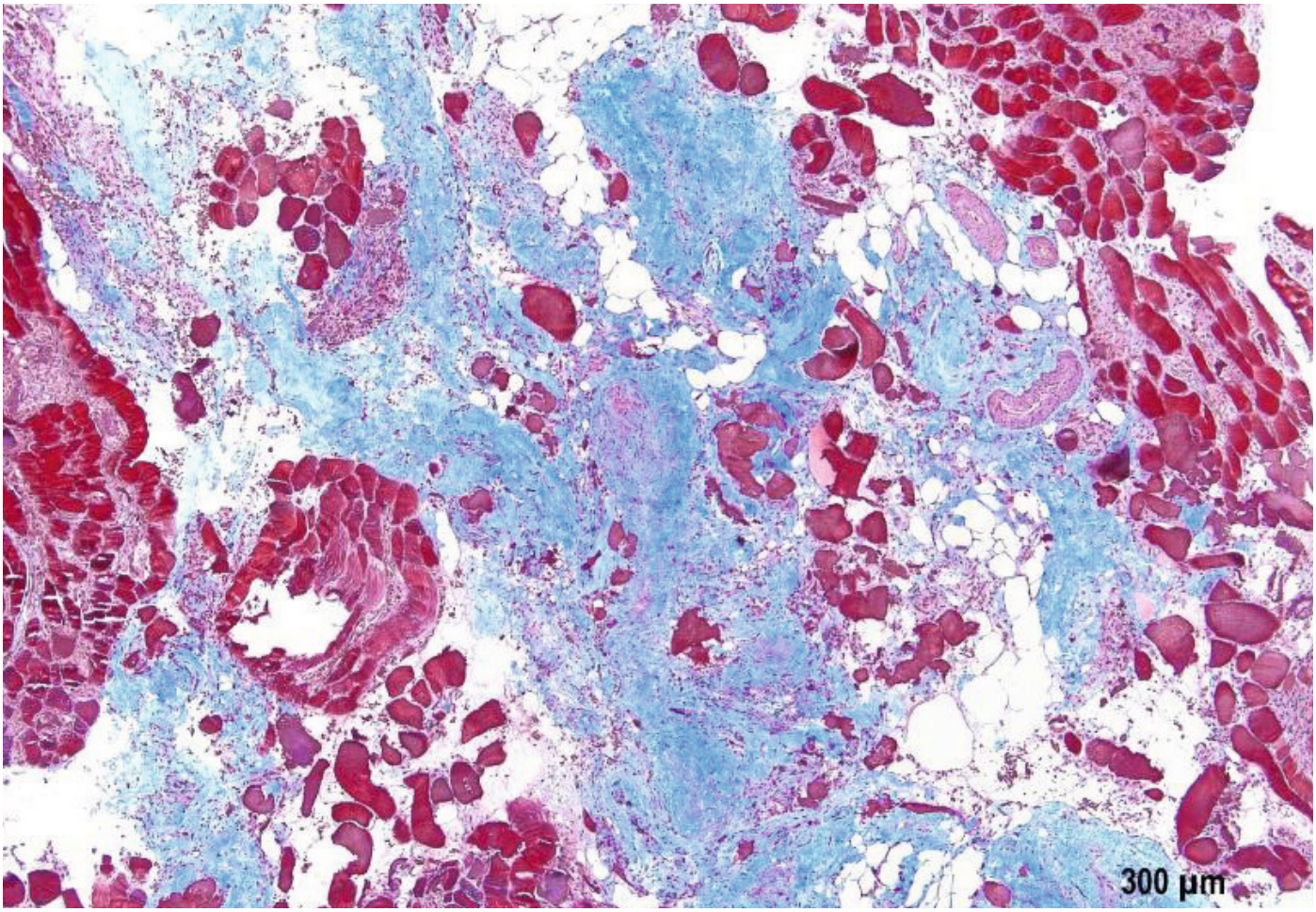

Figure 3: Muscle tissue section, HE. Note the loss of striation of the muscle.

Source: María Luisa Rodríguez Pozo

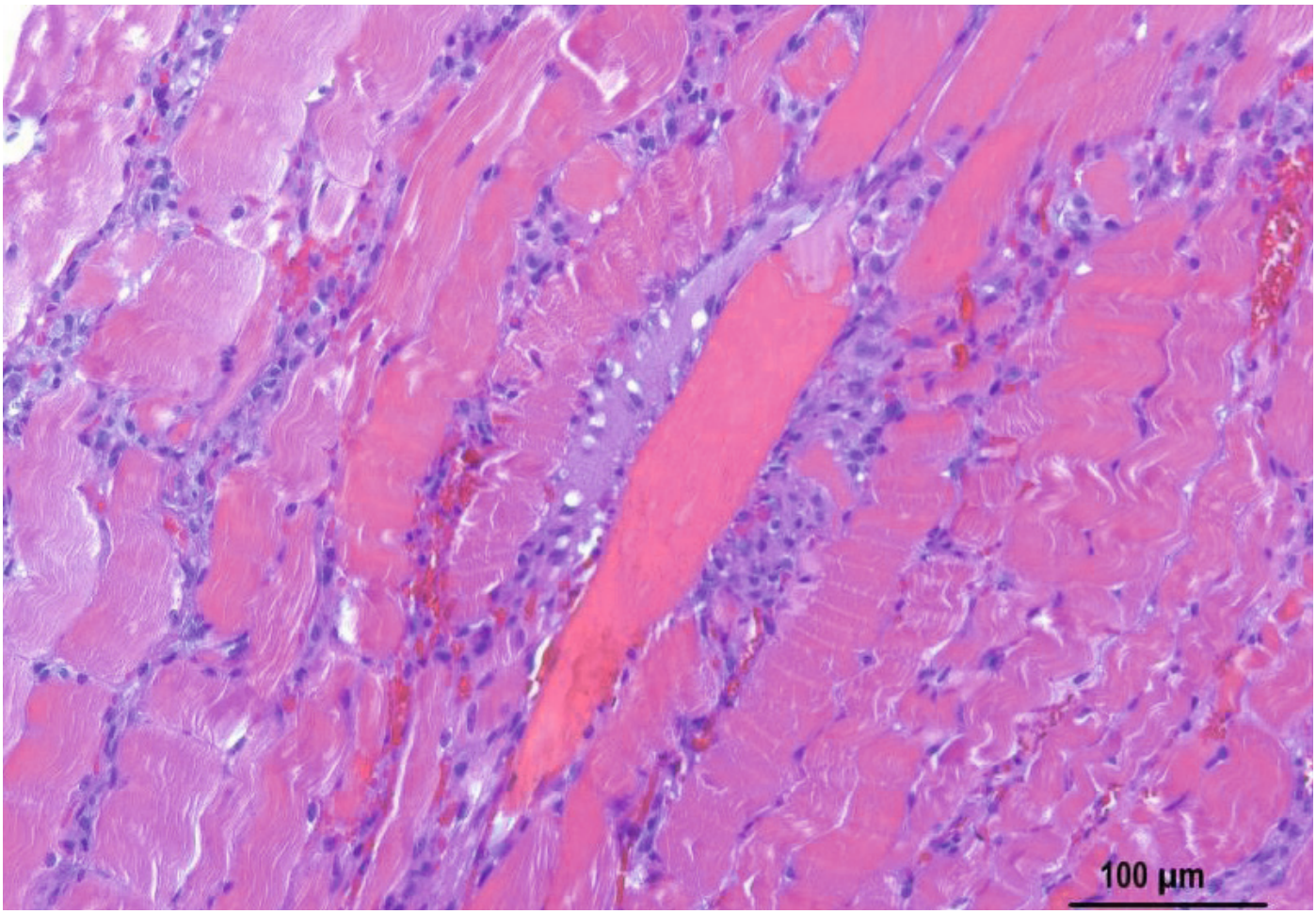

Figure 4: Muscle tissue section, Masson's trichrome. Note the fibrous tissue between the muscular fibers.

Source: María Luisa Rodríguez Pozo

Given the results of the muscular biopsy and the deficiencies of vitamin E and selenium, a definitive diagnosis of nutritional myodegeneration associated to vitamin E and selenium deficiencies was made.

DIAGNOSIS: Nutritional myodegeneration associated to vitamin E and selenium deficiency ("white muscle" disease).

TREATMENT AND FOLLOW UP

Intravenous fluid therapy with isotonic solutions (Lactate Ringer, 4mL/Kg/h), calcium borogluconate 23% (20mL/L) and glucosate solution (1mg/Kg/min) was administered during the first hours after admission. Intravenous dimethylsulfoxide (0,5 g/Kg BID) and flunixin meglumine (0,5 mg/Kg BID) and single intramuscular acepromazine doses (0,03 mg/Kg) were also instituted. Oral supplementation with vitamin E (25 UI/ Kg) and selenium (0,1 mg/Kg) SID was also administered.

After the first 48 hours, the horse progressed well, with gradual decrease of the weakness and improvement of the swallowing. The colour of the urine became normal throughout the days (figure 5) and serial serum CK and AST activities did show significant increase in serum AST activity after day 0 and decrease in serum CK activity (table 5).

Table 5: Evolution of serum AST and CK activities during hospitalization.

Parameter	Day 0	Day 1	Day 3	Day 5	Day 8	Reference intervals	Units
AST	739	–	15.110	–	6.540	150 – 420	U/L
CK	81.860	33.812	17.101	8.852	2.309	60 – 350	U/L

Figure 5: Urine samples obtained during the hospitalization period (days 0, 1, 3, 5 and 8, consecutively). Note the gradual loss of red-brownish pigment until a normal-coloured urine was obtained.

Source: María Luisa Rodríguez Pozo

The horse was discharged ten days after admission. Oral supplementation with vitamin E and selenium was recommended and dietary counselling by a nutritionist. Recommendations about exercise included exercise restriction until complete recovery of muscular enzymes' activities and slow and progressive return to work. Fifteen days after discharge the horse had recovered most of the muscular volume and serum CK and AST activities resulted within normal limits.

SUMMARY

Selenium and vitamin E are essential components of several major metabolic pathways and have complementary roles as antioxidants. A deficiency of selenium and/or vitamin E diminishes protection against cellular oxidative stress, making the cell membrane more susceptible to disruption by free radicals resulting from cellular metabolism. The most common clinical manifestations of decreased anti-oxidant activity associated with vitamin E and/or Se deficiency are muscular and neuromuscular diseases, such as white muscle disease (WMD), equine motor neuron disease, and equine degenerative myeloencephalopathy.
Nutritional myodegeneration is more commonly seen in young foals under two months although cases in adult horse have been also described. Gestating and lactating mares, young growing horses, and performance horses have the greatest need for vitamin E supplementation, especially those that do not have access to lush, green pasture.

In conclusion, when a horse presents clinical signs of weakness, muscular atrophy and pigmenturia, rhabdomyolysis due to a nutritional myodegeneration secondary to vitamin E/selenium deficiency should be considered even in adult patients.

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