



CASE REPORT

Subclinical *Theileria equi* Infection and Rhabdomyolysis in Three Endurance Horses

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ARTICLE HISTORY

Received: July 4, 2012

Revised: July 30, 2012

Accepted: September 9, 2012

Key words:

Exercise

Horses

Performance

Rhabdomyolysis

Theileria equi

ABSTRACT

Three well-trained endurance horses, competing over different distances, developed sudden and unexpected rhabdomyolysis at the onset of exercise. They were treated and afterwards they did not have any other bout of muscle damage. All of them were positive to *Theileria equi* (polymerase reaction chain). The possible reasons of the rhabdomyolysis could have been the direct effect of the parasite on the muscle and/or the result of the anemia and a limited oxygen supply to the exercising muscles. It is suggested that the horses were carriers of *Theileria* and they developed clinical signs because of the immune-suppression caused by prolonged submaximal exercise and/or transportation.

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To Cite This Article: Muñoz A, RGM Rodríguez, C Riber, P Trigo, M Gómez-Díez and F. Castejon, 2013. Subclinical *Theileria equi* infection and rhabdomyolysis in three endurance horses. Pak Vet J, 33(2): 257-259.

INTRODUCTION

Theileria equi and *Babesia caballi* are tick-borne hemoprotozoan parasites that cause piroplasmiasis in horses (Fig. 1). As piroplasmiasis is becoming a disease of increasing international importance and of major constraint to international movement of horses, great attention is turned to its diagnosis, treatment and prevention (Camacho *et al.*, 2005). The present report documents the cases of three horses that were found healthy in the veterinary inspection before endurance competitions, performance before the event was good and unexpectedly, they developed a mild to severe rhabdomyolysis during exercise. In the three cases, a PCR (polymerase chain reaction) was positive to *Theileria equi* (Fig. 2).

History, clinical examination and treatment: Horse 1 was an Arabian stallion, aged 6 years that started an endurance event of 80 km. He was able to successfully finish 6 competitions of 40 km and a competition of 80 km during the same season. The competition was carried out in a rocky terrain with moderate slopes. At km 7 of the competition, he developed a sudden moderate stiffness and slight discolored urine and, the owner decided to leave the competition. At inspection the horse was lethargic, painful, with tachycardia (72 beats/min), tachypnea (32 breaths/min) and mild dehydration. He was treated with phenylbutazone (4.4 mg/kg IV) and fluid therapy (8 l of saline solution IV supplemented with ClK).

After 90 min, heart rate (HR) and respiratory rate (RR) normalized (42 beats/min and 16 breaths/min, respectively), urine was clear, he started to have interest in food. At the end of the day (approximately 12 hrs after the onset of rhabdomyolysis), the horse was examined again and was considered to be ready to leave. He was transported for 6 hrs and arrived home in good conditions. The horse appeared physically normal the following day, but a blood work was recommended (results in Table 1). PCR was positive for *Theileria equi* and negative for *Babesia caballi* and *Anaplasma phagocytophilum*. The horse was treated with dipropionate of imidocarb (4.0 mg/kg IM, every 72 hrs, 4 treatments) and with an oral complement of vitamin B12, other vitamins and Fe. Two months later, the hematological and biochemical analysis were repeated (Table 1).

Horse 2 was a cross-Arabian 12-year-old mare, trained for endurance that started an event of 160 km. Previously the mare took part successfully in several competitions of 160 km. She had been competing in Spanish Endurance Championship, and in International Events. Therefore, her fitness level was considered high. The competition was carried out in a rocky terrain with moderate slopes. The mare underwent a sudden stop after 18 km of competition. When inspected, she was painful, mild excited, with tachycardia (68 beats/min), tachypnea (24 breaths/min), dilated nares and well hydrated. At this moment, urination was not observed. The physical examination showed a moderate to intense pain at the pressure in the gluteal region. The results of blood work

Table 1: Some hemato-biochemical parameters in horses suffering from rhabdomyolysis and *Theileria equi* infection

Parameters	Case 1		Case 2			Case 3		Reference range (Muñoz <i>et al.</i> , 2010)
	Day 1 after competition	2 months later after treatment	At inspection	5 hrs later	1.5 months later	1.5 hrs after stopping exercise	2 months later	
Hemoglobin (g/dl)	10.3	13.3						12.00-14.00
Packed cell volume (%)	26.0	39.0						35.00-45.00
Fibrinogen (mg/dl)	800	200						200-400
Urea (mg/dl)	40.0	34.0						10.0-35.0
Total bilirubin (mg/dl)	2.40	1.10						0.80-1.80
Aspartate aminotransferase (U/l)	6320	579	5430	7320	350	7320	540	220-440
Creatin kinase (U/l)	10340	277	11320	9320	260	12430	296	150-350

are presented in Table 1. A diagnosis of exertional rhabdomyolysis was made and treatment was administered, consisting in phenylbutazone (4.4 mg/kg IV, BID) and a complement of vitamin E and Se. The mare was monitored, and moderate dark urine was observed after 3.5 hrs after initial examination. IV fluid therapy was administered (Ringer Lactate, 5 l IV). Five hours later, the mare had clear urine and results of the blood work are shown in Table 1. Muscle pain still persisted, but it was reduced in intensity. At the evening, the physical examination of the mare was unremarkable and therefore, it was considered safe to leave the competition. Two days later the mare did not want to eat, she presented fever and ictericia. A PCR analysis was made for both *Theileria equi* and *Babesia caballi* and was positive to *Theileria equi*. A treatment with dipropionate of imidocarb (4.0 mg/kg every 72 hrs for 4 treatments) and oxytetracycline (7.7 mg/kg IV, SID, for 7 days) was provided. The mare improved and the results of the blood work 1.5 months later are presented in Table 1.

Horse 3 was a 7-year-old cross-bred male horse that competed in endurance events of 120 and 160 km. He started a competition of 120 km in rocky place, near to the beach. After covering 16 km, the owner noticed that something was wrong with the horse, and he continued the competition but at lower velocities. After 5 km more (i.e. after covering 21 km), the horse was reluctant to move and the owner decided to leave the competition. The initial physical examination was unremarkable. The horse remained monitored and 1 hr later, an increase in RR (32 breaths/min), with dilation of nares, was detected. At that moment, the horse was tachycardic (64 beats/min) and he shown signs of pain, trying to roll down. The nasogastric intubation was unproductive, rectal exploration was unremarkable, dry feces were found in the rectum and intestinal motility was mildly reduced. Deep muscle palpation in the gluteus region produced a moderate discomfort and a muscle contracture was found in the right hind limb. The results of blood work at that moment are presented in Table 1. A treatment consisting in phenylbutazone (4.4 mg/kg IV, Se and vitamin E, IV and diazepam, 0.25 mg/kg, IV, as muscle relaxant) was provided. The horse improved, muscle contracture diminished over the next 6 hrs, although the owner preferred to stay overnight at the place of the competition. Next day the horse was slightly lethargic and anemia was evident. A microhematocrit was made (28%). Muscle pain and contracture still persisted, but they were of lower intensity. Because of anemia, a blood sample was sent for PCR to the laboratory and it was found positive to *Theileria equi*. The horse was transported home and treated (dipropionate of imidocarb, 4.0 mg/kg, IM, every

72 hrs for 4 treatments and oxytetracycline, 7.7 mg/kg IV, SID, for 5 days). Two months later, the horse had recovered, although AST was still higher (Table 1).

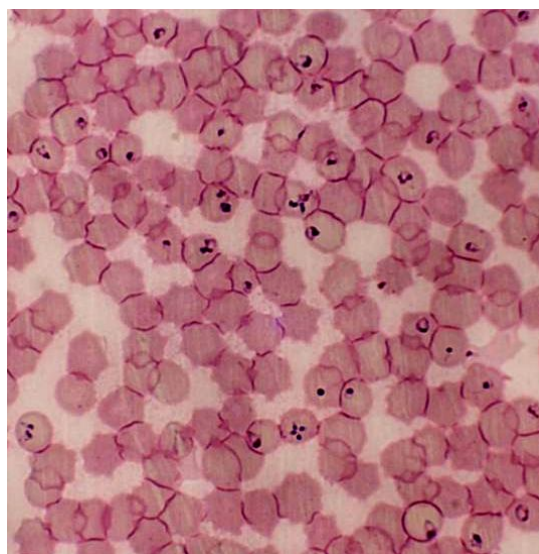


Fig. 1: Blood smear of a horse with *Theileria equi* (image from Dr. Santiago Hernández, Head of the Department of Veterinary Parasitology, School of Veterinary Medicine, University of Córdoba, Spain).

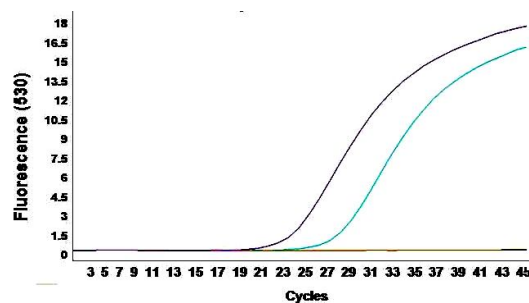


Fig. 2: Amplification curve of the polymerase chain reaction of *Theileria equi* in horses (red line or basal line: negative control; violet line: positive control; blue line: positive sample) (X-axis: PCR cycles; Y-axis: fluorescence) (image from Dr. Bartolomé Garfía, Lab. Garfía, Córdoba, Spain).

DISCUSSION

In this paper, we describe three cases of horses that developed rhabdomyolysis at the onset of the exercise, despite they were properly trained to cover long distances. None of these horses had more rhabdomyolysis bouts after these episodes.

The clinical disease associated to piroplasmosis is characterized by fever, anemia, icterus, hepatomegaly, splenomegaly, lethargy, hemoglobinuria and in some cases, death (Camacho *et al.*, 2005; De Waal, 2012). In endemic areas, acute clinical disease is mild and of short duration, resulting in persistent but low-level infection. Horses born and raised in endemic areas usually develop premonition, characterized by the carrier state, with mild clinical signs (García-Bocanegra *et al.*, 2012). Our three horses were born and they lived in Spain, and it appears that they were asymptomatic carriers.

The most remarkable clinical signs were anemia and rhabdomyolysis during exercise. Anemia was not detected during the physical examination before the competitions, but it was apparent in the blood analysis. It has been shown that endurance training leads to an expansion of plasma volume, in relation to aldosterone-mediated renal mechanisms associated with the retention of Na. For that reason, endurance horses at rest usually have lower hematocrit than other sport horses (Robert *et al.*, 2010). In our experience, this characteristic of the endurance-trained horses makes more difficult to detect clinically anemia. Unfortunately, hematological analyses are not commonly performed in endurance horses the days before the competitions, although this practice, in our opinion, will favor the diagnosis of subclinical anemias.

Some reasons could be implied in the pathogenesis of rhabdomyolysis in these horses. Firstly, it has been suggested that *Theileria equi* induces neuromuscular damage, leading to increased circulating serum muscle enzyme activities (CK and AST) (Camacho *et al.*, 2005). A second hypothesis could be the influence of the anemia secondary to *Theileria equi* infection. This anemia would limit oxygen supply to active muscles in exercise, promoting muscle lysis because of hypoxia.

In the three cases, serum muscle enzymes were normal after 2 months of recovery. However, we were unable to quantify the duration of the muscle damage after the competitions. The IM administration of imidocarb is associated with localized muscle damage and release of

CK and AST to the circulation (Aktas *et al.*, 2005), and therefore, the measurements of the activity of these enzymes did not help to determine the recovery of the rhabdomyolysis.

Horses in endemic areas may live without clinical disease. Heavy exercise, poor nutrition or other disease with a compromise of the immune system may lead to a recrudescent infection. Endurance exercise has been associated with increased release of cortisol, with important immune suppression effects (Robson *et al.*, 2003). In our opinion, the studied horses were subclinical carrier of *Theileria equi* and the stress related to the transportation to the place of the event and/or competition led to clinical manifestations.

In conclusion, carrier of *Theileria equi*, under stressful situations can develop exertional rhabdomyolysis. This disease might appear because of direct muscle of the parasite or secondary to muscle hypoxia because of the anemia.

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