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Case Report

Loss of Performance in an Endurance Horse With Erythrocytosis and Colic During Exercise

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ABSTRACT

A 10-year-old endurance horse was presented because of tiredness in training, inability to finish the races, and colic in competition. The horse was continuously supplemented with four different hematinic compounds for more than 8 months. Physical examination showed mild hyperemia, and blood analysis revealed erythrocytosis, increased γ-glutamyl transferase (GGT), and bilirubin with normal total solids (TS) and albumin. Arterial blood gas analysis and ultrasonography were irrelevant. Serum testosterone was within reference range, and increased serum erythropoietin and cobalamin were found. The horse was subjected to a treadmill endurance exercise and after 20 minutes of exercise, blood had a sticky and dark appearance. Exercise was stopped because the horse presented an episode of colic. Packed cell volume (PCV) of 58% and TS of 6.1 g/dL were found at that moment. An inappropriate secondary erythrocytosis because of supplementation was diagnosed. Supplementation was suspended and in the reevaluation 3 months later, PCV reached 49% after 20 minutes of exercise. Bilirubin, GGT, erythropoietin, and cobalamin values were normalized. Seven months later, resting PCV was 36%, and the horse was competing successfully in longer distances. It is concluded that erythrocytosis in an endurance horse might have detrimental effects on performance.

1. Introduction

Many trainers and owners frequently provide supplements to their sport horses to increase red blood cell (RBC) count and hemoglobin (Hb) concentration. It is supposed that higher Hb concentrations would be associated with a greater oxygen transport and utilization during exercise, leading to enhanced aerobic potential and sport performance. In addition, compounds containing iron, cobalamin or vitamin B_{12}, other vitamins, and trace elements associated with iron metabolism are often administered in sport horses to accelerate recuperation of hematological values after anemic situations.

It appears that IV administration of erythropoietin (EPO) might have an ergogenic effect of performance in unfit Standardbred trotters [1]. However, in this research, packed cell volume (PCV) was lower in the EPO-supplemented group than that in the control group. A survey conducted at a California racetrack indicated that a large majority of trainers had their horses on some type of iron supplement [2]. An early study performed in Thoroughbred horses in light training failed to detect q2 changes in PCV or Hb concentration after 8–12 weeks of supplementation [3]. It is known that the risks of over supplementation with trace elements linked to oxygen transport are higher than the likelihood of deficiencies. In fact, overdoses of injectable iron have been shown to cause toxicosis in horses, causing

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liver damage and cholestasis [4]. However, a more recent experimental study found that PO administration of ferrous sulfate during 8 weeks did not produce adverse clinical reactions or liver histologic lesions in four ponies [5]. Cobalt ions (Co^{2+}) could induce EPO gene expression in human begins, leading to erythrocytosis [6].

We present here a case of an endurance horse with erythrocytosis, loss of performance, and colic during exercise that improved when long-term supplementation (more than 32 weeks) was stopped.

2. Case Description

2.1. History

A 10-year-old gelding well-trained Anglo-Arabian horse was referred to the Equine Sport Medicine Center of the College of Veterinary Medicine of Córdoba because of the loss of performance. The owner reported that the horse appeared tired during the training sessions. In addition, he was unable to finish the last four 80-km endurance races where he competed. In all the cases, the horse was disqualified with marked dehydration, hyperemic mucous membranes, and paralytic ileus. In the last endurance event, the horse presented mild-to-moderate colic episodes and rhabdomyolysis that disappeared when exercise was suspended and medical intervention was not required. Five months before remission, the horse had been competing successfully in the same distance (80 km). The trainer informed that the horse had been receiving continuously vitamin B_{12} and iron supplementation for at least the last 8 months (Biodyl, Methio B12, Hemo 15, and Hippiron). Diet of the horse consisted in a concentrate source and fodder of good quality combined with pasture.

2.2. Clinical Examination

Physical examination at admission was irrelevant with exception of hyperemia in the mucous membranes. Auscultation of the thorax and abdomen did not reveal abnormal findings.

2.3. Laboratory Findings

Blood analysis showed increased PCV (48%; reference values for endurance horses, 35%–38% [7]). Total solids (TS, 6.6 g/dL; reference values for endurance horses, 6.47 ± 0.85 g/dL [7]) and albumin concentrations (2.8 g/dL; reference values for endurance horses, 2.66–2.80 g/dL [7]) were normal. To rule out stress and splenic contraction as a cause of the increased PCV, the horse was kept calm in a box, and three blood samples were withdrawn every hour. Packed cell volume values higher than 46% were found in the three samples. Increased total bilirubin (3 mg/dL; reference values, 0.5–2.2 mg/dL [8]) and γ-glutamyl transferase (GGT, 89 IU/L; reference values, 6.5–24.5 IU/L [8]) were also found. Serum iron (111 μg/L; reference values, 132–186 μg/L [9]) and ferritin (30.1 μg/L) concentrations were within reference limits for horses (ferritin: 31.9 ± 3.4 μg/L) [10]. Serum creatine kinase (CK), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) activities were 208, 183, and 375 IU/L, respectively (reference values: CK, 155.2 ± 18.43 IU/L; AST, 195.1 ± 18.40 IU/L; LDH, 346.0 ± 37.85 IU/L) [7].

2.4. Further Diagnostic Procedures

Diagnostic workout included arterial blood gas analysis, thorax, and abdominal ultrasonography, including echocardiography, measurements of serum testosterone, EPO and vitamin B_{12} concentrations, and endurance treadmill exercise testing.

Results of arterial blood gas analysis were within normal limits for horses: PaO_2, 93 mm Hg (73–108 mm Hg); O_2 saturation, 98% (>94%); pH 7.402 (7.364–7.444); $PaCO_2$, 45 mm Hg (34–50 mm Hg); and bicarbonate, 25 mmol/L (20–34 mmol/L) (VetStat; Idexx). Ultrasonographic findings in thorax and abdomen were unremarkable. Serum testosterone concentration was measured with a competitive enzyme immunoassay validated for horses [11]. A serum testosterone concentration of 6.89 pg/mL was found (35.48 ± 10.89 pg/mL for geldings). Serum EPO concentrations were measured with a chemiluminescent immunometric assay developed for humans (Immulite; Siemens). A value of 3.6 mIU/L was measured. Four age-matched healthy endurance horses were considered controls, and all of them had concentrations lower than 0.6 mIU/L (0.424 ± 0.114 IU/L). Increased serum vitamin B_{12} concentrations were found (3,000 pg/mL; reference range provided by the laboratory, 700–1700 pg/mL).

To assess the adaptation to exercise, the horse was subjected to an endurance treadmill exercise. Environmental temperature was 19°C, and relative humidity was 44%. After 10 minutes of warm-up period (5 minutes at walk and 5 minutes at trot), the treadmill was inclined 3%, and velocity was increased until a stable heart rate of 110–130 beats/min was achieved (6 m/s). Blood samples were taken during exercise every 10 minutes. Values of PCV and TS are presented in Table 1. After 20 minutes of exercise, during blood sampling, it was observed that blood was very sticky. Exercise was interrupted at that moment because the horse started to show colic. Intestinal peristaltism was intensely reduced. Colic signs disappeared after 15 minutes without medical treatment and after the horse drank 5 L of water. Recovery of heart rate (64 beats/min at 7 minutes after exercise) and respiratory rate (120 breaths/min at 5 minutes after exercise) was poor for a well-trained endurance

Table 1
Packed cell volume (PCV) and total solids (TS) during an endurance treadmill exercise in a horse with secondary erythrocytosis, at admission and 3 months later, after interrupting supplementations.

Sampling Times	PCV (%)	TS (g/dL)
Exercise test at admission		
At rest	48	5.6
After 10 min of endurance treadmill exercise	54	6.1
After 20 min of endurance treadmill exercise	58	6.1
Exercise test three months later		
At rest	43	7.0
After 10 min of endurance treadmill exercise	48	7.8
After 20 min of endurance treadmill exercise	49	8.0

Table 2
Packed cell volume (PCV) and total solids (TS) during 80-km endurance event in a horse with secondary erythrocytosis, 10 days after admission and 4 months later, after interrupting supplementations.

Sampling Times	PCV (%)	TS (g/dL)
First competition (10 d after admission)		
At rest	46	5.9
After vet-gate 1	56	7.4
After vet-gate 2	55	7.2
End of competition	57	7.4
Second competition (4 mo after admission)		
At rest	35	6.8
After vet-gate 1	43	7.4
After vet-gate 2	45	7.6
End of competition	Disqualified by lameness	

horse. Serum CK activity was measured 6 hours after treadmill exercise test, and it was a normal value (234 IU/L).

2.5. Diagnosis and Follow-up

A presumptive diagnosis of inappropriate secondary erythrocytosis associated with supplementation was made. It was recommended to stop the administrations of these products. The trainer did not provide an explanation for the increased serum EPO concentrations.

Although not recommended, the horse competed in an 80-km endurance event 20 days later because the owner found that the horse fitness had improved during the training sessions. The animal was able to complete the competition, but his condition was poor. Packed cell volume and TS were measured at rest, after each vet-gate and at the end of competition (Table 2).

Three months later, the horse was reevaluated. Environment temperature was higher during this second exercise test (26.6°C), and, therefore, sweating was more intense. Packed cell volume and TS during this second exercise test are shown in Table 1. Recovery of heart rate improved, and the horse did not show signs of pain during the test. Erythropoietin and vitamin B_{12} concentrations decreased to 0.495 mIU/L and 1,100 pg/mL, respectively.

One month later, the horse competed again in an 80-km endurance event. The results of PCV and TS results are presented in Table 2. The horse showed a better hematologic response to the endurance competition, although he was disqualified after 65 km by a foot lameness causing by a stone.

Seven months after the first examination, the horse completed successfully an 80-km endurance race, with PCV and TS values of 36% and 5.6 g/dL at rest and 42% and 7.2 g/dL at the end of competition. The horse was followed for a year and did not present colic or muscle problems in competition, and his performance recovered. Telephone follow-up was made for an additional 5 months, and the horse was competing successfully in endurance races of 120 km.

3. Discussion

The case of an endurance horse with erythrocytosis, colic in competition, and loss of performance is presented. Erythrocytosis refers to a relative or absolute increase in RBC mass, characterized by increased PCV, RBC, and Hb. Most of the reports of erythrocytosis in horses reported PCV values higher than 60% [12,13]. Endurance horses have low resting PCV, and training even decreases these values [14]. This finding has been attributed to an increased reabsorption of osmotically active substances and tubular conservation of electrolytes as a method of conserving water and sodium. This mechanism, leading to increased plasma volume and hypervolemia, could be protective during prolonged exercise when substantial fluid and electrolytes loss because of sweating [14].

Erythrocytosis can be divided into relative and absolute. In the relative erythrocytosis, the RBC mass is normal, but PCV is increased because a decrease in plasma volume (dehydration) or because of splenic contraction, which may transiently add RBCs into the circulating compartment in the horse [15]. Relative erythrocytosis was ruled out in this horse because he was not clinically dehydrated, and TS and albumin concentrations were within the normal limits. Furthermore, three serial blood samples taken when the horse was calm in the box ruled out the effect of stress.

Absolute erythrocytosis can be primary or secondary. Primary erythrocytosis results from malignant transformation of bone marrow precursor cells and erythropoiesis occurs regardless of EPO stimulation [12,13]. Primary erythrocytosis was considered unlikely based on the age of the patient and the increased concentration of serum EPO.

Secondary erythrocytosis develops because of appropriate or inappropriate EPO production. Appropriate secondary erythrocytosis represents a physiological response to chronic tissue hypoxia, from low environmental oxygen concentration, inadequate oxygen exchange or transport due to lung and cardiovascular disease, abnormal oxygen affinity of hemoglobin, or administration of EPO-like substances. Inappropriate secondary erythrocytosis involves release of EPO or EPO-like substances in renal neoplasia [15]. In horses, this type of erythrocytosis has been reported with liver neoplasias and rarely in non-neoplastic conditions of the liver [13,16]. No cause for systemic hypoxia was evident and results of the arterial blood gas analysis were within reference interval. Thoracic and abdominal ultrasonographic findings did not reveal a neoplastic condition, and liver damage was of minor intensity. Therefore, an inappropriate secondary erythrocytosis was diagnosed, secondary to supplementation. Horse was neither living at high altitude nor moved for training or subjected to other hypoxic conditions. This initial diagnosis was confirmed later when PCV and EPO concentrations decreased after suppression of the supplementations. More than 1 year and half after the presentation to the Center, the horse is healthy, competing successfully in longer distances (120 km), and a neoplastic condition has not been diagnosed.

Exogenous EPO administration has been reported to have an ergogenic potential in horses, increasing PCV values [1]. Although the owner of the horse denied EPO administration, this fact could not have been completely ruled out. In addition, none of the supplements reported by the owner contain Co^{2+}, although other food

sources were not investigated. However, the erythrocytosis disappeared, and feeding management was not changed.

Testosterone concentration was low, as expected in a gelding horse. It has been demonstrated that administration of anabolic steroids leads to significant increase in RBC parameters in horses [17].

The horse in the present study was supplemented continuously for more than 8 months, and the fact that resting PCV decreased after stopping the suppression of supplementation raises the suspicion of an effect of these compounds. It is believed that combinations of different supplements are more effective than one single complement, once metabolism depends on the performance of several compounds simultaneously [18]. In our case, the horse received four different supplements (three of them with vitamin B_{12} and two with iron). Iron supplementation has been related with periportal necrosis of hepatocytes, bile ductule proliferation, fibrous connective tissue proliferation, and cholestasis [4,19]. Although liver ultrasonography was unremarkable, the horse of the present case at presentation had hyperbilirubinemia and elevated serum GGT activity, indicating cholestatic damage. These abnormalities were not found in the second presentation of the horse, 3 months after suspending supplementation.

Administration of hematinic supplements is commonly performed by trainers and horse owners to rise PCV and oxygen-carrying capacity. Aerobic potential is one of the determinants of endurance success [20]. However, in endurance runners, the "paradox" of PCV is a well-known event. When PCV increases excessively, there is a decrease in fitness and a higher score of overtraining [21]. In human athletes, excessive increase in PCV is associated with increased blood viscosity, poor circulation, and clotting, all factors increasing the risk of myocardial infarction [22]. These risks are exacerbated by endurance exercise because sweating and fluid losses also increase blood viscosity. The horse is somewhat unique compared with most other mammalian species because the spleen might store between 6 and 12 L of RBC-rich blood at rest. This great splenic reserve is mobilized during exercise, proportionally to increased requirements for oxygen transport [23]. Therefore, the combined effects of a large increase in PCV after splenic contraction and sweating and dehydration could dangerously increase PCV.

It has been suggested that if PCV rises above 60%, the advantages of greater oxygen transport are overcome by the harmful effects of increased blood viscosity [15]. Endurance horses with PCV equal or higher than 50% in competition are a risk of disqualification and often required veterinary intervention and IV fluid therapy [24]. The increased resting PCV in this horse, together with dehydration in competition, could have led to substantially increased blood viscosity. Unfortunately, blood viscosity was not measured. However, when treadmill exercise was stopped in the first examination, blood samples were difficult to withdrawn, and blood appears sticky and dark. It could be speculated that the increased viscosity would induce altered blood flow to intestines, and muscles led to colic and rhabdomyolysis. In horses, it has been demonstrated that a reduction in intestinal blood flow diminishes intestinal mechanical activity [25]. However, in these reports, although paralytic ileus was detected at auscultation, horses did not show abdominal discomfort. In the present case, when PCV decreased after interrupting supplementations, the horse recovered his performance, and up to now, he did not show any more colic episodes or rhabdomyolysis during training and competition.

4. Conclusions

Equine clinicians, owners, and trainers should be aware that increased PCV is not always associated with a higher endurance potential and race performance. Endurance horses usually have low resting PCV as a protection against fluid losses by sweating during prolonged exercise. Erythrocytosis together with dehydration might have detrimental effects during prolonged exercise. The finding that this horse increased his performance when PCV decreased supports this hypothesis.

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