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Note

A suspected case of hypoxia-induced pre-renal azotemia in an old part-Arab stallion: case report and review of the literature

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Abstract

The kidneys maintain homeostasis and this function is compromised in hypoxic conditions. Hematology and serum biochemistry evaluations were performed on a 17-year old Nigerian part-Arab stallion, who was observed to be docile, cachexic, and has bilateral ocular mucus discharge. Ticks were seen attached around the inguinal region. The mucous membrane of the eyes was congested, animal was partially insensitive to its environment and had an abnormal posture and gait. Blood samples for hematology and clinical biochemistry analyses were collected from the jugular vein. Hematology and serum biochemistry determinations followed standard procedures. Hematological analysis revealed that the stallion had secondary absolute polycythemia, low erythrocyte sedimentation rate. The mean corpuscular volume, mean corpuscular hemoglobin concentration and total leukocyte count were within the respective reference ranges. The clinical biochemistry profile of the horse showed normal serum activity of alanine aminotransferase and elevated serum activities of aspartate aminotransferase and alkaline phosphatase, normal serum total protein, albumin, decreased serum globulin concentrations, with a high albumin: globulin (A/G) ratio. The stallion also had normal total cholesterol level and an abnormally high serum creatinine and blood urea nitrogen levels. These findings were suggestive of hypoxia-induced pre-renal azotemia.

Keywords: hematology; hypoxia; serum biochemistry; old stallion; part-Arab; pre-renal azotemia

Introduction

The kidneys are organs responsible for water and electrolyte homeostatic control. They filter the blood of urea and creatinine and excrete these toxic metabolic end products in urine (Chen and Al Khalili, 2020). They also control red blood cell mass. The kidneys also possess endocrine properties that enables them maintain calcium balance (parathormone and vitamin D), control blood pressure and body fluid volume (renin-angiotensin-aldosterone system) and regulate oxygen transport (Hounkpatin *et al.*, 2019). One of the accurate measures of renal function is the glomerular filtration rate (GFR), which can be determined by repeated blood sample collection to determine serum urea or creatinine clearance or repeated timed urine collections to determine excretion of any to these exogenous compounds (Chen and Al Khalili, 2020). Use of timed urine collections to monitor changes in GFR is most useful over time than at one point in time, therefore, routine measurement of blood urea nitrogen and serum creatinine concentrations as estimators of GFR is better and

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faster when performed (Okoro and Farate, 2019). In mammals, changes in serum creatinine concentration is a better indicator of alterations in renal function than blood urea nitrogen, as increase in blood urea nitrogen is usually due to change in diet, fever and increased protein catabolism (Manoeuvrier *et al.*, 2017).

Azotemia is a condition characterized by abnormally high levels of non-protein nitrogenous compounds in the blood (Suganya *et al.*, 2016). These compounds include blood urea nitrogen, creatinine and other nitrogen-rich compounds in the blood. Azotemia could occur because of decreased excretion of blood urea nitrogen and creatinine, or due to increased urea production by the liver (Jing *et al.*, 2020). Azotemia could be pre-renal, renal or post-renal in origin. Pre-renal azotemia is caused by reduced renal blood flow because of reduced cardiac output due to cardiac insufficiency, increased protein catabolism, fever, and hypovolemic shock. Renal azotemia occurs when disorders affecting the kidneys such as reduced glomerular permeability, loss of nephrons, increased intra-tubular pressure cause a major reduction in the glomerular filtration rate. Renal azotemia is seen in toxic nephrosis, as it is associated with numerous exogenous and endogenous nephrotoxins, renal ischemia/hypoxia, renal hypoplasia/aplasia and hydronephrosis (Suganya *et al.*, 2016). Post-renal azotemia occurs when the inciting factor causing abnormalities in creatinine and blood urea nitrogen levels is distal or outside the kidneys. Conditions associated with post-renal azotemia include urinary tract obstructions caused by uroliths, neoplasia and prostatic disease, and leakage of urine from urinary tract following trauma or neoplasia (Jing *et al.*, 2020). In equine medicine, hematological and serum biochemistry evaluations is not only relevant for diagnosing disorders of the hematopoietic and urinary systems but also play major role in the diagnosis of systemic diseases (Agina, 2017). Most equine clinicians evaluate renal function by measuring serum concentrations of blood urea nitrogen and creatinine (Agina, 2017).

Homeostatic functions of the kidneys are compromised following hypoxic condition (Samanta *et al.*, 2018). Hypoxia is lower oxygen concentration that can alter renal function, impair body fluid balance and blood pressure homeostasis (Samanta *et al.*, 2018). It may promote an increase in erythropoietin production, due to decreased blood flow to the kidneys consequent upon narrowing of the renal arteries. Therefore, this case report described a part-Arab stallion that presented hypoxia induced-pre-renal azotemia. To the authors knowledge, this is the first report of suspected case of renal hypoxia in a Nigerian horse.

Materials and Methods

A 17-year old Nigerian part-Arab stallion presented for sale at the Obollo-Afor horse depot, Udenu Local Government Area of Enugu State, South-Eastern Nigeria was physically examined before blood samples were collected for haematology and clinical biochemistry analyses. The Stallion's age was estimated based on tooth eruption, wear and appearance of Galvayne's groove (Łuszczyński *et al.*, 2019). The full medical history of the horse was not obtained from the head of the horse depot, because they are trade horses slaughtered for meat in the slaughter slab. Five (5) ml of blood was collected from the jugular vein, one ml was put into K2EDTA tubes while four ml was put into non-EDTA blood tube and allowed to clot for one hour. Serum was obtained by centrifuging the clotted blood for 10 minutes at 3000 rev/min. The haematology and clinical biochemistry determinations followed standard procedures (Walton, 2014).

Results

Examination of the 17-year old stallion revealed congested mucous membrane of the eye, prominent rib cages and emaciation. The horse was weak, had few ectoparasites (ticks) and bilateral ocular mucus discharge. No nasal discharge was observed. The animal was partially insensitive to its environment and had an abnormal posture and gait. The perineal area was free from diarrheic faces. There were no wounds on the body. The hematological and clinical biochemistry values are presented in Tables 1 and 2 respectively.

The hematological analysis revealed a very high packed cell volume (PCV), red blood cell (RBC) count and hemoglobin concentration. A normal mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) were recorded. A low erythrocyte sedimentation rate (ESR) and normal total white blood cell count (TWBC) were also observed. No monocytes, eosinophils, basophils or blood parasites were found in the Giemsa stained blood smear (Table 1).

The clinical biochemistry findings include a normal serum alanine aminotransferase, an elevated serum aspartate aminotransferase and alkaline phosphatase activities. A normal serum total protein and albumin level with a decrease in serum globulin values were observed. The albumin: globulin ratio was high while the total cholesterol value was within the reference range. The serum creatinine and blood urea nitrogen levels were elevated (Table 2). Blood gas analysis and urinalysis were not done. Serial performance of the hematology and clinical biochemistry tests was not possible because the horse was slaughtered for meat.

Table 1. Haematological values of an old part-Arab Stallion with a suspected case of hypoxia-induced pre-renal azotemia

Parameters	Value obtained	Reference values
Packed cell volume (PCV) (%)	59	31.5 - 53.50
Haemoglobin concentration (g/dl)	21.6	11.53 - 19.86
Red blood cell count (10^6/µl)	15	6.46 - 11.16
Mean corpuscular volume (MCV) (fl)	39.33	38.37 - 60.96
Mean corpuscular haemoglobin concentration (MCHC) (g/dl)	36.61	27.67 - 55.03
Total white blood cell count (TWBC) (10^3/µl)	5.7	5.40 - 13.90
Differential leucocyte count	Absolute (10^3/µl)	
Band neutrophil	0	0.00 - 0.97
Segmented neutrophil	4.85	2.05 - 8.83
Lymphocyte	0.855	2.05 - 8.83
Monocyte	-	
Basophil	-	
Eosinophil	-	

Table 2. Clinical biochemistry values of an old part-Arab Stallion with a suspected case of hypoxia-induced pre-renal azotemia

Parameters	Value obtained	Reference values
Alanine aminotransferase (ALT) (U/L)	24.95	3.01 - 29.43
Aspartate aminotransferase (AST) (U/L)	138.01	74.38 - 115.06
Alkaline phosphatase (ALP) (U/L)	185.63	34.24 - 109.76
Total protein (g/dl)	5.72	5.57 - 7.74
Albumin (g/dl)	3.96	2.77 - 4.06
Globulin (g/dl)	1.76	2.16 - 4.50
Albumin:Globulin	2.25	0.6 - 1.4
Total cholesterol (mg/dl)	121.05	66.67 - 185.36
Creatinine (mg/dl)	4.0	0.8 - 2.0
Blood Urea Nitrogen	41.49	8 - 27

Discussion

The finding of secondary absolute polycythemia, characterized by significant elevations in the packed cell volume, hemoglobin concentration and erythrocyte cell count suggests an increase in erythropoietin concentrations observed during hypoxia. It was also observed that the mean corpuscular volume and mean corpuscular hemoglobin concentration of the stallion were within the reference range. Therefore, these erythrocytes were normal-sized erythrocytes with normal hemoglobin content, which is a characteristic feature of erythrocytic indices in secondary absolute polycythemia (Walton, 2014). Hypoxia with polycythemia and azotemia, and increased serum erythropoietin has been reported in renal T-cell lymphoma in dogs (Durno *et al*., 2011).

Kidney function can be compromised by polycythemia of hypoxia in several ways. They include increased viscosity of polycythemia blood which tends to reduce renal blood flow and reduced plasma fraction decreases plasma flow relative to renal blood flow (Chen and Al Khalili, 2020). Response to renal hypoxia increases cellularity and viscosity of the blood and may cause a reduction in renal blood flow that cannot be compensated by the higher oxygen-carrying capacity of the blood, so that renal oxygen delivery is reduced, exacerbating renal hypoxia and producing a vicious cycle of increasing polycythemia and increasing renal hypoxia. In other words, decreased renal oxygenation could have triggered erythropoietin production and its resultant increase in erythrocytic parameters as observed in this horse. A classic adaptation of the tissues to hypoxia is the stimulation of erythrocyte production (erythroid hyperplasia) (Hirakawa *et al*., 2017). The hypoxia inducible factor-2 (HIF-2) not only stimulates erythropoietin synthesis when partial pressure of oxygen is low, but also enhances intestinal iron uptake and utilization, and promotes erythroid progenitor maturation in the bone marrow (Haase, 2013). This mechanism is now seen as a therapeutic opportunity in human medicine for the treatment of anaemia associated with chronic kidney disease (Hirakawa *et al*., 2017). Dehydration was excluded as a possible cause of polycythemia because of the normal total protein and albumin levels observed in the horse.

Aspartate aminotransferase is a leakage intracellular enzyme therefore, an elevation in its serum activity could be attributed to cellular hypoxia (Walton, 2014; Agina, 2017). The concurrent increases in blood urea nitrogen and creatinine (azotemia) could be attributed to the kidney's damage to hypoxia. Tissue hypoxia is believed to be an important implicating factor in both acute and chronic kidney diseases, as impaired fluid regulation could contribute to pulmonary oedema and progression from acute to chronic kidney disease (Samanta *et al*., 2018) and may serve as a physiological biomarker of early diagnosis of these diseases (Evans, 2019). In health, the oxygen tension in the kidney is relatively lower in mammals as the kidneys receive approximately 20% of blood pumped from the heart (Hirakawa *et al*., 2017). Most of the oxygen in the renal tissues are utilized to fuel Na-K-ATPase, which controls tubular sodium reabsorption and controls the movement of various solutes, glucose and amino acids across cellular membranes (Haase 2013). The low oxygen tension is due to the oxygen shunt between the artery and the veins that run parallel in the kidney (Kuo and Kurtcuoglu, 2017). This oxygen shunt affects renal oxygenation and account for the high oxygen tension in renal veins than in efferent arterioles and oxygen tension also decreases deeper in the renal surface. In humans, oxygen tension is 50 mm Hg on the renal surface and 30 mm Hg in the renal medulla (Nordquist *et al*., 2015). A lower oxygen tension in normal kidneys has been shown in transgenic mice (Safran *et al*., 2006). Partial pressure of oxygen (pO_2) in the kidney is maintained at a stable level by a complex functional interplay between renal blood flow, GFR, oxygen consumption and arterio-venous oxygen shunting (Haase, 2013).

Conclusions

Our findings were suggestive of hypoxia-induced pre-renal azotemia and they include secondary absolute polycythemia, decreased erythrocyte sedimentation rate, normal sized red cells that are normochromic, elevated serum activities of AST and ALP, normal total protein and albumin levels, high A/G ratio, low globulin, normal cholesterol level with abnormally high serum creatinine and blood urea nitrogen levels. Renal failure is a relatively uncommon problem in horses but has a poor prognosis if not recognized and properly treated.

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Conflict of Interests

The authors declare that there are no conflicts of interest related to this article.

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