Case Report

Iron storage disease (ISD) in a captive toco toucan (*Ramphastos toco*): a case report

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Abstract

A captive, male toco toucan (*Ramphastos toco*) presented with a 1-month history of anorexia, hypodynamia and inability of flying. On physical examination, conscious and responsive, cataract and body condition score were found to be 4/5. Blood chemistry analysis revealed high levels of AST and CK. Radiological examination showed the lungs had increased soft-tissue opacity with loss of the normal reticulated pattern. A necropsy revealed a yellowish discoloration of the liver, pericardial fluid, hemorrhagic pancreatitis and hemorrhagic nephritis. The histopathological examination showed that the liver had modulate autolysis, diffuse sinusoidal congestion and mild hydropic degeneration. Diffuse hemosiderin pigment in cytoplasmic hepatocyte was detected by Prussian blue strain. Histopathological examination confirmed the iron deposition in the liver of the toco toucan. Problems often arise from feeding foods containing ascorbic acid (vitamin C), which is an important factor for iron absorption. Therefore, it is recommended that fruits and vegetables that are high in vitamin C should not be given at the same time as food with high levels of iron. Diagnosis is not always possible until a biopsy. Diagnosis should be based on signalment, history taking and clinical signs, laboratory data and special examination. Our findings will benefit veterinarians in the investigation, diagnosis, prognosis and treatment in ISD in a frugivorous bird.

Keywords: iron storage disease (ISD), toco toucan, ascorbic acid, diagnosis, management

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Introduction

Iron storage disease (ISD) or hemochromatosis mostly reported in captive frugivorous birds (Lowenstine *et al*., 1999; Sheppard and Dierenfeld, 2002; Klasing *et al*., 2012; Pence, 2019). ISD is caused by high iron levels in the dietary or increased iron absorption affect to an accumulation of iron in the tissues (Crissey *et al*., 2000; Sheppard and Dierenfeld, 2002; Klasing *et al*., 2012; Pence, 2019) while some bird species are genetically susceptible to this condition (Cubas, 2007; Pence, 2019). It can be found commonly in birds including 1) Ramphastidae such as the toco toucan (*Ramphastos toco*), 2) mynahs, birds of paradise and Sturnidae, 3) turacos 4) Psittaciformes such as starlings and tanagers (Sheppard and Dierenfeld, 2002; Pence, 2019) and softbilled birds (Johnston, 1999). Toco tocans are the most susceptible species to iron accumulation in breeding and captive individuals (Lowenstine *et al*., 1999). Clinical signs found were either subclinical or nonspecific signs such as anorexia, dyspnea, and ascites (Cubas, 2007). Occasionally there are problems with the respiratory system and also ascites due to cirrhosis and associated with blood circulation problems resulting in sudden death due to drowning (Pence, 2019). Sudden death is often found or increased chronic signs including malnutrition, dyspnea, dropsy, and balance disturbances (Roels *et al*., 1996). In the group of toucans, sudden death occurred before clinical signs appear (Mitchell and Tully, 2016). These clinical signs included loss of ability to fly and weight loss (Connor and Garner, 2018).

This case of iron storage disease in a toco toucan was a rare case at general animal hospitals. This case report adds to the clinical practice guideline for diagnosis and management of iron storage disease (ISD) in a captive toco toucan (*Ramphastos toco*).

Case Presentation

A captive, male toco toucan (*Ramphastos toco*) of unknown age presented with a history of anorexia for approximately 1 month. The usual daily diet includes dragon fruit, corns, apple and banana in morning meals. The evening diet included green pellet bird food (myhna formula) with fish and boiled eggs each day.

For the physical appearance and from examination (Figure 1), the toco toucan was responsive to stimulation, hypodynamia with inability of flying. The bird had a high body condition score of 4/5 and weighed 0.700 kg. It appeared well feathered and hydrated, but both eyes had cataracts.

A blood sample was taken from the basilic veins for hematological and biochemical profiling. Hematological results were within normal limits and biochemical results indicated high levels of aspartate aminotransferase (AST) and creatine kinase (CK) as showed in Table 1. In addition, radiological examination showed that the lungs had increased opacity with interstitial lung pattern when compared to the size of the abdomen (Figure 2).

The toco toucan was treated with meloxicam 1 mg/kg (Metacam®, Labiana life Sciencs S.A., Terrassa, Barcelona, Spain), marbofloxacin 5 mg/kg (Marbocyl®, VETOQUINOL, Lure, Cedex, France) in the pectoral muscle together with a dietary adjustment. All treatments were administered for 1 week prior to its sudden death.

The necropsy report identified that it died suddenly and revealed a yellowish discoloration of the liver, mild swelling edema, heterogeneous texture, pericardial fluid, hemorrhagic pancreatitis, and hemorrhagic nephritis (Figure 3). The histopathological examination showed the liver section related modulate autolysis, diffuse sinusoidal congestion and mild hydropic degeneration of hepatocytes. The examination also showed severe diffuse hepatic hemosiderosis and mild hydropic hepatopathy (Figure 4).

Figure 1 Physical appearance and examination of the case. (A) The toco toucan was responsive to stimulation, hypodynamia with inability of flying. (B) It appeared well feathered and hydrated, but both eyes had cataracts.

Table 1 Hematological and biochemical profiling of the toco toucan

Parameter	Result	References [a]
HCT (%)	47	46-60
WBC (10^3/ul)	9.0	4-10
Heterophil (10^3/ul) (%)	64 (5,760)	35-65
Lymphocyte (10^3/ul) (%)	34 (3,060)	25-50
Eosinophil (10^3/ul) (%)	2 (180)	0-4
Basophil (10^3/ul) (%)	0	0-5
AST (U/L)	493	130-330
BA (umol/L)	35	20-40
CK (U/L)	8,275	207-1,279
Total protein (g/dL)	3.5	3-5
Albumin (g/dL)	1.6	1.4-2.4
Globulin (g/dL)	1.9	1.4-2.2
UA (mg/dL)	11.1	4-14
Glucose (mg/dL)	292	220-350
Calcium (mg/dL)	10.8	10-15

[a]Exotic formulary 4th edition

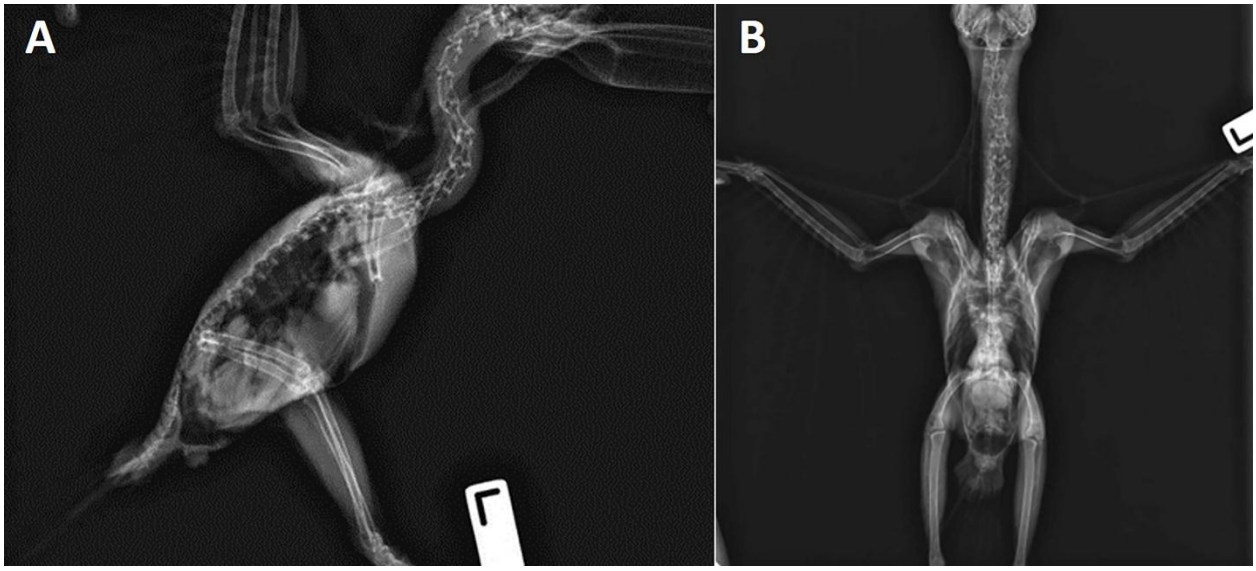

Figure 2 Radiological examination of skeletal system, (A) Left lateral recumbency posture showing content in gastrointestinal tract. (B) Dorsoventral posture showing increased soft tissue opacity of the lungs with loss of the normal reticulated pattern and normal liver size.

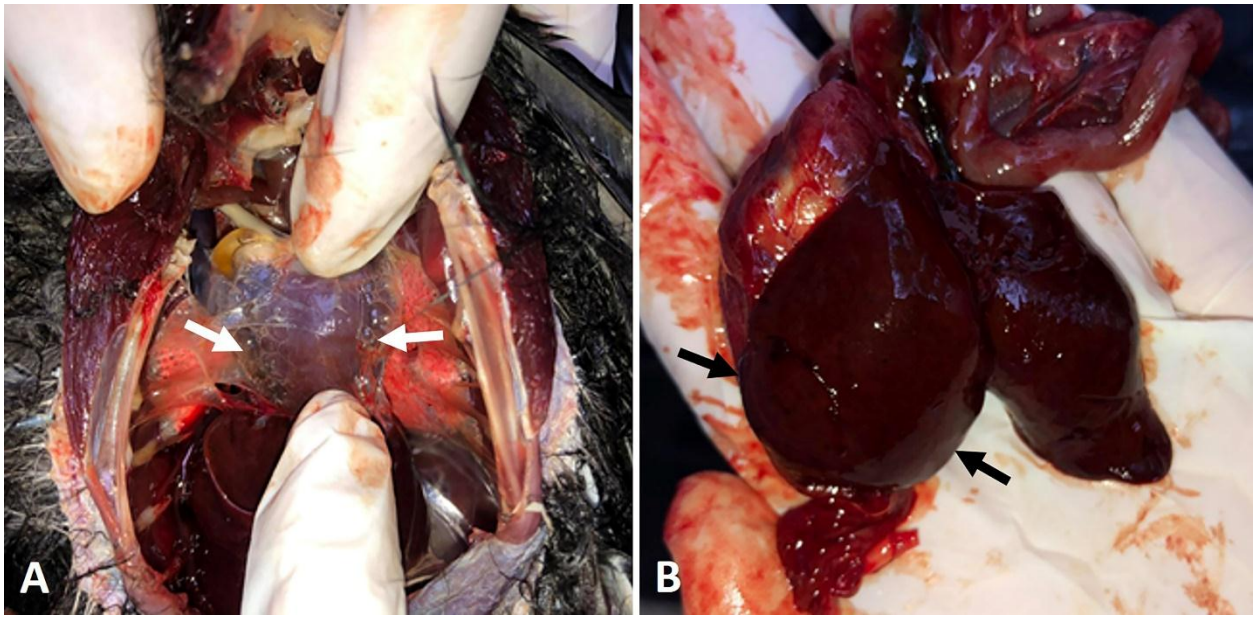

Figure 3 A necropsy was performed immediately after death, (A) shows pericardial fluid (white arrow) and (B) shows a yellowish discoloration (black arrow) of the liver.

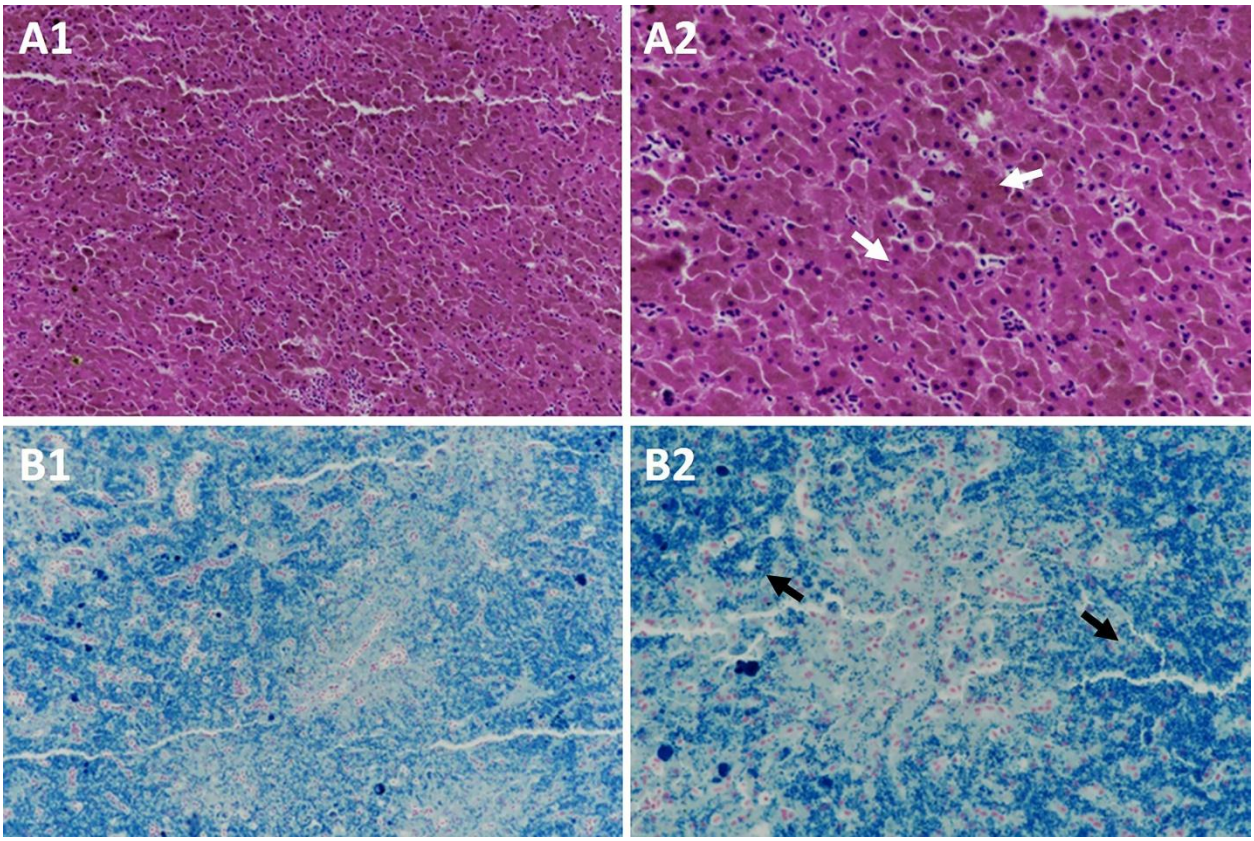

Figure 4 The histopathological findings, A1 and A2 show hepatocytes contained diffuse brown black small pigment in their cytoplasm (white arrow). B1 and B2 show obvious iron diffusion (hemosiderin pigment) by Prussian blue special straining (inorganic iron with potassium ferrocyanide in acidic solution forms ferric ferrocyanidem) and small round nuclei (black arrow).

Discussion

The results of hematological and biochemical profile indicated that hematocrit values were in the lower boundary of the lowest threshold (47%; 46-60%). In addition, anemia should be further monitored as follow up. Elevated enzyme values for AST (493 U/L; 130-330 U/L) and CK (8,275 U/L; 207–1,279 U/L) were above the threshold (O'Connor and Garner, 2018). Hematology and serum biochemical analysis appear to be of little specific diagnostic value (Sheppard and Dierenfeld, 2002). AST is an enzyme that is well used to assess the liver, but it is not specific because elevated AST can also be caused by tissue damage and therefore must be evaluated along with CK, which if both values are abnormal, it is more likely to be caused by tissue damage (Rosenthal, 2019). Presumptive diagnostics based on liver enzyme values suggested metabolic disease, myopathy or liver disease. In addition, the diagnosis is supported by neoplastic diseases, parasitism and systemic bacterial infections causing the hemosiderin pigment (Cork, 2000).

During rehabilitation, veterinarians are suggested to give antibiotics and anti-inflammatory drugs. In addition, dietary management should be considered as well as clinical signs and behavior should be monitored continuously.

In the case that a bird is found with accumulated iron in tissues, the chelation therapy treatment is suggested by using the ability of the iron chelator dessferioxamine (Roels *et al.*, 1996).

Dietary management and husbandry are important factors for reducing iron accumulation in birds. In some cases, certain pellet foods contain high levels of iron content, which can result in iron accumulation in toucans and toucanets (Drews *et al.*, 2004). An appropriate diet should be chosen with a recommended iron value of <100 ppm (Drews *et al.*, 2004; Pence, 2019) and phlebotomy has been used which was successful in the toucan group (Roels *et al.*, 1996). This results in reduced iron levels by removing ferritin, and stores of iron in the bloodstream that binds to transferrin out of the blood circulation (O'Connor and Garner, 2018).

Iron chelator of dessferioxamine has been considered as a suggested treatment for ISD in birds (Roels *et al.*, 1996). The administration of deferoxamine mesilate is at 100 mg/kg/day SC for 110 days or deferiprone at 50 mg/kg PO bid for 30 days (Cubas, 2007). Use of deferiprone (75 mg/kg PO, SID for 90 days) showed that iron level in the liver decreased rapidly in 3 hornbills using histopathological assessment which can be monitored ISD by three methods (Sandmeier *et al.*, 2012); quantitative image analysis (QIA), chemical analysis by liver biopsy, and magnetic resonance imaging (MRI).

Phlebotomy was successful in the toucan group (Roels *et al.*, 1996) by taking approximately 10% of body blood volume (approximately 1% of body weight) every 2 weeks. The reason for the treatment is that the regeneration of blood affects the accumulation of iron to create new hemoglobin (Pence, 2019). This resulted in reduced iron levels by removing ferritin,

which stores circulating iron in the bloodstream that binds to transferrin out of the blood (O'Connor and Garner, 2018; Pence, 2019).

For best treatment, rapid, correct and accurate diagnosis is important. Hematological and biochemical examination cannot confirm the presence of iron accumulation until the biopsy (Gerlach *et al.,* 1998). Initial diagnosis should be based on signalment, history taking and clinical signs, laboratory data and other special examinations.

Diet and husbandry management are important factors in reducing the incidence of iron accumulation in birds. Reducing the dietary iron component to this safety level did result in significant reductions of hepatocellular iron levels (Drews *et al*., 2004). It is important to choose a suitable diet with a recommended iron value of <100 ppm (Pence, 2019). In birds of the Ramphastidae family, there is a tendency for ISD (Vincent, 2007). When feeding a diet high in ascorbic acid, organic acids and low pH effected increased iron absorption by reducing non-heme iron from the insoluble form Fe^{3+} to Fe^{2+}, which is more easily absorbed. (Sheppard and Dierenfeld, 2002; Pence, 2019). Duodenal cytochrome b accepts intracellular electrons from the oxidation of ascorbic acid to dehydroscorbic acid, and uses these acids to accelerate the reduction of Fe^{3+} to Fe^{2+} (Yiannikourides and Yemisi, 2019). Therefore, it is recommended that fruits and vegetables high in vitamin C, should not be fed at the same time as foods high in iron (Sheppard and Dierenfeld, 2002; Pence, 2019). Iron chelating agents in food, such as tannins can be diluted in drinking water or green tea leaves used in food and phytate plants, it reduces the absorption and dispersion of iron by transforming it into an insoluble complex (Pence, 2019). This problem can be prevented by supplementing with non-citrus fruits. A diet high in vitamin C is recommended on alternating days with a diet comprised of iron chelating agent.

Thus, high dietary iron level, nutritional interactions increasing the bioavailability (absorption and excretion) and genetically or physiologically sensitive species are all contributing factors to ISD (Cork, 2000; Sheppard, 2002).

In husbandry, there should be an understanding of the basic requirements, diseases or health problems that are often encountered. The veterinarian should be consulted for advice on nutrition management. If the owner encounters health problems in the bird, it should be taken to the veterinarian as soon as possible. All this information is used for the benefit of veterinarians for investigation, diagnosis, prognosis and treatment in ISD in birds.

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