

CRANIAL EDEMA ASSOCIATED WITH A PROTEIN-LOSING NEPHROPATHY IN A GOLDEN-MANTLED FLYING FOX (*PTEROPUS PUMILUS*)

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Abstract: An adult golden-mantled flying fox (*Pteropus pumilus*) was diagnosed with nephrotic syndrome on the basis of the findings of proteinuria, hypoalbuminemia, hypercholesterolemia, and cranial edema. Membranoproliferative glomerulitis and interstitial nephritis were confirmed antemortem by renal biopsy. The bat had received seven injections of oxytocin in the period immediately prior to presentation. The possible role of oxytocin in the development of the nephropathy is discussed. Supportive care and treatment with a single plasma transfusion, furosemide, and prednisone led to a gradual but complete resolution of the nephrotic syndrome in this animal.

Key words: Nephrotic syndrome, oxytocin, cranial edema, *Pteropus pumilus*, flying fox, bat.

CASE REPORT

An adult, 208-gm, intact female golden-mantled flying fox (*Pteropus pumilus*) with a swollen head of 8-days duration was evaluated on 28 March 1996 at the University of Florida Veterinary Medical Teaching Hospital. At the time of presentation, the bat was suckling a healthy 30-day-old pup. The bat was a subject in a study of nutritional ecology and energetics of fruit-eating bats that included analysis of milk changes during lactation. The bat had been injected with oxytocin (Anthony Products Co., Arcadia, California 91006, USA; 3 IU i.p.) to enhance milk let-down beginning on the day after parturition, then every 2–5 days, for a total of seven injections during the period immediately preceding presentation.⁸

The animal had been wild caught in the Philippines and then transported in May 1992 to the Lube Foundation, a private bat breeding and research facility in north central Florida. The animal was housed in an indoor/outdoor enclosure and was fed a mixture of fruits, vegetables, commercial primate chow (Zu/Preem Canned Marmoset Diet, Premium Nutritional Products, Inc., Mission, Kansas 66202, USA, and Hill's New World Monkey Chow, Hill's Pet Products, Topeka, Kansas 66601, USA), and a vitamin/mineral supplement (Vionate Vitamin-Mineral Powder, ARC Laboratories, Atlanta, Georgia 30340, USA). The bat had no previous history of illness. An idiopathic leukocytosis with a lympho-

cytosis and monocytosis were present at the time of its entry examination in 1992, and a subsequent examination in 1993 revealed a neutrophilic leukocytosis with a lymphocytosis (Table 1).

The bat was anesthetized with isoflurane (Aerane®, Ohmeda Pharmaceutical Products Division Inc., Liberty Corner, New Jersey 07938, USA) in 100% oxygen for physical examination. The initial examination revealed no abnormality except for a cool, pitting edema of the head (Fig. 1). Blood was collected from the median vein on the medial surface of the humerus and submitted for a CBC and plasma biochemical panel. Whole body radiographs were made, and the thorax and abdomen were evaluated ultrasonographically. The animal was discharged with instructions to discontinue the oxytocin pending laboratory results. Significant findings included leukopenia, hypoproteinemia, hypoalbuminemia, low albumin/globulin (A/G) ratio, hypocalcemia, hyperphosphatemia, hypercholesterolemia, and hyperbilirubinemia (Tables 1, 2). Abdominal ultrasonography revealed a small amount of free peritoneal fluid and bilateral hyperechoic renal cortices. Whole body radiographs and thoracic ultrasonography were unremarkable.

The bat was reevaluated 5 days later (2 April 1996). Subjectively, the cranial edema was less pronounced and abdominal palpation was unremarkable. Blood and a free-catch urine sample were submitted for a plasma biochemical panel and urinalysis, respectively. Significant findings on the plasma biochemical panel included hypoglycemia, hypoproteinemia, hypoalbuminemia, low A/G ratio, hypocalcemia, hypercholesterolemia, and hyperbilirubinemia (Table 2). Urinalysis revealed a specific gravity of 1.008 and 300 mg/dl protein (Table 3). On 16 April 1996, an increase in cranial edema was

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Figure 1. Cranial edema (arrowheads) in an adult female golden-mantled flying fox (*Pteropus pumilus*) with a protein-losing nephropathy.

sample were submitted the following day (17 April 1996) for another plasma biochemical panel and urinalysis, respectively. Significant findings included hypoproteinemia, hypoalbuminemia, low A/G ratio, hypocalcemia, hyperphosphatemia, hypercholesterolemia, and hyperbilirubinemia (Table 2). The urine specific gravity was 1.006 and protein was $>2,000$ mg/dl (Table 3). The bat was hospitalized

ma collected in heparinized tubes from three healthy golden-mantled flying foxes as well as furosemide (Lasix®, Hoechst-Roussel Pharmaceuticals Inc., Somerville, New Jersey 08876, USA; 1 mg/kg i.m.).

The cranial edema improved during the following 7 days of hospitalization. Therapy included furosemide 1 mg/kg i.m. b.i.d., which was decreased

Table 3. Specific gravity, protein content, and pH of urine from a golden-mantled flying fox (*Pteropus pumilus*) with a protein-losing nephropathy.

| Parameter | Apr 2 1996 | Apr 17 1996 | Apr 22 1996 | Apr 30 1996 | May 17 1996 | Jul 19 1996 | Aug 15 1996 | Oct 29 1996 | Reference values ^a |
|------------------|---------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------------------------|
| Specific gravity | 1.008 | 1.006 | 1.009 | 1.005 | 1.007 | 1.013 | 1.010 | 1.011 | 1.017–1.030 |
| Protein (mg/dl) | 300 | >2,000 | >2,000 | 300 | 300 | 100 | 30 | 100 | Negative |
| pH | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 | 5.0 |

^a Reference values are based on five golden-mantled flying foxes in the collection.

nificant findings included hypoglycemia, hypoproteinemia, hypoalbuminemia, low A/G ratio, hyperphosphatemia, hypercholesterolemia, and hyperbilirubinemia (Table 2). The significant findings on the urinalysis included a specific gravity of 1.009, >2,000 mg/dl protein, and one waxy cast with small clumps of epithelial cells (Table 3). The bat was discharged on day 7 of hospitalization (23 April 1996) with the instructions to continue oral furosemide at 1 mg/kg and prednisone syrup at 2 mg/kg once daily.

The bat was clinically normal on reevaluation 7 days later (30 April 1996). Total protein and albumin were increased compared with previous samples (Table 2). Urine specific gravity was 1.005 with proteinuria (300 mg/dl) (Table 3). Oral furosemide and prednisone s.i.d. were continued. Two weeks later (14 May 1996), the total protein and albumin were increased and the cholesterol decreased from the previous sample (Table 2). The CBC was unremarkable (Table 1).

Fifty days after the initial evaluation (17 May 1996), the cranial edema recurred with proteinuria and isothermia (Table 3). The dosage intervals of oral furosemide 1 mg/kg and prednisone 2 mg/kg were increased to b.i.d., and an abdominal exploratory laparotomy was performed by a ventral midline approach 5 days later (22 May 1996). Biopsies were collected with a small biopsy forceps from both kidneys and the liver margin. A blood sample was collected at the time of surgery. Significant findings included a neutropenia with a left shift, monocytosis, hypoalbuminemia, hypocalcemia, hyperphosphatemia, and hyperbilirubinemia (Tables 1, 2).

Grossly, the left kidney was irregular and appeared slightly larger than the right kidney. Hematoxylin and eosin, periodic acid–Schiff (PAS), and Congo red stains were performed on the kidney tissue for histologic evaluation. Microscopically, the kidney biopsies revealed occasional moderate dilation of tubular lumens and dense eosinophilic accumulations of homogenous PAS-positive mate-

and glomerular tufts had thickened capillary walls with narrowed capillary lumina. Leukocytes were seen occasionally within capillaries. Mesangial cells were prominent, were clustered in the tufts, and had enlarged, hypochromatic nuclei. Adhesion of visceral epithelial cells to the Bowman's capsule was occasionally noted. In some glomeruli, parietal epithelial cells were prominent. Amyloid was not detected in glomeruli by Congo red stain. Rare small interstitial accumulations of predominately plasma cells and lymphocytes with fewer neutrophils were noted. Minimal fibrosis was found in these interstitial areas. The histopathologic diagnosis of the renal lesions was moderate, multifocal, chronic, membranoproliferative glomerulitis and interstitial nephritis with focal glomerulosclerosis.

Histologic evaluation of the liver biopsies revealed moderately to markedly swollen hepatocytes with a pale, eosinophilic, vacuolated cytoplasm. Frequently, the hepatocytes formed confluent sheets of dense anastomosing cords with poorly defined sinusoids. Inflammation was not a feature. The histologic diagnosis was diffuse, moderate to marked vacuolar degeneration of the hepatocytes, most consistent with glycogen deposition or hydropic degeneration.

The bat was discharged the day after surgery (23 May 1996) with continuing therapy of oral furosemide 1 mg/kg b.i.d. and oral prednisone on a tapering schedule of 2 mg/kg b.i.d. for 3 days, s.i.d. for 3 days, then e.o.d. for three doses over the next 2 wk.

The last episode of cranial edema was on 17 May 1996. To date, no other episode of cranial edema has occurred. The bat has been off all medications since June 1996. Laboratory results from blood and urine samples collected during July–October 1996 revealed persistent hypocalcemia with resolving nephropathy and an unremarkable CBC (Tables 1–3).

DISCUSSION

This golden-mantled flying fox was diagnosed antemortem with a membranoproliferative glomer-

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