A CLINICIAN'S APPROACH TO LIVER DISEASE IN TORTOISES

Stephen John Divers, BSc(Hons) CBiol MIBiol BVetMed MRCVS
Elands Veterinary Clinic
Station Road, Dunton Green
Sevenoaks, Kent TN13 2XA
United Kingdom

Abstract: This paper describes the historical indicators and clinical signs of liver disease in tortoises. The importance of medical stabilization is stressed and a logical and practical case work-up is described.

Key words: liver, disease, reptile, tortoise, Chelonia, diagnosis, endoscopy, biochemistry

INTRODUCTION

Liver disease represents a known cause of morbidity and mortality in captive tortoise populations[1]. Hepatitis can be due to a variety of infectious agents including various bacteria, fungi, viruses, protozoal and occasionally helminth parasites, as well as acute toxicological insults. Degenerative liver disease, or hepatosis, is due in the main to poor captive nutrition and chronic fatty changes leading to hepatic lipidosis. Rarely, chronic low grade exposure to toxins or poisons can also lead to hepatosis. Unfortunately, owners are seldom aware of chronic disease until the functional capacity of the liver has been exceeded. Therefore, tortoises suffering from either acute or chronic liver disease will often present as critically ill animals.

This paper attempts to provide the clinician with a practical approach to investigating and diagnosing liver disease in Chelonia.

CLINICAL INVESTIGATION

History

In cases of acute liver disease there will often be very little history with the tortoise in apparent good health and eating normally and then suddenly becoming depressed, lethargic and anorexic. If several tortoises in a large collection are affected simultaneously, then an infectious agent must be considered above all else. Owner records will be of use in identifying any new additions (last 6-12 mo) to the collection, or the provision of a novel, potentially toxic food item[2].

In cases of chronic liver disease, detailed owner records may indicate a gradual reduction in appetite, reduced activity, reduced fecundity and fertility, reduced weight gain or gradual weight loss, hibernation problems including post-hibernation anorexia, and changes in fecal character and color. However, apart from zoological collections, most owners will miss these early signs resulting in the chronically diseased animal presenting as an acute emergency during the terminal stages of pathogenesis.

Clinical Findings

In cases of acute liver disease the animal may appear in good condition with normal weight, normal muscle coverage over limbs and with no obvious abnormalities. Diarrhea is not uncommon and if the urates are pigmented (yellow-green) then the excretion of bile pigments (biliverdin and bilirubin) may indicate severe liver compromise. Regurgitation usually involves liquid and not food material, and is considered to be a poor sign. The animal will usually be very depressed, lethargic and weak, mucous membranes may be pale, hyperemic or jaundiced. The eyes may be closed.

In cases of chronic liver disease the animal will usually be in poor body condition. The limbs are often flaccid and weak with poor muscle coverage. The weight is usually below normal, often critically so, although in cases of hepatic lipidosis or ascites weight may be normal or even increased. Diarrhea is less common as these animals have often been hypophagic and anorexic for a prolonged period of time. It is often during periods of increased physiological stress that the underlying liver disease becomes clinical, for example, hibernation, breeding, episodes of concurrent disease, etc. Unfortunately, the chronic nature of the disease may be missed and signs of severe liver compromise (anorexia, diarrhea, regurgitation, jaundice etc.) may confuse and convince the clinician that this is an acute hepatitis rather than the end stage presentation of chronic disease. A full clinicopathological investigation is essential to accurately differentiate between all cases of acute and chronic liver disease.

Medical Stabilization

The aim must be to stabilize the patient prior to diagnostic work-up. Take a blood sample for laboratory investigation prior to initiating i.o. or i.v. fluid therapy at 20-30 ml/kg/d. The provision of a suitable thermal environment must never be overlooked.

Laboratory Findings

A basic data base including fecal, complete blood count and basic biochemistry is essential in any reptile presenting with anorexia and other gastrointestinal signs and will direct the clinician towards further more specific liver biochemistries and ancillary diagnostics. (Table 1).

Diagnostic Imaging and Endoscopy

Unfortunately radiography is of limited use in assessing liver disease in most chelonians. Occasionally, lateral views may indicate an increase in hepatic size, but the gastrointestinal contents and superimposition of the shell make this very difficult. Ultrasonography has been used to visualize the liver and although useful for identifying gross changes in liver size, discrete neoplasms and abscessation, the author has found if of limited use in categorizing subtle changes in liver structure and pathology.

Endoscopy represents a very useful diagnostic tool and enables the clinician to visualize the liver's surface, appreciate its size, contours and color. More importantly it facilitates the taking of hepatic biopsies for both culture and sensitivity and histology which in the vast majority of cases provides a definitive diagnosis and prognosis. The site of entry is the inguinal or femoral fossa, with the animal positioned in lateral recumbency. Air inflation is not always required but useful. In cases of severe, chronic liver disease it may be wise to perform a coagulation profile before embarking on biopsy.

Treatment (See Table 2)

Certain treatments are broadly applicable to most if not all cases of liver disease. For example, fluid therapy, reduced protein intake (no dog/cat food!), anabolic steroids, and multivitamins (especially water soluble B and C). Ascites may require the very careful and judicious use of diuretics while infectious hepatitis will necessitate antimicrobial medications based upon culture and sensitivity. In cases of hepatic encephalopathy, oral neomycin may be employed to reduce the gastrointestinal production of ammonia.

In cases of severe, chronic disease such as hepatic lipidosis, a pharyngostomy tube may be necessary to provide sufficient nutritional support for weeks or months until the animal is able to feed normally again.

The concept of diagnosing and treating 'liver disease' is a fallacy! Liver disease is the problem not the diagnosis. A diagnosis is hepatic lipidosis, mycotic hepatitis, herpes virus hepatitis, toxic hepatosis, mycobacterium hepatitis, cholangitis or any number of other specific disorders. Only once you have a specific diagnosis can you provide specific therapy and maximize your chances of success.

LITERATURE CITED

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TABLE 1

Blood Parameters Used in the Assessment of Tortoise Liver Disease

Blood Parameter	Normal Range[5]	Diagnostic Use
Total WBC ($x10^9$/L)	2.0-10.0	Raised during inflammation and infection, may be depressed or low during hibernation/post-hibernation
Heterophils ($x10^9$/L)	0.5-4.0	Classic reptile inflammatory cell, usually raised in sepsis and necrosis
Lymphocytes ($x10^9$/L)	0.75-4.0	Highly variable but may be elevated in cases of viral disease
Azurophils ($x10^9$/L)	0.075-0.7	Elevated during bacterial infections and necrosis
Monocytes ($x10^9$/L)	0.02-0.5	Elevated in cases of chronic disease and chronic immunogenic stimulation
Eosinophils ($x10^9$/L)	0.025-0.8	Variable in number, elevated in protozoal and helminth infections
PCV (L/L)	0.20-0.35	Useful to assess hydration status, anemia
RBC ($x10^{12}$/L)	0.12-0.75	Decreased in cases of chronic disease
Hb (g/dl)	3.5-8.6	Decreased in cases of chronic disease
ALT (U/L)	5-120	Often raised in cases of liver disease but not liver specific as also present in muscle
ALKP (U/L)	20-150	Widespread tissues distribution, not specific or very sensitive of liver disease
AST (U/L)	20-150	Very sensitive indicator of both liver and muscle disease, also elevated in cases of renal disease
GGT (U/L)	0.0-3.0	Liver specific but unfortunately not very sensitive in most reptiles
Bile acids (μmol/L)	<10μmol/L	Liver specific and very sensitive for liver function not necessarily active disease; normal values yet to be elucidated for most species; serial samples probably most useful to monitor liver function
Bilirubin/biliverdin	na	Bilirubin produced in very small quantities (intermediate metabolite), biliverdin is the major bile pigment but no commercial assays yet available
Cholesterol (mmol/L)	0.6-5.8	May be elevated secondary to triglycerides in cases of hepatic hepatitis
Triglycerides (mmol/L)	0.6-5.4	May be elevated in cases of hepatic lipidosis
Total Protein (g/L)	32-66	Decreased with malnutrition, blood loss, intestinal disease, chronic liver and kidney disease; alpha globulins decrease with hepatic disease
Albumin (g/L)	10-35	May fall as a result of prolonged anorexia or hepatic disease; rises due to dehydration
Glucose (mmol/L)	2.5-5.5	Varies with metabolic state, nutrition and stress but reduced in severe hepatopathies; rare cases of diabetes mellitus with hepatic lipidosis
Uric acid (μmol/L)	10-200	Raised during dehydration but hepatic production may be reduced in cases of liver disease; normal range highly variable between species but more precise within a species
Urea (mmol/L)	0.0-16.7	Production and excretion highly variable, may have some limited use as a guide to early dehydration but not considered clinically useful

Please note that these values will vary with species, gender, nutrition, environment, season, and reproductive status.

TABLE 2

Drugs Commonly Employed in the Treatment of Liver Disease

Drug	Dose	Comments
Acyclovir	80 mg/kg p.o. q 24 hr	Herpes virus hepatitis
Amphotericin B	0.5-1.0 mg/kg i.ce., i.v. q 24-72 hr x 14-28 d	Mycotic hepatitis FT HT
Itraconizole	5 mg/kg p.o. q 24 hr	Mycotic hepatitis FT HT
Miconazole	5 mg/kg i.v., i.m. q 24 hr	Mycotic hepatitis FT HT
Ceftazidime	20-40 mg/kg i.m. q 72 hr	Reconstituted solution viable for 12 hr at +4°C or 4 mo if frozen
Doxycycline	2.5-10 mg/kg p.o. q 12-24 hr x 10 d	
Enrofloxacin*	5-10 mg/kg i.m., p.o. q 24 hr	
Neomycin	10 mg/kg p.o. q 24 hr	Do not give systemically NT
Piperacillin	50 mg/kg i.m., then 25 mg/kg q 24 hr x 10 d	FT
Furosemide	2-5 mg/kg i.m., i.v. q 12-24 hr	Diuretic used to reduce ascites; beware of dehydration
Hydrochlorothiazide	1 mg/kg q 24-72 hr	Thiazide diuretic used to reduce ascites; beware of dehydration
Metronidazole	250 mg/kg p.o., can repeat in 7-10 d	Protozoal hepatitis
Oxfendazole	68 mg/kg p.o. once	Nematodes; benzimidazole of choice
Praziquantel	8 mg/kg i.m., p.o. , repeat in 14 d and 28 d 30 mg/kg p.o. once	Cestodes and trematodes
Prednisolone	5-10 mg/kg i.m., i.v., i.o. as required 0.5-1.0 mg/kg s.c., i.m. q 24-48 hr	Shock; antifibrotic?
Vitamin B_{12}	0.05 mg/kg i.m., s.c.	Appetite stimulant
Vitamin B complex	0.1 ml/kg i.m.	
Vitamin C	10-200 mg/kg i.m. as required	
Nandrolone	1 mg/kg i.m. q 7-28 d	Anabolic steroid

Reference should also be made to the table of antibiotic regimes derived from published pharmacokinetic studies.
Where a particular temperature is not stated, the reptile should be maintained at species-specific PBT.

FT - fluid therapy recommended
HT - potentially hepatotoxic
NT - potentially nephrotoxic
* - pain/irritation/inflammation at injection site