More than just blood work – first opinion approach to hepatopathy

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Categories: Vets

Date: September 16, 2013

AT the time of writing, I’m on maternity leave enjoying the hot, sunny weather, so I’ve had to look at my surroundings for inspiration.

Many horses are sporting sunburnt noses and farmers are frantically cutting hay, which made me consider photosensitivity reactions, ragwort poisoning and assessment of underlying liver disease within a first opinion setting.

The liver has a large range of actions, including formation of plasma proteins, formation and excretion of bile salts, formation of blood clotting factors and detoxification, including detoxification of photodynamic agents. As liver disease is often diffuse, the clinical signs are varied and non-specific.

Many equines present with lethargy, depression and weight loss, but ventral oedema, polyuria, polydipsia and gastrointestinal disturbances may also be apparent. As these are nonspecific symptoms, a complete clinical examination should be undertaken to eliminate other disease processes. It is rare to see severe icterus as the primary presenting sign due to the pigmented nature of equine skin. Sometimes hepatopathies are diagnosed on a routine blood sample without any evidence of clinical disease.

Photosensitivity is an important, though rarer, sign of hepatopathy and any individual animal showing erythematous reactions of the non-pigmented skin should be fully examined and a screening biochemistry profile taken. Owners often just keep applying sun block, yet careful history taking may reveal this horse has never suffered from sunburn in previous years. In other cases, if the horse has white markings on the distal limbs, the owners may be unsuccessfully treating for mud fever. Other than hepatic disease, ingestion of toxic plants, such as St John’s wort, may cause similar actinic reactions.
Blood testing

Often, raised gamma-glutamyl transferase (GGT) levels are the primary parameter used to diagnose liver disease, yet simple in-house biochemistry and haematology tests can offer much more comprehensive information, without referral for specialist veterinary intervention.

GGT is the most liver specific enzyme and is taken to denote hepatocellular damage and cholestasis. As suggested, it is routinely used to screen for equine hepatopathy and is also the only enzyme that may be used to provide an indication of prognosis. Horses in training will often have a mildly raised GGT, so care must be taken not to over-interpret results.

Aspartate aminotransferase and alkaline phosphatase are routinely found in in-house biochemistry profiles. These are useful, although non-specific indicators of liver pathology if interpreted in conjunction with other parameters. Raised glutamate dehydrogenase and lactate dehydrogenase are also useful, non-specific indicators, although they are not so commonly available in-house. There may be plasma proteins derangements, as failure of albumin synthesis will often result in hypoalbuminaemia and consequently a reduced total protein level.

Occasionally, hyperglobulinaemia is observed, which can indicate chronicity. Total bilirubin is also likely to be increased, although this can also increase after a period of inappetence, therefore cannot be taken as a definitive diagnosis of hepatopathy. Assessment of the inflammatory proteins serum amyloid A and fibrinogen can also be useful. Leukocytosis and neutrophilia may be noted in more chronic conditions.

Unfortunately, none of the above parameters evaluate hepatic function. This is routinely done by measuring serum bile acid concentrations and usually requires use of an external laboratory. Measurement can help distinguish between damage, compromise and failure, with levels greater than 30mol/L showing reduced survival. Even if the practice laboratory only requires a heparinised and ethylenediaminetetraacetic acid blood sample, taking a plain tube avoids returning for resampling. Rarely, liver function is assessed using plasma levels of ammonia and bromsulphthalein clearance.

Is a blood sample all that is required?

Although blood samples provide an easy method of diagnosing and assessing hepatopathies, much more can be achieved either at the yard or in a first opinion clinic situation.

Ultrasonographic assessment of limited portions of the liver can be done using the standard 5MHz scanner that most practices have for rectal examinations. There is usually no need to clip the hair in all but the hairiest of animals – soaking with surgical spirit should provide adequate contact.

Unfortunately, there are only limited windows for hepatic ultrasonography – between the 10th and
14th intercostal spaces on the right side is the most accessible. The liver should be assessed for size, homogenous echogenicity and dilation of bile ducts. Most liver pathologies are diffuse, so there is limited concern about “missing” any problems.

Hepatic biopsies are easily obtained in first opinion practice and should not be viewed as a specialist procedure. Although complications are rarely encountered, they include haemorrhage, peritonitis, mild pneumothorax and the potential of sampling the wrong tissue. The most significant of these is intraabdominal haemorrhage due to a lack of clotting factors. There continues to be debate about whether clotting factors should be assessed prior to biopsy. Ideally, these should be checked, although most clinicians routinely perform biopsies without this information.

Biopsies are usually taken from between the 12th and 14th intercostal spaces on the right side. This can be done with a blind technique, although ultrasound guidance is preferable to minimise potential complications. This simple technique is performed using local anaesthetic under standing sedation, allowing multiple small samples of tissue to be taken with a Tru-Cut needle through one small incision\(^4\). Samples should be preserved in an appropriate volume of formal saline solution and can also be placed in transport media for culture and sensitivity.

Biopsies provide a histopathological diagnosis, help assessment of the expected prognosis and help treatment planning. Severe periportal and bridging fibrosis usually indicate a poor prognosis. Neutrophilic or lymphocytic infiltrates may also be observed, as may biliary hyperplasia and haemosiderin accumulation. Megalocytosis is pathognomic for pyrrolizidine alkaloid toxicity. A scoring system has been devised to help correlate histopathological changes with prognosis\(^5\).

**Treatment options**

Without the benefit of a biopsy, cases of liver disease are usually prescribed a prolonged course of antibiotics and management supportively. As unnecessary use of antibiotics is inadvisable, this option should be based on neutrophilic infiltrates noted on biopsy. Culture and sensitivity of a tissue sample is the preferable option and will help direct the antibiotic choice.

It is presumed most infectious cholangiohepatitis cases are due to retrograde bacterial spread from the small intestine\(^3\). Trimethoprim sulphonamide is often chosen, as it is broad spectrum, easily administered and relatively inexpensive. Contrary to data sheet recommendations, this is often prescribed twice daily.

In some cases, the biopsy shows an inflammatory pattern, in which case corticosteroids are usually prescribed. Again, a biopsy will justify this approach, which is especially important if the animal has a previous history of laminitis.

**Management options**
It is advisable to feed a low protein, high carbohydrate diet. As such, alfalfa-containing products should be avoided. Beet pulp can be a useful feed, as it has a favourable branched chain to aromatic amino acid ratio, which may reduce the incidence of hepatoencephalopathy\(^1\).

S-Adenosylmethionine (SAMe) is an oral supplement that may help protect and repair hepatocytes after oxidative injury and is becoming more commercially available in equine specific formulae. Feed supplements, such as milk thistle (silymarin) and vitamin E, can also be used for their antioxidant action. An increase in dietary vitamin B may help support hepatic function. Care should be taken to avoid feed supplements with excessive amounts of iron.

All animals with hepatopathies should be shielded from the sunlight. This is especially important if there are existing signs of photosensitivity at presentation. Field-kept animals can usually graze during the hours of darkness instead.

**Ragwort toxicity**

Common ragwort (\textit{Senecio jacobaea}) is one of the weeds subject to the Weeds Act 1959 and the \textit{Code of Practice on How to Prevent the Spread of Ragwort} (2004) was published by Defra\(^6\). This should protect grazing land, yet it is still common to see an abundance of ragwort plants in the UK countryside.

Normally, ragwort, which contains pyrrolizidine alkaloids, is not highly palatable, although palatability increases after drying, such as in hay. The toxins are metabolised in the liver where they are cytotoxic. Megalocytosis results in a fibrotic response within the liver and, as this accumulates, hepatic function becomes compromised. Once clinical signs are evident, the condition becomes irreversible, although treatment and management can improve the clinical signs for a short time.

**Hepatoencephalopathy**

It is always debatable whether to treat an equine exhibiting signs of hepatoencephalopathy. Arguably, hepatoencephalopathy occurs more frequently after acute liver disease rather than chronic disease\(^1\).

It is usually appropriate to treat hepatoencephalopathy in acute cases of hepatic disease in young horses. In other cases, especially those involving chronic disease such as pyrrolizidine alkaloid toxicity in older equines, it may not be appropriate to undertake treatment. Ultimately, this is governed by the owner’s wishes, finances and the welfare of the animal. If a biopsy has been taken, this can help guide this decision.

Hepatoencephalopathy cases that show manic behaviour should be sedated with small doses of alpha-2 agonists and their head should be kept in a normal position. Treatment can then be
instigated, with oral lactulose to reduce circulating ammonia levels\(^1\), dietary management and possibly hospitalisation for appropriate supportive therapy.

**Follow up**

Once the diagnosis and treatment have been established, many clinicians follow the progress of treatment using repeat biochemical profiles; however, a repeat biopsy is much more informative and not dramatically more costly.

**Summary**

Although liver disease is often not evident until damage is severe, it is worthwhile investigating further to provide the horse with the most appropriate treatment and the owner with valuable prognostic information. Treatment can be very rewarding, especially in the cases of septic cholangiohepatitis.

**References**

Only a simple kit is required for liver biopsy.
Left: common ragwort continues to proliferate in the UK countryside.
Below: site for liver biopsy between 12th and 14th intercostal spaces.