Inappetence and dullness in a pony

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In this instalment of BattLab box our colleague presents an interesting case which turns out to have a potential life threatening condition.

SIGNALMENT

10 years old, female entire, pony.

HISTORY

The pony presented with a history of inappetence, tachycardia and reduced faecal output of 12 hours duration. Her clinical sings did not resolve after she was medicated by the referring veterinarian with butylscopolamine, metamizole and flunixin meglumine.

PHYSICAL EXAMINATION

On presentation she was dull in demeanour but responsive and showed a mild interest in grazing. Her temperature was normal at 37º C. She was tachycardic (80 bpm) and had reduced gut sounds. Her body conditions score was 9/9. No dental disease was found on oral examination. A rectal examination was within limits.

INVESTIGATION

Biochemistry

Biochemistry was performed (see Table 1).

Parameter	Value	Equine reference range
Sodium (mmol/L)	140	125 - 150
Potassium (mmol/L)	2.8	2.8 - 4.5
Chloride (mmol/L)	105	95 - 105
Urea (mmol/L)	3.8	3.3 - 6.7
Creatinine (µmol/L)	77	71 - 159
Glucose (mmol/L)	**7.9**	3.05 - 4.99
Total Protein (g/L)	58	55 - 75
Albumin (g/L)	25	25 - 54
Globulin (g/L)	33	24 -51
Total calcium (mmol/L)	2.76	2.5 - 3.4
AST (IU/L)	**2515**	< 250
CK (IU/L)	**5708**	< 130
GGT (IU/L)	**1434.9**	< 25
GLDH (IU/L)	6.9	< 8
Bile acids (µmol/L)	**25**	< 12
Total bilirubin (µmol/L)	**71.3**	8.6 - 59.9
Triglyceride (mmol/L)	**8.0**	< 0.97

Table 1. Biochemistry results. Values in bold were outside the equine RI.

Urinalysis
Urine dipstick showed a trace of glucose and 4+ erythrocytes/haemoglobin.

Haematology
Haematology was performed and revealed borderline erythrocytosis (haematocrit = 0.51 L/L, reference interval: 0.30 - 0.50 L/L). Other haematology parameters, as well as, plasma protein and fibrinogen were within limits.

Imaging
Abdominal ultrasonography revealed an enlarged liver of increased echogenicity with rounded edges (Figure 1). Colic was ruled out.

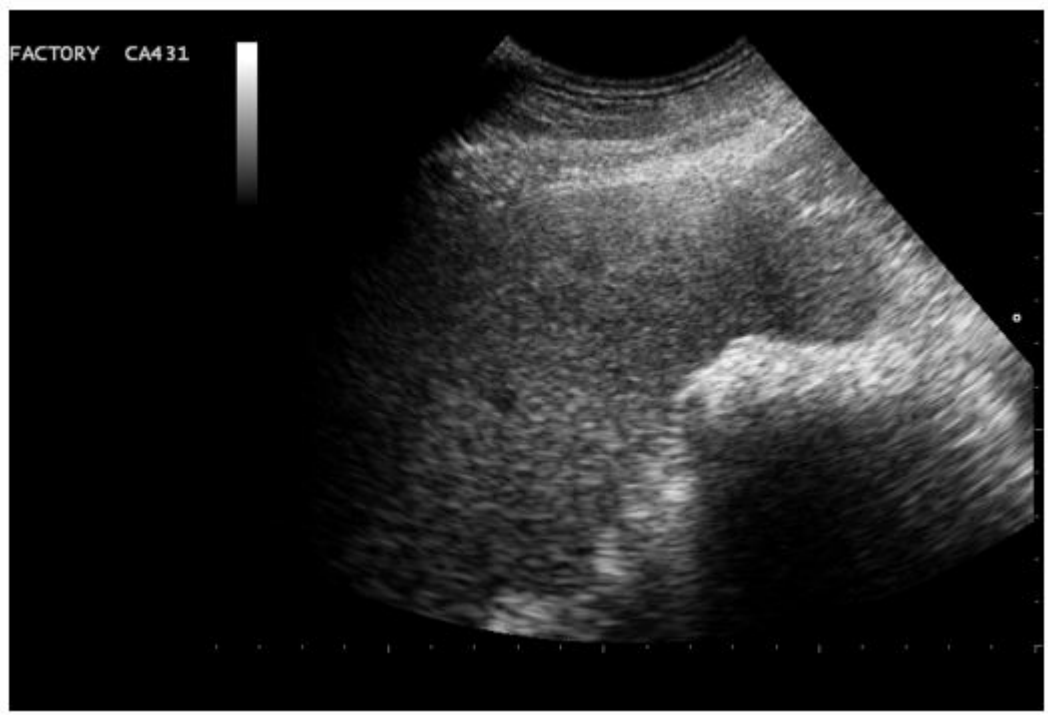

Figure 1. Abdominal ultrasound showing enlarged liver with rounded edges.

What is your interpretation of the clinicopathological findings?
What further tests would you perform in order to reach final diagnosis?

Biochemistry
Moderate to marked hypertriglyceridaemia most likely reflected primary or secondary hyperlipaemia. Equine hyperlipaemia is a consequence of a negative energy status which in this case was most likely secondary to anorexia, obesity or hepatopathy. Other causes of secondary hyperlipaemia were less likely (stress, neoplasia, gastrointestinal disease, pituitary pars intermedia dysfunction [PPID]) or were ruled out (laminitis, renal failure, dental disease, endotoxaemia).

CK was markedly elevated indicating myocyte injury (mostly likely skeletal but also cardiac) which could be secondary to lipid accumulation, intramuscular injections or hypoxia. Nutritional causes, toxicity, trauma, rhabdomyolysis, inflammatory and infectious diseases were considered unlikely causes of muscle injury based on the clinical picture.

Moderate elevation of AST could reflect myocyte and/or hepatic injury – supported by increases in CK and GGT.

GGT was markedly elevated which indicated hepatobiliary (cholestasis, biliary hyperplasia) or hepatic disease – most likely associated with hepatic lipidosis. Other disorders, such as cholangiohepatitis and liver flukes were still a consideration. Acute hepatocyte necrosis was less likely given normal GLDH. Toxicosis was also less probable given the history.

Cholestasis was supported by mild increases in bile acids and bilirubin. Both parameters could be also elevated due to liver dysfunction. Hyperbilirubinaemia could be also secondary to anorexia; haemolytic disorder and sepsis were ruled out.

There was mild hyperglycaemia which could be stress-related, could reflect excitation or insulin resistance due to obesity (e.g. metabolic syndrome). Postprandial increase was much less likely. Hyperglycaemia could be also secondary to PPID but corresponding clinical signs were not observed. Diabetes mellitus was ruled out given the magnitude of hyperglycaemia.

Urinalysis

Trace of glucose on urine dipstick most likely reflected hyperglycaemia. The presence of 4+ erythrocytes/haemoglobin could be secondary to myoglobinuria (considering the increased CK) or inflammation/infection, bleeding, trauma in the kidneys or urinary tract (less likely given lack of corresponding clinical signs). Sediment examination was not performed.

Haematology

Although plasma protein was not high to support this, erythrocytosis was most likely secondary to dehydration. Splenic contraction caused by excitation/pain was another likely consideration. Cardiorespiratory disease and endotoxic shock were unlikely given the lack of corresponding clinical findings. Other less common causes of erythrocytosis (e.g. erythropoietin-secreting tumour, primary erythrocytosis or polycythaemia vera) were excluded based on the mild character of the changes.

Severe inflammatory disease/acute inflammation was considered very unlikely given lack of significant haematological changes and normal fibrinogen.

FURTHER TESTS

Faecal examination

Faecal examination was performed and the worm egg count was zero, making parasitism unlikely.

Liver biopsy and histology

A liver biopsy was performed and histology showed mild hepatocellular steatosis, moderate to marked chronic hepatocellular swelling (glycogen accumulation), moderate lymphocytic inflammation and moderate portal/porto-portal bridging fibrosis (Figure 2a-d).

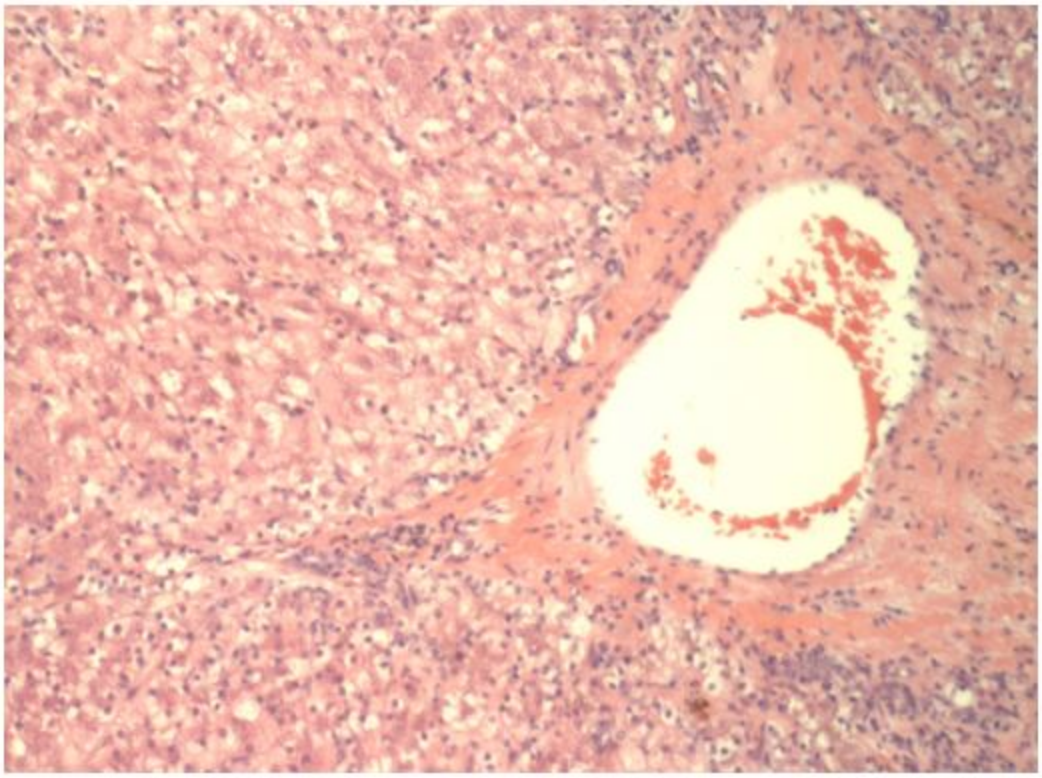

Figure 2a. Histology of the liver showing portal/porto-portal bridging, fibrosis and lymphocytic inflammation (haematoxylin and eosin stain, 10x objective).

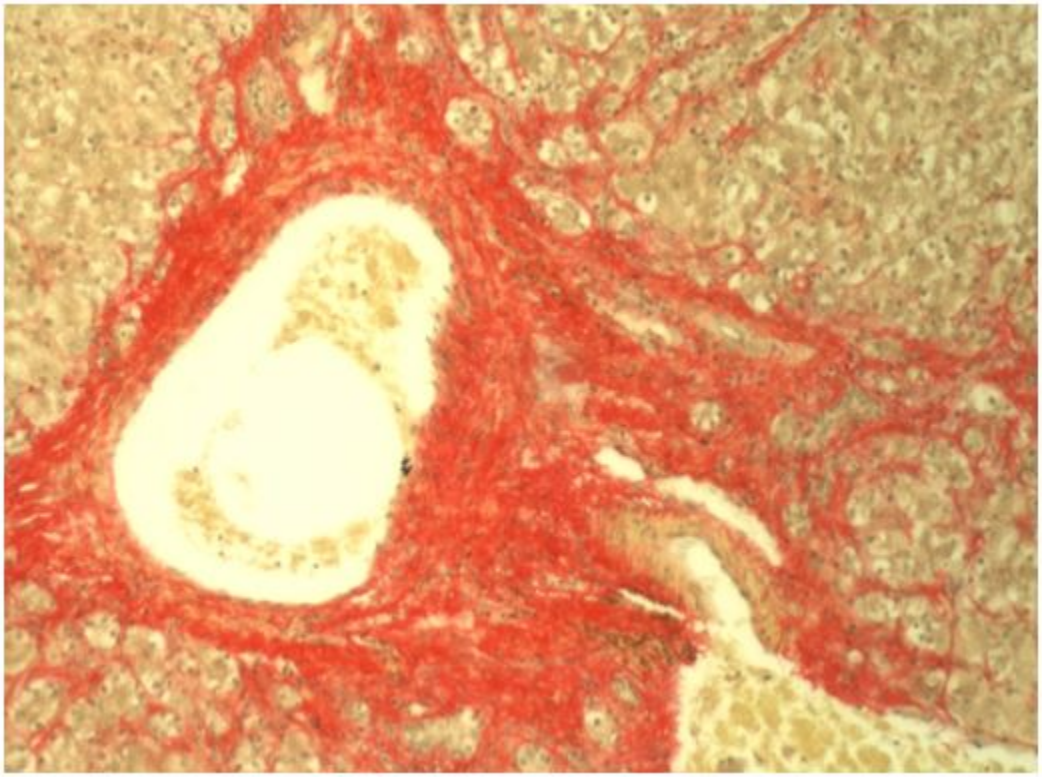

Figure 2b. Histology of the liver showing porto-portal bridging and fibrosis (Sirius red stain, 10x objective).

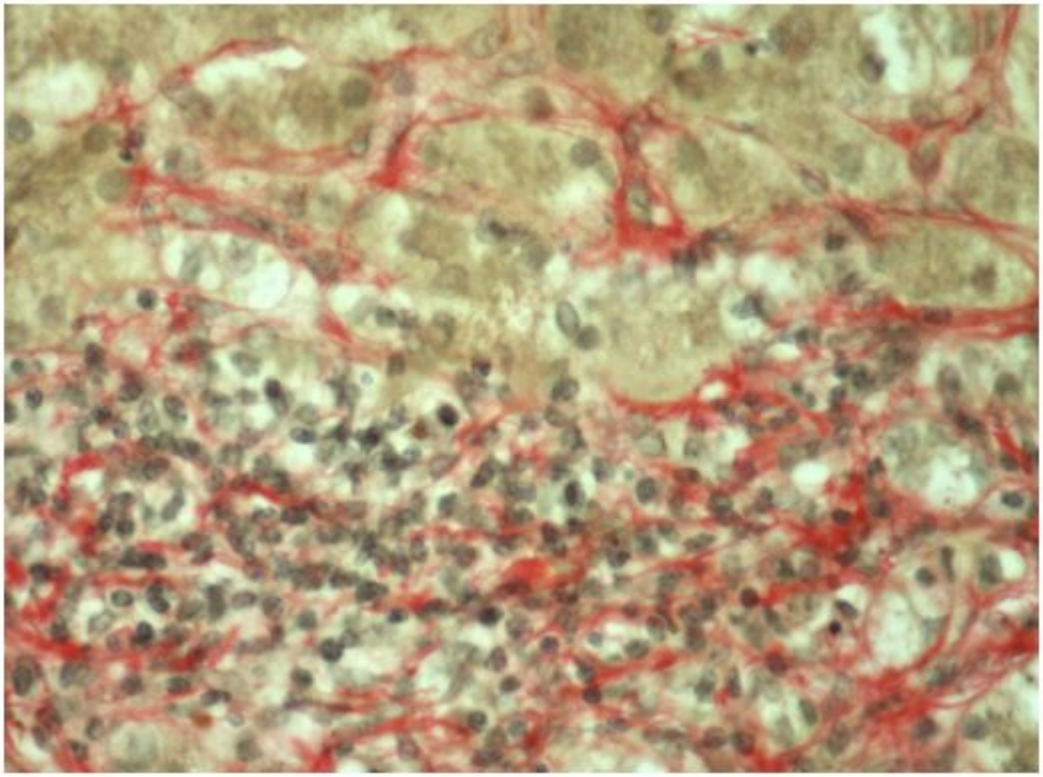

Figure 2c. Histology of the liver showing portal/porto-portal bridging, fibrosis and lymphocytic inflammation (Sirius red stain, 40x objective).

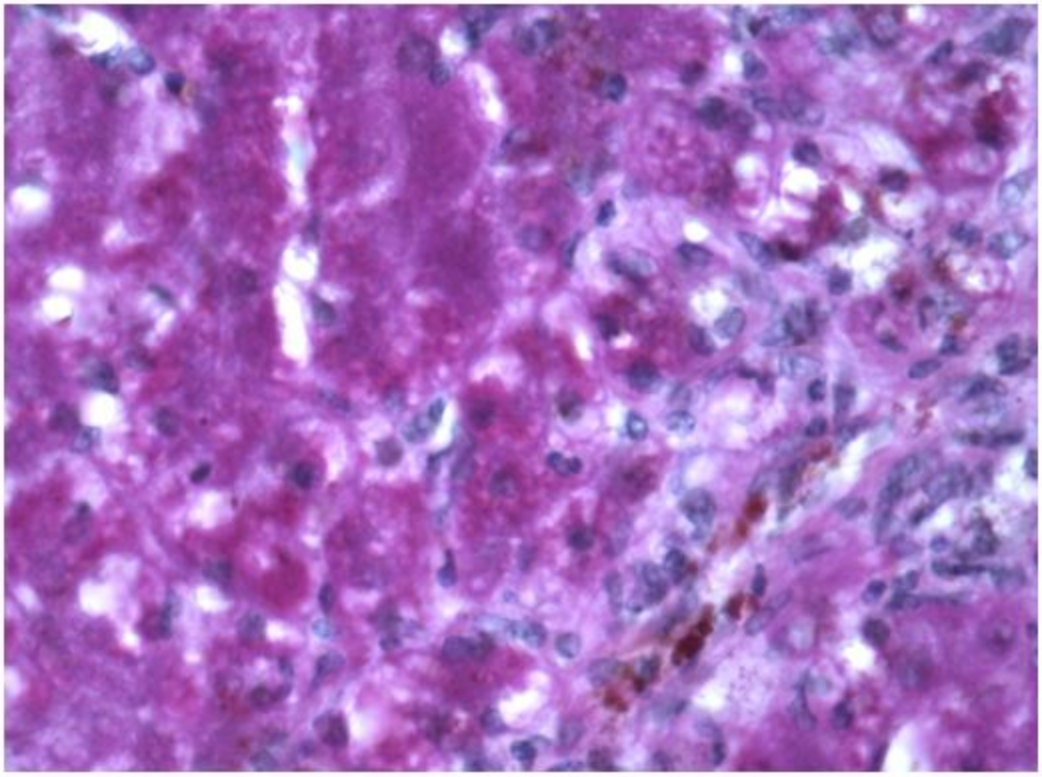

Figure 2d. Histology of the liver showing hepatocytes exhibiting abundant intracytoplasmic accumulation of periodic acid–Schiff positive material (presumptive glycogen) (haematoxylin and eosin stain, 40x objective).

Other

Nasogastric intubation did not yield any gastric reflux. Abdominocentesis was performed but no peritoneal fluid was obtained.

Troponin I measurement, which would be required to rule out cardiac myocyte injury, was not performed.

Tests for metabolic syndrome and PPID, which could both predispose the animal to hyperlipaemia, were not performed due to low clinical suspicion for these diseases. Measuring blood insulin and performing a glucose tolerance test would be required to rule out metabolic syndrome. An ACTH measurement and a dexamethasone suppression test would be recommended to exclude PPID.
Analysis of urine sediment and urine culture which would be helpful in determining the cause of a positive erythrocyte/Hb dipstick were also not performed.

DIAGNOSIS: HYPERLIPAEMIA, CHRONIC HEPATOPATHY WITH CHOLESTASIS, LIVER DYSFUNCTION AND MILD HEPATIC LIPIDOSIS

TREATMENT AND FOLLOW-UP

During hospitalisation she was managed with intravenous fluids, intravenous glucose supplementation and protamine zinc insulin. She responded well to therapy and quickly regained her full appetite/bright demeanour. Her faecal output became normal in frequency. Her triglyceride, total bilirubin, bile acids and CK normalized during hospitalization. GGT, AST and glucose decreased but remained elevated. She remained tachycardic (around 60 bpm) despite marked clinical improvement.

Electrocardiography confirmed normal sinus rhythm.

Ten days after presentation she was discharged with instructions to return to normal management. It was recommended that she is fed soaked hay (with minerals, vitamins and milk thistle) to prevent further weight gain. It was advised to assess her liver status in four weeks' time.

DISCUSSION

Hyperlipaemia is a potentially life-threatening disorder of ponies, miniature horses and donkeys, rarely affecting standard-sized horses. The disease is characterized by a markedly elevated triglyceride concentration. It can occur as a primary condition, or it can be secondary to any physiologic or pathologic conditions which induce a negative energy balance and therefore change the metabolism of lipoproteins. The most common underlying causes/predisposing factors include anorexia, obesity, pregnancy, lactation, renal failure, endotoxaemia, stress, PPID, laminitis, gastrointestinal disease, hepatopathy, dental disease, neoplasia or surgery.

Its development is associated with mobilization of fatty acids from triglycerides in adipose tissue, occurring mostly in response to hypoglycaemia, which is not stopped when the energy demand is met. Fatty acids which are not utilized by the tissue are taken up by the liver where only a part of them can be used as a source of energy or converted into ketones. The majority being reesterified to triglycerides and deposited in hepatocytes or released into circulation as triglyceride-rich lipoproteins, i.e. VLDL. Marked hyperlipaemia leads to hepatic lipidosis and secondary hepatocyte injury/dysfunction. Lipid deposition can also occur in kidneys and other organs leading to renal and multi-organ failure.

In this case it was not possible to identify the exact cause of the syndrome. In general, ponies are susceptible to this metabolic derangement due to innate insulin resistance. Obesity and sex could also

be considered as the initiating factors. Chronic hepatopathy seen in this case was likely a pre-existing condition.

Treatment can include fluid therapy, glucose infusion (with/without insulin), nutritional support and correction of the underlying disorder. Prognosis is often poor.