HUMONGOUS HEPATOCYTES IN A PREMATURE FOAL

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HISTORY

• From a herd of pregnant horses, a ~292 day pregnant mare was presented for premature udder development and thin, yellow vaginal discharge

• Vaginal discharge and cervix cultured

• Empirically treated for presumed placentitis with trimethoprim sulfonamide, altrenogest, and flunixin meglumine
HISTORY

ONE WEEK LATER

- Vaginal discharge
  - Bacterial culture negative
  - Creatinine = 46.3mg/dL (considered to be urine)

- Ultrasound
  - Fetal heartbeat 80bpm (normal 75 +/- 7bpm)
  - Minimal placental separation at cervical star

- Within 12 hours, the foal was prematurely born; agonal/unable to stand

- Euthanized and submitted, with fetal membranes, for necropsy
GROSS FINDINGS

FETAL LIVER

- Mildly enlarged
- Diffusely tan/orange
- Normal texture and consistency
GROSS FINDINGS

Villi are multifocally:

• Blunted
• Sparsely arranged
• Normal
• Dissociation of cords
• Mild, multifocal congestion
• Lymphocytic portal inflammation
• And...
Large hepatocytes containing:

- Multiple nuclei (3 to 15)
- Vacuolated cytoplasm
- +/- yellow-green pigment
HISTOPATHOLOGY

FETAL LIVER, CD3
Fetal liver: Giant cell hepatitis
MULTINUCLeleATED GIANT HEPATOCYTES

• Binucleated hepatocytes common (i.e. young animal, regenerative process)

• Multinucleated (>2 nuclei) hepatocytes uncommon in domestic animals

• Significance uncertain

• Form by either:
  1. incomplete cell division
  2. cell fusion
MULTINUCLEATED GIANT HEPATOCYTES

Form in response to the following:

• Nutritional deficiency
• Abnormal storage disease
• Toxin exposure
• Bacterial or viral infection
# ANCILLARY TESTS

<table>
<thead>
<tr>
<th></th>
<th>Fetal Liver</th>
<th>Placenta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equine herpesvirus 1 (EHV1) IHC</td>
<td>No immunoreactivity</td>
<td>Fungal organisms not identified</td>
</tr>
<tr>
<td>Steiner silver stain</td>
<td>Spirochetes not identified</td>
<td>Bacterial organisms not identified</td>
</tr>
<tr>
<td><em>Leptospira spp.</em> IHC</td>
<td>Immunoreactivity equivocal</td>
<td>Spirochetes not identified</td>
</tr>
<tr>
<td>Gomori methenamine silver stain (GMS)</td>
<td>Fungal organisms not identified</td>
<td></td>
</tr>
<tr>
<td>Gram stain</td>
<td></td>
<td>Bacterial organisms not identified</td>
</tr>
<tr>
<td>Steiner silver stain</td>
<td>Spirochetes not identified</td>
<td></td>
</tr>
</tbody>
</table>
HISTOPATHOLOGY

PLACENTA, H&E

PLACENTA, Leptospira IHC

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**SEROLOGY: DAM**

*Leptospira pomona* titer

Post-foaling 12,800
Two weeks later 6,400

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Giant cell hepatitis and multifocal lymphoplasmacytic placentitis secondary to *Leptospira spp.* infection.
DISCUSSION

In foals, giant cell hepatitis is most commonly associated with:

- Subclinical, gestational infection of dam by Leptospira serovar pomona (North America)
- Hematogenous spread and diffuse placentitis
- Third trimester abortion or premature foaling
- Placentitis alone vs. placentitis + fetal infection
- Flooding and wildlife interaction are risk factors for infection
Multinucleated giant hepatocytes have also been reported in other animals in association with the following diseases*:

<table>
<thead>
<tr>
<th>SPECIES</th>
<th>ASSOCIATED DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cats (2)</td>
<td>Thymic lymphoma</td>
</tr>
<tr>
<td>Lioness</td>
<td>Renal medullary AA amyloidosis</td>
</tr>
<tr>
<td>Shorthorn calf</td>
<td><em>Lantana</em> hepatotoxicosis</td>
</tr>
<tr>
<td>Parakeet</td>
<td>Pacheco’s disease</td>
</tr>
<tr>
<td>Mice</td>
<td>Coronavirus</td>
</tr>
<tr>
<td>Cynomolgus monkeys</td>
<td>*None (incidental finding)</td>
</tr>
</tbody>
</table>
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• Dr. Stephanie Shrader, DVM
• Histo techs Lisa and Beth
• Dr. Elizabeth Welles, DVM, PhD, DACVP
REFERENCES

5. JPC Systemic Pathology, Digestive System. JPC #2289065, November 2015.

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