University of Mosul
Lecture No.: 5
College of Veterinary Medicine
Date: 14 / 10 / 2024
Unit of Scientific Affairs
Website: https://uomosul.edu.iq/veterinarymedicine/

Fatty Liver الكبد الدهني

Department of Internal and Preventive Medicine

Summary:

- Fat-mobilization syndrome
- Fat-cow syndrome
- Hepatic Lipidosis
- Pregnancy Toxemia in cattle

In about 30% of high-producing cows, fatty infiltration in the liver is severe and is associated with reversible but significant effects on liver structure and function.

Etiology

- Mobilization of excessive body fat to liver during periods of negative energy balance in:
  - Early lactation of dairy cows
  - Late pregnancy of beef cows.
- Normal lipid levels (hepatic triglyceride levels) in the liver of cows should be range between 10% to 15% of the liver weight.

Epidemiology

- Fatty liver is common in high-producing dairy cattle a few weeks before and after parturition.
- The percentage of cattle dying or being culled because of disease is
  - 15% in mild cases (Less than 20% lipid = less than 50 mg lipid /g liver).
  - 31% in moderate cases (20% to 40% lipid = 50 to 100 mg lipid /g liver).
  - 42% in severe cases (greater than 40% lipid = more than 100 mg lipid /g liver).

  } histologically
- Any disease of early lactation that affects appetite and food intake can contribute to fatty liver.
  - Predisposing diseases include ketosis, left-side displacement of the abomasum, mastitis, retained fetal membranes, milk fever, and downer-cow syndrome.
- Under usual circumstances, the disease in beef cattle occurs sporadically:
  - the morbidity is about 1%, but the mortality is usually 100%.
- Overfeeding during the dry period predisposes cows to accumulate fat in adipose tissue.
  - Before parturition, adipose tissue from overfed cows has higher rates of esterification than the adipose tissue of cows fed a restricted energy intake.
  - In the fatty livers of these overfed cows, the rate of gluconeogenesis is not optimal, which results in prolongation of lipolysis.
  - The increased lipolysis after parturition leads to a major increase in the hepatic triacylglycerol concentration and to a shift in hepatic fatty acid composition.

- Fatty liver occurs because of a sudden demand of energy in the immediate postpartum period in well-conditioned lactating dairy cows.
- Fatty liver also occurs because of a sudden deprivation of feed in fat pregnant beef cattle, and is especially severe in those bearing twins.

Pathogenesis

- Fatty liver develops because of failure of the metabolic adaptive mechanisms to the negative energy balance.
- A substantial drop in dry matter intake is initiated in late pregnancy and continues into early lactation. This decrease is caused by:
  - Physical constraints in the abdomen as a result of the enlarging gravid uterus
  - Changes in reproduction status, fat mass, and metabolism in support of lactation.
- Body fat, especially subcutaneous fat, is mobilized and deposited primarily in the liver, as well as in muscle and kidneys.
- Fat mobilization begins about 2 to 3 weeks before calving and is probably induced by a changing hormonal environment before calving rather than an energy deficit.
- Up to 50% of all cows have some accumulation of triacylglycerol in the liver.
- Excess lipids are stored as triacylglycerol in the liver, and excessive lipid in the hepatocytes can decrease the metabolic function of the liver.
  - The body prepares for these demands through hormonal signals to ensures the availability of the energy for the demands of the upcoming lactation period.
    - Increased levels of cortisol and catecholamines enhance lipolysis to provide energy.
- Mobilization of an excessive amount of nonesterified fatty acids (NEFAs) results in:
  - Increased hepatic lipogenesis.
  - Accumulation of lipid in the hepatocytes.
  - Depletion of liver glycogen.
  - Inadequate transport of lipoprotein from the liver.
- Most of the lipid infiltration of the liver in dairy cows after calving is in the form of triacylglycerols because of the increased uptake of NEFAs.
  - When carbohydrates are abundant, energy from fatty acids may be used more for immediate energy needs rather than being converted into ketones.
- Fat and thin cows respond differently to the metabolic demands of early lactation.
  - Fat cows appear less able to utilize mobilized fatty acids, and as a result they accumulate esterified fat in tissues.
  - Cows that are not fat initially do not develop fatty liver syndrome.

Fatty Liver or Ketosis?

Each cow's metabolism, body condition, genetics, and health status can influence whether they develop ketosis or fatty liver.

The specific metabolic responses can lead to one disease:

- If the liver becomes overwhelmed with excessive NEFAs and cannot process them effectively, fat accumulates within liver cells, leading to hepatic lipidosis.
- If the production of ketones exceeds the cow's ability to utilize them, it leads to ketosis.

Dietary Influences: diet high in readily fermentable carbohydrates might promote ketosis, while one without sufficient energy might lead to fatty liver.

Clinical Findings

- Affected cows are usually excessively fat, with a BCS of 4/5 or higher.
- The temperature, heart rate, and respiration are within normal ranges.
- Rumen contractions are weak or absent, and the feces are usually scant.
- Periods of prolonged recumbency are common, and affected cows may have difficulty in standing.
- Severe ketosis that does not respond to the usual treatment may occur.
- Affected cows gradually become weaker and progress to totally recumbent (die in 7 to 10 d).
- Some cattle exhibit nervous signs consisting of a staring gaze, holding the head high, and muscular tremors of the head and neck.
- Terminally there is coma, tachycardia, and marked hyperglycemia.
- In fat beef cattle shortly before calving, affected cows are:
  - Aggressive, restless, excited, and uncoordinated with a stumbling gait.
  - Sometimes they have difficulty in rising; and they fall easily.
  - The feces are scant and firm.
  - Tachycardia.
  - Eventually they become sternally recumbent.
  - The feces are usually scant; terminally, there is often fetid yellow diarrhea.
  - The disease is highly fatal; the course is 10 to 14 days.
- In dairy cattle with moderately severe fatty liver, the clinical findings are much less severe, and most will recover within several days if they continue to eat even small amounts of hay.
- Complications:
  - Inferior reproductive performance as a result of a delay in the onset of normal estrus cycles and a reduction in the conception rate.
  - Increased incidence of parturient paresis.
  - Unresponsive treatment for ketosis.
- Prognosis: unfavorable.

Clinical Pathology

- **Serum Biochemistry (depends on the severity)**
  - Increased plasma/serum nonesterified fatty acid (NEFA), acetoacetate, BHB, and total bilirubin.
  - Decreased serum fructosamine (marker for average blood glucose levels).
  - Increased plasma/serum hepatic enzyme activity (particularly AST).
  - High plasma NEFA : cholesterol (high liver fat percentage):
    - NEFA concentration reflects a metabolite that has not been cleared by the liver
    - cholesterol concentration reflects the rate of hepatic reesterification and export as a VLDL.
  - Hyperbilirubinemia as a result of decreased hepatic uptake of bilirubin due to the competition between bilirubin and NEFA for the same binding site on hepatocytes
  - Decreased plasma fibrinogen due to interference of its synthesis because of intracellular lipid accumulation.
- **Hemogram**
  - leukopenia, neutropenia, and lymphopenia; may be related to the increased incidence of postparturient diseases, such as mastitis and endometritis.
- **Liver Biopsy and Analysis**
  - Presence of triglyceride in the hepatocytes.
- **Ultrasonography of the Liver**
  - Identification of hepatic enlargement.
  - Echogenicity or brightness of the liver.

Necropsy Findings

- Enlarged, pale yellow, friable, and greasy liver.
- The histologic changes include the occurrence of fatty cysts or lipogranulomas, enlarged hepatocytes.

Differential diagnosis

- Left-sided or right-sided displacement of abomasum.
- Milk fever.
- Abomasal impaction.
- Vagus indigestion.
- Peritonitis.
- Primary ketosis (characterized by inappetence, marked ketonuria, and good response to glucose).

Treatment

- Treatment strategies
  - Decrease the rate of fat mobilization leading to decrease of the plasma NEFA concentration
  - Facilitate the complete oxidation of NEFAs in the liver.
  - Increase the rate of export of VLDLs from the liver.
- therapeutic approaches
  - Propylene glycol (300 mL daily for 5 days, PO).
  - Dextrose (500 mL of 50% dextrose once, IV).
  - Dexamethasone IM.
  - Isoflupredone (synthetic glucocorticoid) 20 mg, IM, multiple injections.
  - Cyanocobalamin (vitamin B12, 1 to 4 mg IV, daily for 2 to 3 treatments).

Control

- Avoid overfeeding during late lactation and dry period.
- Avoid situations that reduce feed intake at time of parturition.

---------- END ----------

References:

- Constable PD, Hinchcliff KW, Done SH, et al. (2017). Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats. 11th ed. Elsevier, St. Louis, Missouri, USA. P: 1716.