Marek’s Disease

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- Marek's disease (MD) is a tumoral and fatal disease in chickens
- The disease is a common lymphoproliferative disease of chickens, characterized by mononuclear cellular infiltrates in peripheral nerves and various other organs and tissues including iris and skin
- Marek's disease also caused significant economic losses with deaths and productivity loss in Turkey
- It is an immunosuppressive disease

Etiology

- The agent of Marek's disease is Marek's disease virus, one of the Herpesviruses, which has an oncogenic
- There are three serotypes of Marek's disease virus.
- Serotypes are detected by monoclonal antibodies. Genome structure and antigens of all three serotypes were determined. All three serotypes have common antigens.

Serotypes

- Serotype-1 (*Gallid alphaherpesvirus*-2): The group includes virulent and oncogenic viruses. The virulence of the viruses in this group was determined as moderate, virulent and very virulent.
- Serotype-2 (*Gallid alphaherpesvirus*-3): includes non-oncogenic MDV. Serotype-1 which isolated in 1978 is included in serotype-2.
- Serotype-3 (*Meleagrid alphaherpesvirus*-1, Herpesvirus of turkey (HVT)): Contains virus isolated from turkeys. Turkey herpes virus (HVT) does not cause disease in chickens

Etiology

- ✓Marek's disease viruses are cultured in day-old chicks, tissue culture and embryonated eggs
- ✓Marek's disease lymphoma cell cultures are also used in virus proliferation.
- ✓Serotype-1 grow in chicken kidney cells (CKC) and duck embryo fibroblasts (DEF) and produce small plaques.
- ✓Serotype-2 grow best in chicken embryo fibroblasts (CEF) and produce medium plaques.
- ✓The virus can only survive inside the cell. For this reason, MDVs are called cell-dependent viruses.
- ✓HVT grow best in chicken embryo fibroblasts (CEF) and produce large plaques. It is not cell dependent. They are easily lyophilized.

Epidemiology

- Marek's disease has only been seen in chickens. Experimentally, infection has been established in turkeys, pheasants and quails.
- The disease is most common in chickens less than 16 weeks of age.
- The disease has been detected in hens and breeder flocks in the egg period.
- In addition, it has been reported that Marek's disease has been diagnosed in commercial turkey flocks in Israel and France in recent years.
- Transmission occurs by respiratory route.
- **Vertical transmission does not occur**

Epidemiology

- Virus is transmitted to susceptible chickens by direct contact.
- In contaminated flocks, the disease spreads by indirect horizontal transmission.
- MDV multiplies in the feather follicles of infected chickens, epithelial cells in the keratinized layer. Follicle epithelium and skin rashes are the source of viruses.
- Most chickens that appear normal in the infected flocks are porters. As a result of the continuous spread of infectious virus in the flock, the infection remains continuously
- Young chickens are more susceptible to infection. However, the disease can be seen in chickens of any age
- Clinical symptoms are not seen before 3-4 weeks

Epidemiology

- The incubation period varies according to the virulence of the virus, the dose, the transmission route, the genetic characteristics of the chicks and whether they are female or male.
- It is difficult to determine the incubation period in infection that occurs under natural conditions.
- Outbreaks can sometimes be seen in 3-4 week old chicks.
- The most severe cases in Marek's disease appear after 8-9 week

Symptoms

- Marek's disease is a progressive disease
- The symptoms of the disease are different. Symptoms are mainly neurolymphomatosis, acute signs of Marek's disease, ocular, lymphomatosis, and skin lesions.
- After the peripheral nerves are affected, a particular or complete paralysis is seen in the leg and wing.
- In the infected flock, paralysis may have occurred in only a few chickens. Paralysis may not be seen in other infected chickens.
- Symptoms resulting from the involvement of peripheral nerves vary according to the affected nerves

- When the wing nerves are affected, the wing falls.
- When the neck nerves are affected, the head is kept down and sometimes torticollis is seen.
- When the vagus is affected, the crop expands and hangs, and breathing is observed.
- Because locomotory disturbances are easilt recognized, incoordination or stilted gait may be the first observed sign
- A particularly characteristic clinical presentation is a bird with one leg streched forward and the other back as a result of unilateral parasis or paralysis of the leg

- In infection with some highly virulent MDVs, lesions develop in the eye, resulting in blindness.
- In the acute form of Marek's disease, most of the chickens are weakness and depressed.
- Incoordination and paralysis begin in a few days in infected chickens.
- Nonspecific symptoms such as weight loss, paleness, anorexia and diarrhea occur
- Usually, chickens that have clinical symptoms die.
- Not all infected chickens in the flock develop clinical symptoms.
- Morbidity was 60% or higher in some commercial flocks

- Appropriate and effective vaccines are applied to almost all laying hens. Therefore, morbidity and mortality in Marek's disease is below 5%.
- Broiler chickens are vaccinated in some countries. Therefore the death rate is between 0.1% and 5%.
- In broiler chickens, skin lesions are seen and causing cascade losses

Necropsy Findings

- Thickening (2-3 folds) and discoloration are seen in the affected peripheral nerves. Nerve thickening is unilateral.
- Lymphoid tumors are formed in different organs. These organs are lung, genitalia, ovary, spleen, liver, pancreas, proventriculus, muscle, and skin.
- Enlargement of the viscera may be several times bigger the normal organ size.
- Grayish discoloration is usually seen.
- Diffuse enlargement and nodular tumors are seen in the liver
- Some follicles in the ovary are normal and some are tumorous
- Mature follicles continue their function
- The proventriculus thickens and hardens.

- The affected heart is pale
- Macroscopic changes in the eye include discoloration of the iris (gray eye) and smooth removal of the pupil and progressively smaller hole.
- Bursa Fabricius is atrophic
- Rarely, a diffuse thickening may be seen
- Changes in the skin can be seen after the cut hairs are plucked
- Gray-white interactions occur in the muscles

Diagnosis

- Clinical symptoms and necropsy findings
- Laboratory examinations

a) Virus isolation

b) Antigen detection

c) Antibody detection

d) Histopathological examinations

e) Molecular analysis

Protection and Control

- Layers and breeders should be vaccinated.
- The important thing in vaccination against Marek's disease is to vaccinate before the virus of the disease enters the body. For this reason, Marek's disease vaccines are applied as early as possible after chicks hatch.
- In recent years, in many farms, chicks are vaccinated before hatching, on the 18th day of incubation (in ovo)

Neoplastic Diseases

- Neoplastic diseases of poultry are divided into two groups according to their etiological agents.

➢ The first group includes neoplasms of known etiology,

➢ The other group includes neoplasms of unknown etiology.

- Tumors caused by viruses are of mesodermal origin and transferable.
- Neoplastic diseases or disease complexes can be grouped into 5 groups according to their etiological differences

1. Marek's Disease
2. Leukosis/ Sarcoma Group
3. Reticuloendotheliosis group
4. Lymphoproliferative Disease (LPD)
5. Neoplasms of unknown etiology

1. Marek's Disease

- It is a lymphoprolative disease that affects the nervous system and visceral organs
- The agent of the disease is the *Herpesvirus*

2. Leukosis/sarcoma Group

- They are neoplastic diseases caused by RNA retroviruses
- Lymphoid leukosis is the most well-known disease
- In lymphoid leukosis, the bursa Fabricius and visceral organs are mainly affected.
- In addition, other neoplasms of hematopoietic origin are also included in this group.
- These are;
  - Erythroblastosis
  - Myeloblastosis
  - Myelocytomatosis
  - Nephroblastoma
  - Osteopetrosis

3. Reticuloendotheliosis group

- Some members of this group, which are antigenically related to RNA-containing retroviruses, cause neoplastic diseases in ducks
- Others are the cause of lymphoid neoplasms in turkeys

4. Lymphoproliferative Disease (LPD)

- This group pathogens are retroviruses associated with a number of neoplastic diseases
- These viruses are grouped into different envelope subgroups

5. Neoplasms of unknown etiology

- Neoplasms in this group, which includes a wide range of benign and malignant neoplasms, are derived from muscle, epithelium, nervous tissue, serous membranes and pigmented cells

Leukosis/sarcoma Group Virus Infections

- Lymphoid leukosis is known to be of siginifant economic importance
- Other diseases occur sporadically, with some exceptions
- In recent years, subclinical cases without neoplastic disorders caused by avian leukosis virus have also be seen

Etiology

- Avian type C oncoviruses of the Retroviridae family are divided into 6 subgroups (A, B, C, D, E and J) according to the differences in their envelope glycoproteins
- Type E viruses are endogenous leukosis viruses and have negligible oncogenicity for chickens. Those excluded from this group are exogenous viruses of external origin
- A and B are the most common exogenous viruses in the field
- C and D viruses have been reported rarely
- Type J has recently been isolated from meat type chickens
- Cross neutralization between subgroups is also insignificant except for B and D
- They are enveloped viruses

Epidemiology

- Chickens are natural hosts for all viruses in the ALSV group
- The diseases they cause are seen in all poultry except pheasant, partridge and quail
- The virus causes tumors in chickens, turkeys, ducks, and other poultry
- Females are more susceptible to lymphoid leukosis than males
- Most commercial chickens are susceptible to exogenous ALSV and carry the endogenous leukosis virus. However, a small percentage of them develop lymphoid leukosis or other tumors
- Losses rarely exceed 30%

- Mortality and economic losses from lymphoid leukosis occur in layers and breeder layers in 5-9 month old
- Other neoplastic diseases occur sporadically.
- Vertical and horizontal transmission is seen.
- In vertical transmission originating from the mother, ALSV infects the egg albumin from the oviduct and then the embryo.
- The virus does not reproduce in sex cells.
- Cocks have no role in transmission.
- Since the infected cocks have virus they can be porters

Symptoms- Lymphoid leukosis

- After inoculation of RPL12, B15, F42 or RAV1 strains of the virus into susceptible embryos or 1-14 day old susceptible chicks lymphoid leukosis is seen in 14-30 weeks.
- The disease is rarely seen under 14 weeks of age
- The incidence is usually much higher after reaching sexual maturity
- Lymphoid leukosis always begins with the formation of a tumor in the bursa Fabricius and is localized in this organ until the bursa Fabricius disappears
- When the chicken enters the laying age, the tumor metastasizes and spreads to other organs. Therefore, the incubation period is long
- Due to diffuse enlargement of the liver the disease also known as "**Major liver disease**"
- The clinical symptoms of the disease are not very clear.
- Comb is pale, wrinkled and rarely cyanotic

Symptoms- Lymphoid leukosis

- There is anorexia and weakness.
- The abdominal region is often enlarged.
- Feathers may be contaminated with green-colored diarrhea.
- The liver, bursa Fabricius, and/or kidneys are enlarged and can be noticed by palpation. After clinical signs appear, the disease progresses very rapidly.
- Visible tumors can be found in the liver, spleen, and bursa Fabricius at necropsy. Apart from these organs, tumors can also be seen in the kidney, lung, gonad, intestine, heart, bone marrow and mesenterium. Tumors are soft, smooth and glistening, a cut surface appears grayish to creamy White and seldom has areas of necrosis
- Tumor growth may be nodular, miliary, diffuse, or a combination of these forms.

Symptoms-Erythroblastosis

- Erythroblastosis usually ocuur in birds between 3-6 months of age
- It is a sporadic disease
- The agent of the disease Regional Poultry Research Laboratory isolate (RPL)-12, R, F24, ES24 and 13
- The primary cell involved is erythroblast
- Severe anamia is seen
- General weakness, and pale comb is seen. As the disease progresses, there is usually cachexia in animals
- Diarrhea
- Bleeding may occur in the hair follicles

- The course of the disease can extend from a few days to several months.
- Depending on the severity of the anemia, the comb can change color from slightly yellow to white.
- Petechial hemorrhages ocur in various organs such as muscles, subcutis and viscera
- Thrombosis, infarction and rupture of the liver and spleen may be observed.
- Edema of the lıngs, hypopericardium and fibrinous clot on the liver may ocur
- The most characteristic lesion is diffuse enlargement of the liver, spleen, and sometimes kidneys

Symptoms-Myeloblastosis

- Natural cases of myeloblastosis are uncommon and usually ocur adult chickens
- In circulating myeloblasts from birds with myeloblastosis induced by BAI-A virus
- A severe leukemia exists, with myeloblasts comprising pf peripheral blood cells
- The liver is greatly enlarged
- The spleen and kidneys are also diffusely infiltrated and enlarged

Symptoms-Myelocytomatosis

- Myelocytomatosis has a shorter incubation period than lymphoid leukosis but longer than erythroblastosis and myeloblastosis
- In experimental studies, disease can be produced with MC29 virus in young chicks
- Clinical symptoms are similar to myeloblastosis

Symptoms-Osteopetrosis

- It can be produced by inoculation of RPL 12 virus to day-old chicks
- It is characterized by thickening of the long bones in the leg.
- The incubation period is about 1 month.
- It is most common in 8-12 weeks old animals.
- Leg and wing bones are particularly affected in the disease.
- At the beginning of the disease, the thickened areas are hot and painful. As the disease progresses, the warmth and pain disappear.

- Animals with thickened leg bones look like they are wearing boots
- Animals usually do not develop and remain stunted.
- Anemia can occur
- Sometimes the medulla is lost.
- Affected bones are yellowed and hardened
- In microscopic examination

an advanced degree of calcification is observed

Diagnosis

1. Clinical and Necropsy Findings
2. Laboratory Examinations

a) Virus Isolation

b) RIF Test (Resistance Inducing Factor Test)

c) Cofal Test (Complement Fixation Test for Avian Leucosis Viruses)

d) NP Test (Non producer Test)

e) Other tests: Apart from the tests mentioned above, tests such as fluorescent antibody technique, Enzyme tests, PCR, hematopoietic transformation test are applied.

f) Serological tests: Plasma, serum and egg yolk can be used as samples for antibody screening.

Neutralization test,

indirect immunoperoxidase absorbance test and ELISA techniques are important serological tests.

Protection and Control

- There is no known treatment or vaccine.
- Control can be performed by flock management to reduce infection in the environment, good quality care and feeding, high standards of hygiene and the use of animals from genetically resistant.
- Because the infection is transmitted by eggs, retrospective virus isolation can be done

RETICULOENDOTHELIOSIS

- Reticuloendotheliosis is a neoplastic disease of chickens that is caused by retroviruses other than leukosis/sarcoma group viruses and includes various pathological syndromes.

Etiology

- Reticuloendotheliosis virus (REV) is one of the avian type C onco viruses of the retroviridae family.
- However, it is separated from the leukosis/sarcoma group.
- The most isolated strain is T in the REV group.
- The T strain is acutely oncogenic and cause reticuloendotheliosis.
- The virus can be cultured on embryonated chicken eggs and tissue cultures

Epizootiology

- Poultry such as turkey, duck, goose, pheasant and quail are susceptible to the disease
- Infection has been reported in many countries of the world
- The disease is transmitted vertically as well as horizontally
- Contaminated vaccines also cause disease.
- Contamination is more common especially in smallpox and marek’s disease vaccines

Symptoms

- Symptoms are not pathognomonic
- Acute or chronic liver and spleen tumors are seen. A similar situation can be seen in the heart, kidney, and pancreas
- Macroscopic tumors similar to Marek's diseasde occur in peripheral nerves 3 weeks after experimental inoculation
- Paralysis can occur in some animals
- The disease can also cause immunosuppression

Diagnosis

- Clinical signs, necropsy and histopathological findings are insufficient
- Isolation and identification of the virus is required
- Virus inoculation is performed on embryonated eggs, tissue cultures and susceptible animals
- The presence of infection in the flock can be determined by detection of disease antibodies in blood serum by tests such as ELISA, agar gel precipitation, plaque reduction, pseudoneutralization, or fluorescent antibody tests

Neoplasms of Unknown Etiology

- This group includes neoplasms of unknown etiology
- They do not have much importance for chicken
- No negative effects of these diseases on human health were detected

Fowl Pox Infection

Etiology

- *Fowlpox* virus, a DNA virus belonging the family *Poxviridae*
- Avianpox viruses infecting various avian species are recognized within the *Avipoxvirus* genus in the family *Poxviridae*
- *Avipox* virus reproduces on the chorioallaotic membrane (CAM) of embryonated eggs and forms **gray-white pocks**. Also, it can grow in embryo fibroblast and kidney cells and produce cytopathic effects (CPE)
- The inclusion bodies (**Bollinger bodies**) formed by the virus in the cytoplasm of the cells and the virus particles (**Borrel particles**) contained in them can be easily seen with light microscopes (1500x magnification)

- The virus is resistant to environmental conditions, drying and some disinfectants
- They can survive on scabs, skin rashes, feathers and dust and remain infective for a long time (months, sometimes years)
- Some strains of poultry pox viruses (chicken and pigeon pox viruses) have hemagglutination ability
- Chicken pox virus is resistant to phenol (1%) and formalin (0.1%) for up to 9 days
- Can be inactivated at 50°C, 30 min and 60°C, 8 min

Epizootiology

- Infection can occur in almost any season
- Mortality may exceed 50%
- If animals also have parasitic, bacterial, viral, hidden, or chronic infections, mortality may be even higher
- Young people are more susceptible to infection
- Males (especially those who are aggrasive) may have more disease than females
- The virus can easily enter through the lesions on the skin and mucous membranes and initiate the infection
- Fights, hard foods, scratches, and the resulting microscopic and macroscopic lesions play an important role in the entry of the virus into the body and the spread of the infection

- Fowl pox disease has been reported in more than 60 species of wild poultry
- Transmission is usually ocur by direct contact from body portants or by dusts, droplets, hairs, etc. It occurs as aerogen with the viruses in it.
- Also, the virus can be carried to distant places and spread the infection by wind, wild birds, stinging flies and insects, etc.
- While infected pigeons are feeding their chick, they can transfer the virus to their offspring and infect them through food contaminated with the virus in the in their esophagus, crop and pharynx

Clinical Symptoms

- After the virus enters the body, the first symptoms begin to appear within 4-15 days, depending on the sensitivity, age, breed, immune status, environmental conditions, stress factors, pathotype of the virus, virulence and other conditions.
- The incubation period differs between bird species

1. **Skin form (cutaneous form, flower form):** Develops in the form of small lesions and blisters on the face, comb, beard, mouth and eyes of chickens, around the hairless parts of the body. **In mild forms** of the disease, significant clinical signs cannot be observed. However, reductions in egg production and regressions in growth can be noticed. As the lesions enlarge and their number increases, weakening and death occur (**in severe forms**).In mild forms of infection, scabs may shed within 1-3 weeks, and open wounds may heal if there is not much contamination

2. **Diphtheric form**: Occurs in mucous membranes. Yellow, necrotic pseudomembranes develop in the mouth, tongue, pharynx, esophagus, larynx, crop, trachea. These also grow over time and can merge with each other. When these membranes are lifted by holding them with forceps, bleeding surfaces occur in their places. Since these lesions prevent feeding and breathing, they cause weakening, wheezing and difficulty breathing, asphyxia and death in animals.

- Mortality can reach up to 60% in unhealthy flock conditions and in susceptible animals under stress. In postmortem examinations, in addition to the lesions that can be easily seen in the head region, disorders are observed in the mouth, pharynx, tongue, pharynx, larynx, esophagus and trachea, crop and sometimes the lungs. Lesions are not observed in other organs and tissues in general. However, formations in the larynx and trachea may be large enough to cause asphyxia and death.

Diagnosis

1. **Clinical and necropsy findings**: Lesions developing on the skin and mucous membranes in fowl pox disease may be sufficient to diagnose the disease. However, some bacterial (CRD, Infectious coryza, chronic cholera, Infectious sinusitis, etc.), viral (ILT, IB, ND, etc.), fungal (moniliasis, aspergillosis, etc.) and other disorders (skin sores, A avitaminosis, etc.) they can be complicated
2. **Laboratory examinations**

a. Microscopy

b. Virus isolation

c. Serological tests

d. Biotechnological methods

Treatment

- Since fowl pox disease is a viral infection, it cannot be treated with antibiotics. However, broad-spectrum antibiotics can be used to prevent bacterial contamination and secondary infections
- Glycerin iode is applied on the lesions on the face and mouth of the animals and the application is continued until the wounds heal. The crusts of the wounds formed in the mouth are removed by holding them with a forceps and glycerin iode is applied to the wound surface. Antibiotic pomade and solutions can also be used for the same purpose

Protection and Control

- Biosecurity
- Vaccination

Avian Encephalomyelitis (Epidemic Tremor)

Etiology

- *Avian encephalomyelitis virus* (AEV), *Enterovirus*, *Picornaviridae*
- Isolates serologically similar
- There are two pathotypes

1. Field strains, enterotropic
2. Embryo-adapted strains, neurotropic

Epidemiology

- Chicken, turkey and duck susceptible to disease
- There is vertical transmission
- Infection also occurs horizontally
- The incubation period is 1-7 in vertical transmission, at least 11 days in horizontal transmission

Clinic and Necropsy

- Depression, ataxia and tremor in young animals
- Decrease in egg production in layers, decrease in hatchability in breeders
- Single and/or double sided opacity in the lens
- Nervous symptoms appear 1 week after hatching
- Although the disease is usually seen at 5-6 weeks of age, it has also been reported in older animals
- Mortality up to 15% and morbidity 60% in infected poultry
- Clinical signs are more severe in turkey
- 5-10% decrease in egg production reaches normal level after 2-3 weeks
- Approximately 5% decrease in hatching yield
- Weekly mortality in animals increases by 0.2-1% in egg production
- Macroscopic findings are usually absent

Diagnosis

- **Clinical and necropsy**: It should be differentiated with ND, MD, and nutritional encephalomalacia. Clinical signs are not sufficient to diagnose the disease.
- **Laboratory diagnosis**:
  - Histopathological examinations
  - Virus isolation; 5-6 days old egg yolk inoculation
  - VN, ELISA, FAT
  - Molecular analysis

Control

- Vertical transmission
- Biosecurity
- Vaccination
  - Live vaccine