CHICKEN INFECTIOUS ANEMIA

A Continuing Education Program Prepared
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INTRODUCTION

Chicken infectious anemia (CIA) is a disease characterized by aplastic anemia, generalized lymphoid depletion, subcutaneous and intramuscular hemorrhages, and immunodepression. Because of the immunodepression, increased mortality due to secondary complications is often observed. The causative agent of CIA, first identified in Japan in 1979, has been called, at various times, chicken anemia agent (CAA), parvovirus-like virus (PVLV), chicken anemia virus (CAV), or chicken infectious anemia virus (CIAV). Clinical signs and lesions described previously in cases of aplastic anemia, hemorrhagic syndrome, and anemia-dermatitis may have been caused by CIAV.

INCIDENCE AND SUSCEPTIBLE HOSTS

Chicken infectious anemia virus is ubiquitous in all major chicken producing countries of the world. Serological data indicate that the virus is widely spread in the United States in both layer and broiler-type breeder chickens. The chicken appears to be the only host for CIAV.

TRANSMISSION

The disease readily spreads horizontally, but vertical transmission

appears to be the most important means of dissemination. Vertical transmission occurs following the infection of hens in lay. The hen continues transmitting CIAV until antibodies appear in her blood, a period of approximately 7 days. From a single infected breeder flock, however, CIAV infected chicks can be produced for 3 to 6 weeks.

PATHOGENESIS

Chickens of all ages are susceptible to infection with CIAV. However, clinical disease is seen only during the first two to three weeks of life although immunocompromised chickens may suffer from anemia later in life. Chicken infectious anemia virus persists only for 3 to 4 weeks in chickens with an intact immune system, but for as long as 7 weeks in immunocompromised chicks.

Age resistance to clinical disease caused by CIAV develops rapidly and becomes complete by 2 to 3 weeks of age. Maternal antibodies from immune hens prevent clinical disease in young chicks. Because of passive immunity and age resistance, most infections with CIAV are subclinical.

ETIOLOGY

Chicken infectious anemia virus is a spherical, nonenveloped virus

with a diameter of 19 to 24 nm. The genome consists of a circular single-stranded molecule of DNA. Two other viruses with similar characteristics are the psittacine beak and feather disease virus (PBFDV), and swine circovirus (SC). However, antigenic and nucleic acid sequence studies have detected no relationship among them. It has been suggested that these three viruses should be placed in a new viral family, Circoviridae. Chicken infectious anemia virus is a remarkably hardy virus and is resistant to treatment for 2 hours at 37 C with 5% solutions of invert soap, amphoteric soap, orthodichlorobenzene, iodine disinfectants, and sodium hypochlorite. It is completely inactivated by treatment with 10% iodine disinfectants and sodium hypochlorite in 2 hrs at 37 C. Heating at 100 C, but not at 80 C for 15 minutes destroys CIAV infectivity.

CLINICAL SIGNS

The only specific clinical sign of CIA is anemia, which reaches a peak at 14 to 16 days post infection. At this time, hematocrit values can range from 6 to 27% (normal 35%). Levels of thrombocytes and white blood cells are reduced and the blood may be slow to clot. Affected birds appear depressed and pale, and may show signs of secondary bacterial,

fungal or viral infections. Morbidity and mortality rates are influenced by several factors such as immunodepression by other agents [infectious bursal disease virus (IBDV) and Marek's disease virus (MDV), among others], secondary infections, age of infection, route of infection, and environmental factors. Mortality is usually between 5 and 10%, but can be as high as 60%. Morbidity and mortality are severe if chicks are dually infected with CIAV and MDV, reticuloendotheliosis virus (REV) or IBDV. Infection of chicks with CIAV in the early part of life can interfere with vaccination against MDV or IBDV.

GROSS LESIONS

Bone marrow of the femur can be fatty and yellowish due to severe anemia. Moderate to severe thymic atrophy is one of the most consistent lesions seen in chicks affected with CIA. Atrophy of the bursa of Fabricius can also be seen. Enlarged and mottled livers, hemorrhages in the proventricular mucosa, and subcutaneous and muscular hemorrhages are often seen in association with severe anemia. Secondary bacterial infections can cause airsacculitis, pericarditis, pneumonia, etc. Gangrenous dermatitis resulting from secondary bacterial infections is

often observed. Skin lesions usually develop on the wings as seen in "blue wing disease", but may also appear on other parts of the body.

MICROSCOPIC LESIONS

Hypoplasia of both erythroid and myeloid series cells is seen in the bone marrow by 8 days post-infection. Hematopoietic cells are replaced by adipose tissue or proliferating stromal cells in the early stages of the disease. Immature erythrocytes and granulocytes are present in increasing numbers by 20 days post-infection, and there is a period of hyperplasia by 20 to 24 days post-infection. The hematological parameters return to normal by 28 to 36 days post-infection. Anemia, thrombocytopenia, and leukopenia appear to be due to the direct cytotoxic affect of CIAV on bone marrow hematopoietic precursor cells. Severe lymphoid depletion can be seen in the thymus with a loss of architecture between the medulla and cortex. Lymphoid depletion can also be seen in the bursa of Fabricius, cecal tonsils and spleen. Various organs such as pancreas, heart, adrenal gland, lung, liver, and kidney can be infiltrated with lymphocytes and/or occasional blast-like cells. Characteristic eosinophilic (red) intranuclear inclusion bodies, which are sometimes multiple can be observed in the

large mononuclear cells in various organs such as thymus, spleen, bone marrow, bursa, pancreas, lung, liver, kidney, adrenal gland, etc. The true nature of these inclusion bodies is not currently known.

DIAGNOSIS

A presumptive diagnosis of infectious anemia can be made based on clinical signs and gross lesions, such as decreased packed cell volume ($\geq$ 26%), pale bone marrow, severely atrophied thymus and small bursa. Serological tests including indirect immunofluorescence, ELISA and virus neutralization can be used to detect antibodies to CIAV.

Chicken infectious anemia virus does not replicate in primary chicken embryo cell cultures or in cultured mammalian cells. However, the virus can be cultured in some lymphoblastoid cell lines established from Marek's disease lymphomas, most commonly in MDCC-MSB1 cells. Inoculation of susceptible 1-day-old chicks followed by observation of characteristic lesions is one of the most reliable methods of diagnosis.

Other tests for detection of CIAV such as immunostaining, in-situ hybridization and polymerase chain reaction may become commercially

available in the future.

DIFFERENTIAL DIAGNOSIS

Other diseases including MD, IBD, and RE can cause lymphoid depletion and atrophy of bursa and thymus. However, they rarely cause anemia. Osteopetrosis virus can also cause atrophy of the thymus and bursa of Fabricius, depressed immune responses, and aplastic anemia but not pancytopenia. Certain toxic agents such as sulfonamides and some mycotoxins such as aflatoxin can cause aplastic anemia and a hemorrhagic syndrome. Aflatoxin may also impair the immune system. However, such intoxications are rare in commercial chicken flocks.

PREVENTION AND TREATMENT.

Infectious anemia can be controlled by assuring immunity to CIAV in parental flocks before the onset of lay. This probably occurs in many flocks through natural exposure, but it may not be consistent. A live-virus vaccine is available for this purpose in Europe. At present, a commercial CIAV vaccine is not available in the United States.

In practice, in spite of the risks of introducing other diseases, and the lack of uniformity in the exposure, breeder flocks are being exposed to

CIAV to assure immunity by the time they reach sexual maturity. Non-immune breeder flocks are exposed during their growing period to CIAV by rearing them on litter from affected parent flocks, or by administration through the drinking water of homogenized liver tissue obtained from affected chicks. There is no treatment for chicken infectious anemia. Prevention and treatment of secondary bacterial infections is important.

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DESCRIPTION OF SLIDES

Most of the slides are from 14-day-old experimental chicks inoculated with CIAV at 1 day of age, unless otherwise mentioned. Infected chicks are compared with uninoculated control birds. (Directions i.e., top 'vs' bottom, left 'vs' right are according to the projected view on the screen.)

1. A 15-day-old chick with dermatitis naturally infected with CIAV.
2. Hematocrit tubes showing low Packed Cell Volume (15% to 22%) in 3 naturally infected birds with CIAV compared to a normal (35%).
3. Blood in the syringes showing pale blood due to anemia in a CIAV infected bird compared to blood from an uninfected bird.
4. Pale yellow, fatty bone marrow in the femur of a chick infected with CIAV compared to that of a normal control chick (top).
5. Severely atrophied thymus in a chick infected with CIAV; normal thymus at the top.
6. Moderate atrophy of bursa of Fabricius in a chick infected with CIAV compared to the normal bursa on the left.
7. Severe gangrenous dermatitis on the wing of a chick from a field case.
8. Petechiae and ecchymotic hemorrhages on the pectoral muscles in two chicks

with hemorrhagic syndrome probably secondary to CIAV.

9. Necrotic enteritis in a 16-day-old chick probably secondary to CIAV.

10. Bone marrow: Severe hypoplasia of both erythroid and myeloid cells and replacement by adipose tissue in a chick infected with CIAV compared to normal on the left. H&E, 12.6x

11. Bone marrow: Higher magnification of slide number 10. H&E, 78.5x

12. Thymus: Atrophy of lobules and loss of distinction between medulla and cortex with chick infected with CIAV compared to normal on the left. H&E, 9.5x

13. Thymus: Higher magnification of slide number 12. H&E, 63.3x

14. Thymus: Severe lymphoid depletion and infiltration of large blast-like cells. Notice one large cell has multiple eosinophilic intranuclear inclusion bodies. H&E, 156x

15. Thymus: Mild lymphoid atrophy with infiltration of a large number of blast-like cells. H&E, 156x

16. Bursa of Fabricius: A plica showing lymphoid depletion and increased interstitium in a chick infected with CIAV compared to normal on the left. H&E, 30.2x

17. Spleen: Moderate lymphoid depletion and few blast-like cells in a chick

infected with CIAV compared to normal on the left. H&E, 78.5x

18. Spleen from an infected chick showing the presence of eosinophilic intranuclear inclusion bodies in several mononuclear cells. H&E, 316.5x

19. Lung: Hyperplasia of bronchus-associated lymphoid tissue in an infected chick. Notice eosinophilic intranuclear inclusion bodies in the mononuclear cells. H&E, 125x

20. Heart: Lymphocytic myocarditis in an infected chick. H&E, 93x

21. Pancreas: Lymphocytic pancreatitis with occasional eosinophilic intranuclear inclusion bodies in the mononuclear cell of an infected chick. H&E, 185x

22. Adrenal: Infiltration of lymphocytes in the adrenal gland of an infected chick. Notice occasional eosinophilic intranuclear inclusion bodies in the mononuclear cells. Normal adrenocortical cells on the left side. H&E, 93x

23. Testis: Lymphocytic orchitis with a few eosinophilic intranuclear inclusion bodies in the mononuclear cells. H&E, 125x

24. Fluorescent antibody staining of MSB1 cells infected with CIAV. Notice the positive intranuclear fluorescence.

25. Thymus: Peroxidase anti-peroxidase staining (reddish-brown) of CIAV antigen in the nucleus of infected cells.