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Studies of the Association of Leukemogenic and Oncogenic Properties in Avian Leukemia Viruses

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A. Introduction

The transmission of avian leukosis virus (ALV) in chickens doesn't cause only leukosis, but also nonleucocytic neoplasias (Carr 1960; Graf and Berg 1978; Löliger 1964). After inoculation with avian myeloblastosis virus (AMV), kidney tumors (nephroblastomas) and osteopetrosis or osteosarcomas distinctly different to leukemia may develope in the infected, susceptible chickens. The nephroblastomas, which might be compared with the Wilm's tumor in man, are mostly consisting of different neoplastic cellformations, such as cystoma, adenoma, endothelioma, hemangioma and fibrocytic neoplasias. It is not known that other avian tumor viruses, which don't belong to the ALV group, such as the Marek's disease herpes virus (MDHV), reveal a similar tumor spectrum.

Investigations to separate and characterize the non leucocytic tumor factors (Ogura et al. 1974; Smith and Moscovici 1969) might suggest that this factor of the AMLV is not identical with the leucocytic factor but belongs to the same ALV subgroup antigens A and B. In order to determine the susceptibility of chicken lines having different homozygous cell type properties – c/A, c/B, c/AB, c/O – for AMLV, we investigated the development of leucocytic and nonleucocytic neoplasias in the individual chicken lines to clarify the following:

1. Influence of the chicken lines on incidence and type of the leucocytic and the nonleucocytic neoplasias;
2. Identification of the leucotic and non leucocytic tumor inducing factors in the standard AMLV by differential susceptibility of host cells to ALV subgroups; and
3. Comparison of the tumor development in chicken following experimental infection with AMLV and MDHV.

B. Material and Methods

I. Chicken Lines

The following lines were used: Leghorn line R with sublines celltype c/0, c/A and c/AB;
2. Leghorn line M with sublines celltype c/0 and c/AB;
3. Leghorn line G with subline celltype c/B;
4. Line UM of dysgammaglobulinemic chicken, celltype c/0; and
5. SPAFAS line, free from endogenous ALV, celltype c/0.

The homozygoty of celltype properties were tested by challenge with RSV BH-RAV-1 and BH-RAV-2 (14).

II. Virus Strains

Standard avian myeloblastosis virus (AMV) – strain BAI-A – were obtained by Dr. Bauer, Giessen; – also used was MDHV, strain Celle. Chickens were infected by the intraperitoneal route within 48 h after hatching with the plasma of birds with acute AMV leukemia or the whole blood of birds with acute Marek's disease. The observation extended over 140 days in the first trial and 112 days in the second.

III. Clinical and Pathomorphological Observations

Blood smears and hematocrit were taken from the chicks at the 11th, 15th and 21st day after infection and from moribund chicken before killing. Autopsies were performed on all dead chickens. Touching smears of bone marrow and histologic preparation from bone marrow, liver, bursa, and kidney were done.

C. Results and Discussion

Leukemia and nephroblastomas developed after infection with standard AMV in chickens of all the tested lines homozygous for celltype c/0, c/A, and c/B, but not for cell type c/AB. MDHV induced only lymphoid cell reticulosis, but no leukosis, nephroblastomas, or osteosarcomas within 20 weeks (Table 1).

Pretumorous lesions in the kidney by proliferation of capillary endothel and retothelial cells in the nephron can already be observed in 3-week-old chicks. Gross lesions with clinical symptoms and death by nephroblastoma occur at the earliest at 56 days and mostly between 70 and 112 days after infection. In general leucocytic lesions are not present in chickens older than 50 days (Fig. 1).

Table 1. Incidence of leukemia, nephroblastoma (incl. ovarycystoma), and osteosarcoma in chickens of various lines and different cell susceptibility for the ALV subgroup viruses after experimental inoculation with standard AMV at 1 day age. Observation time: 112 and 140 days

chicken			leukemia complex %			Nephrobl. %	Osteosarc.[a] %	Total %
Line	Cell type	n	Anemia	Erythrobl.	Stemc.-1.			
R	C/0	59	0	0	57.6	35.6	0	93.2
R	C/A	58	0	0	22.4	48.3	1.7	70.7
R	C/AB	46	0	0	0	0	0	0
M	C/0	51	0	0	68.6	25.5	7.8	94.1
M	C/AB	84	0	0	0	0	0	0
G	C/B	58	0	0	8.6	32.8	0	41.4
UM	C/0	146	4.8	0	89.7	4.8	22.6	99.3
SPAFAS	C/0	18	11.1	44.4	11.1	33.3	16.7	100.0

[a] Osteosarcoma occurs together with leukosis or nephroblastoma

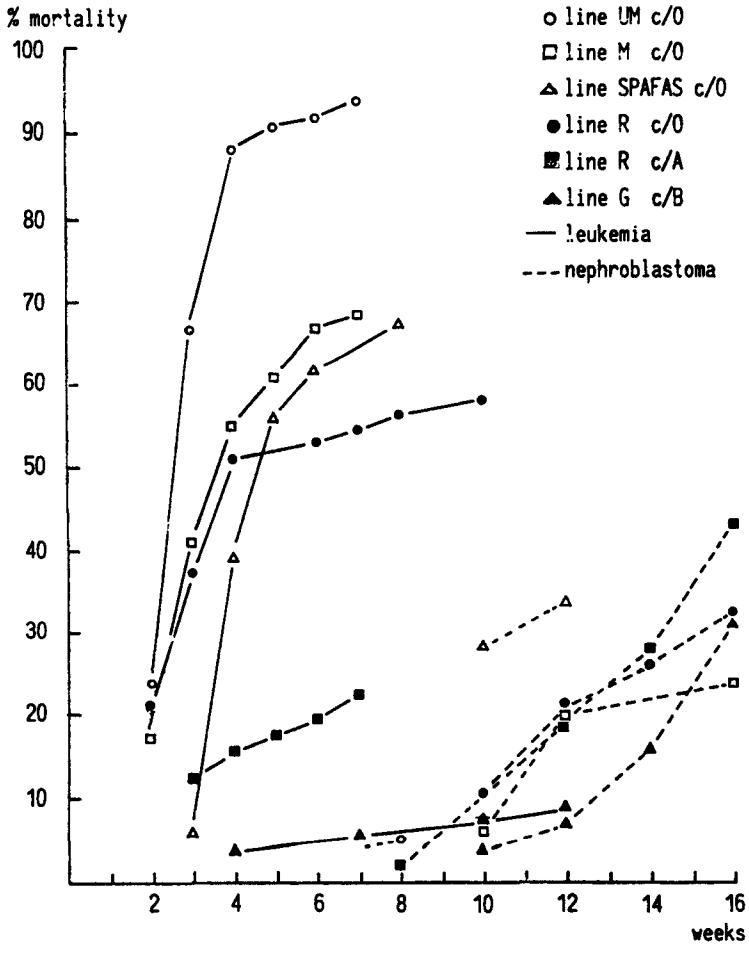

Fig. 1. Development of leukemia and leucocytic neoplasias (nephroblastoma) in chicken of different lines after infection with standard AMV

Osteopetrosis and osteosarcomas occur most often in chicken of lines M, UM, and SPAFAS. Osteosarcomas were observed in young chicken with acute stem cell leukemia as well as in older pullets with nephroblastomas (Table 1).

The frequency of clinic-evident nephroblastomas increases at low frequency of acute leukemia among the young chickens. AMV-infected susceptible chicks, which survive the acute leukemia stage, sicken mostly at a high percentage for nephroblastomas (Fig. 1).

In susceptible chickens of lines R, M, and G the acute stage of AMV infection is evident from agranulocytic stem cell leukemia at 2 to 5 weeks after infection. Among the dysgammaglobulinemic chicken of line UM the first stage observed within 12–15 days was an aplastic anemia with medullar fibrosis which was followed by the stem cell leukemia stage. In the SPAFAS chicken at first an erythroblastosis occurs, followed by stem cell leukemia and later by chronic nephroblastomas (Table 1).

These results indicate that leukemic lesions, nephroblastomas of mixed cell type, and osteosarcomas are caused only by the RNA avian leukosis viruses. Within AMLV both subgroup antigens A and B comprise leukemogenic and nonleucocytic tumor properties. The target cell of these seems to be the pluripotential retothelial cell of mesenchymal origin in the young chicks.

The kind of evident lesions, i.e., leukemia or nonleucocytic tumors, depends on the pathogenicity or amount of the infective agent and on the genetical susceptibility of the retothelial target cells. The more intensive the early hemoblastic disorders (aplastic or leukemic) in the host, the lower is the chance of development of nonleucocytic tumors, especial the late nephroblastomas, by neoplastic transformation of other cells with AMV-infected retothelial cells.

Basing on these etiologic relationships between leukemias, nephroblastomas and osteopetrosis or osteosarcomas in chickens it might be allowed to inaugurate, speculatively, similar etiologic relationships between the leukemias. Wilm's kidney tumors and osteosarcoma in man, especially in young man. This comparative speculation is the mind of our contribution about the association of leucemogenic and oncogenic properties in avian leukemia viruses.

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