

2. Title: Gibbon Leukemia

Principal Investigators: Dennis O. Johnsen, Major, VC
Prayot Tanticharoenyos, D.V.M.
James D. Pulliam, Major, VC

OBJECTIVE

The objective of this study is to determine the incidence as well as the clinical, pathological, and etiological characteristics of the leukemias that have occurred among gibbons in the SMRL colony.

DESCRIPTION

Over the period of the last twenty months, four gibbons in the SMRL colony have died from generalized malignant lymphomas. The extreme variations in the clinical and pathological features of this disease in gibbons is demonstrated by the following summary of each of the cases.

Case #1: Gibbon S-17. This gibbon was a splenectomized male that had been used for over two years in a malaria research project. Approximately one week before his death he showed clinical signs of diarrhea and an upper respiratory infection. This animal was treated with terramycin and neomycin for the respiratory infections and with oral vermifuges for Strongyloides sp. and tapeworms, whose ova were found in a fecal examination. The mucous membranes of the animal were pallid and a low hematocrit and hemoglobin of 3 mg./% showed that the animal had a severe anemia. Transfusions of gibbon blood were given several times, and the diet of the animal was supplemented with iron and ferrous sulphate. The condition was diagnosed as parasitic anemia secondarily complicated with an upper respiratory infection. The animal died approximately one week following the time that clinical signs were first observed. Multiple masses that resembled fat were distributed throughout right and left lung lobes and also formed adhesions to the diaphragm. The liver contained the same type of tissue and was rather soft and enlarged. The kidneys were yellowish and tough and also contained similar lesions. The mesenteric lymph nodes were enlarged. Microscopically, the cause of death was diagnosed as a widespread infiltrative tumor of lymphoid cells distributed in most organs of the body. The neoplasm was diagnosed as a malignant lymphoma of the poorly differentiated lymphocytic type.

Case #2. Gibbon S-19 was a splenectomized mature female gibbon. Before being used for dengue virus studies, this animal had been utilized for malaria studies for a period of time and had been artificially infected with malarial parasites. In July 1968, S-19 was inoculated with Dengue 1 virus and on each day following this time, blood samples were drawn to check for viremia. Two days following inoculation the animal was observed to be anorexic, and passed a soft stool; the temperature was 105°F. The temperature remained elevated at 105°-106°F. and the condition of the animal deteriorated during the next seven days at the end of which time it died. Before necropsy the most likely cause of death was considered to be experimentally induced hemorrhagic fever. At necropsy the heart showed epicardial and sub-endocardial petechial hemorrhages and the lungs were congested. The external surfaces of both kidneys revealed small gray infiltrates 1 mm. in width which extended in linear streaks vertically through the renal cortex. The liver tissues showed a loss of hepatic architecture, were soft, and were a deep red in color. Infiltrates of atypical mononuclear cells were observed in the lung, kidney, liver, and lymph nodes. The pathologic diagnosis was lymphoma leukemia.

Case #3. Gibbon S-77 was a mature female that had been previously infected with malarial parasites one and one half years before the time she was sacrificed. Following malaria experiments, this animal was also placed on the dengue virus study. In September 1968 a veterinary examination showed that the lower abdomen was enlarged. A radiograph showed a diffuse opacity around the urinary bladder. At this time a tumor of the urinary bladder was diagnosed and an exploratory laparotomy was performed to determine if the tumor could be removed. The abdominal cavity was found to be filled with what appeared to be fat and there were generalized adhesions among all the organs of the abdominal cavity.

The liver was hard and pale and there was approximately 20 ml. of fluid in the peritoneal cavity. The duodenum had a small perforating ulcer and there was marked inflammation around the site. The animal was sacrificed during surgery and necropsied immediately. Microscopically, the alveolar walls and vessels of the lungs were filled with masses of adult and immature lymphocytes. The kidney also contained masses of interstitial infiltrates of lymphocytes as did the liver, the bladder, intestinal wall and brain. These findings supported a pathological diagnoses of generalized severe malignant lymphoma.

Case #4. Gibbon S-85 was an adult female gibbon that had previously been splenectomized for work in malaria studies and then placed on the dengue virus study for one year prior to its death. Three days before it died the animal was found paraplegic in its cage. Because this condition was regarded as the result of an unobserved accident, the animal was radiographed. There seemed to be some gapping between several intervertebral spaces in the lumbar area although no definite lesions were observed. Three days later the animal died. Post mortem examination revealed that the cardiac lobe of the lung was gray and shrunken and some focal hemorrhages were observed on the bladder. Hemorrhage was also observed at the interface of the intervertebral spaces from about the seventh thoracic to the first sacral vertebrae to the sacral vertebrae. On close examination the sublumber muscles were slightly off color and softened in this area. When they were examined microscopically the lungs were found to be affected with a severe focal pneumonia. In the heart one of the valves contained a large nodule consisting of mature and large immature lymphocytes. The sub-lumbar muscular tubes contained interfibrillar accumulations of lymphocytic cells. In some areas, the accumulations of cells were so dense that the architecture of the muscle was obliterated. The cell type was a mixture of mature dark lymphocytes and a preponderance of a pale large lymphocytic cells. Several large accumulations of lymphoblastic cells were also present in the ovary. The liver contained medium to large size accumulations of lymphoblasts present in many of the central veins and periportal areas. The periosteum of the lumbar vertebrae was eroded and infiltrated by lymphoid cells. The pathologic diagnosis in this case was a severe focal pneumonia, a mild interstitial pneumonitis, and a generalized severe lymphoblastoma.

Considering the relatively high incidence of this disease in this colony and the current interest in the medical field concerning viral agents as possible etiologic agents in neoplasia, tissues were collected from both gibbons B-72 and S-63 for virological follow up and possible animal inoculation experiments later. Investigators at the National Institutes of Health, Cancer Research Institute were contacted concerning the method of properly preserving specimens that might be taken from developing cases of leukemia. Furthermore, a project was initiated to detect possible developing cases of leukemia in the gibbon colony. Each quarter every gibbon is closely examined for evidence of physical disease with particular emphasis placed on the enlargement of the lymphoid tissues. Blood samples are drawn and checked for anemia, which seemed to be the most consistent clinical finding among the cases of leukemia observed so far; high white counts with predominant ratios of lymphocytes are also followed closely.

PROGRESS

In the two quarters that have passed since the initiation of the leukemia screening program, no new cases have been discovered. Blood values that appeared to be unusual after a first examination were rechecked following a period of several weeks; in all cases the blood values at the time of second examination were within normal limits and there were no other indications of leukemia. Efforts by the Department of Virology to isolate an infectious agent on tissue cultures from the tissue specimens submitted from the necropsy of gibbon S-77 and gibbon S-85 were unsuccessful.