Virus Nephritis, Preliminary Note

By

Akira Sakamoto, Sakae Suzuki, Hideko Kato and
Takashi Ariyoshi

(From the Department of Pediatrics, Nagoya University, Nagoya; Director: Prof. A. Sakamoto)

(Received for publication, January 26, 1952)

We have succeeded in isolating a new virus from 5 patients of typical acute glomerulonephritis. Strains derived from different patients proved identical. The following is a summary of our studies to date.

EXPERIMENTAL

Materials and Methods

In most cases fresh, bacteriologically sterile samples of patients' urine, taken on the 10th to 49th day of illness, were administered intraperitoneally to young guinea pigs (around 250 Gm.). Occasionally patients' blood served as material for inoculation. Urine, diluted with an equal amount of saline, in a dose of 2.5 cc., or 1 cc. of patient's whole blood was used. In subsequent passages the liver or kidney of the animals, which died following the injection, was consistently employed. Emulsions of the organs were strongly centrifuged and the supernatant, with or without filtration through Chamberland L3, was administered to guinea pigs by a variety of routes (usually intraperitoneal, peroral or intranasal).

Results

Guinea pigs invariably died following a single administration mostly in about 2 weeks. Time of death varied from a day to 141 days. The animals showed no significant symptoms until several hours prior to death, when they abruptly became weak. The infection is serially transmissible to guinea pigs by means of inoculation by the organ emulsions proved free from ordinary bacteria, covering at the longest 12 months through 11 generations. When mice were tried, they did not reveal any evidence of infectious manifestations, even though large amounts of the pathogenic materials were given to them.

Routes of infection. Almost all routes of infection can be used to produce the disease and death. The following characteristic pathologic features
are seen. It is especially noteworthy that both peroral and intranasal routes proved to be the most efficient for successful infection; feeding of a 0.1% liver emulsion to animals may cause the acute infection leading to death.

**Demonstration of the virus.** The pathogenic virus was isolated in all 5 patients examined from the urine, and in some cases from the blood or an oral washing, the last of which was used after heating at 65°C for 30 minutes. It is of special interest that the virus can readily be isolated late in the course of the disease, contrary to the usual condition in virus disease. The infective agent increased in pathogenicity when cultured in chick embryo, especially on the chorioallantois. Occasional capillary hemorrhage is to be noted.

**Symptoms and signs.** Gross examination: animals tested regularly exhibited no symptoms except at the time immediately prior to death, when they showed suddenly weakness. Rarely they passed formed stools stained with fresh blood. Urine: albumin mostly positive; red blood cells often present microscopically, white cells frequently found, but casts only occasionally. Blood picture: erythrocytes showed no significant changes, excepting that normoblasts may in a moderate number appear transitorily after the injection. White cell counts revealed slight leucocytosis or the normal range of variation, in either case with consistent preponderance of polymorphonuclear cells.

**Autopsy.** (a) Gross findings: hemorrhage occurs in the body cavities, occasionally causing death due to massive hemorrhage into the abdominal cavity. The most frequent site of the condition is the gall-bladder where a sanguinous fluid is seen in about one-third of the animals injected. Next comes in frequency the abdominal hemorrhage; ascites with blood-tinged exudate, occasionally with pure blood. Bacteriologic studies of these fluids result mostly in no growth on anaerobic and aerobic cultures. Further, gastrointestinal hemorrhage is rarely encountered. Kidneys are dark red in color with no hemorrhagic areas. No apparent edema in the skin. (b) Microscopical findings: the most significant and intensive lesions are found in the liver and kidney. Liver: there is marked hyperemia in general, and degeneration of varying degrees in hepatic cells, which predominates in the central zone with pictures of more or less severe cellular destruction associated often with hemorrhage with no evidence of cell accumulation in the interstitium or in the Glisson's capsule. Kidney: generally hyperemia is extremely marked. The glomeruli are mostly normal in size and shape and not poor in erythrocytes. In some of them, however, capillary endothelial cells are swollen and often proliferate, with occasional hemorrhage. In others the epithelial cells of the capsule may proliferate and there may be thickening and fibrinoid
degeneration of the Bowman's capsule. The principal site of renal lesions, however, is the tubule. It is particularly intensive and diffuse in the proximal convoluted portion, showing marked swelling of the endothelial cells, and, in subacute cases, advanced fatty, granular or albuminoid degeneration. Casts may be found. There is no evidence of cell infiltration. In brief, essential features of this infection manifest themselves as the picture of nephrosis, associated with localized glomerular changes already in an early stage of the disease. The spleen reveals some findings of splenitis with some reticuloendothelial response, while marked hypertrophy and hyperplasia of the reticuloendothelial cells may often be encountered in the lymph nodes.

Acute symptoms and death of animals infected are to be attributable to liver damage, nephrosis and exudative hemorrhagic effusion in the body cavities. The above mentioned gross and microscopical changes in acute cases are considered suggestive evidences for the presence of a specific virus, causing widespread capillary damage with systemic involvement of the whole body.

Immunologic studies concerning the virus and on the infected patients are in progress.

SUMMARY

A new virus was demonstrated by means of the urine or blood taken from patients with typical acute glomerulonephritis. The infection is transmissible to guinea pigs in series with fatal consequence. Some of the properties of the agent and the essential pathologic findings of animals infected are presented.