Astrakhan Scrub Typhus: Time Course of Infectious Process According to Electron Microscopy Findings

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 134, No. 10, pp. 435-436, October, 2002
Original article submitted July 8, 2001

Structural changes in the liver and spleen of albino mice with Astrakhan scrub typhus were studied by electron microscopy. Rickettsia invasion and formation of granulomas induced structural (destructive) and metabolic changes in hepatocytes. Rickettsia were degraded in cytophagosomes and cytolysophagosomes of hepatic macrophages (Kupffer cells) and blood capillary endotheliocytes. In the spleen rickettsia were seen in the extracellular spaces and in various cell populations.

Key Words: *rickettsia; granuloma; hepatocytes; metabolic disorders*

Increasing incidence of endemic rickettsiosis and appearance of new foci of acute febrile infections caused by various strains of the scrub typhus group rickettsia dictates the need for their detailed investigation.

Electron microscopy plays a special role among other methods of investigation. This method reveals ultrastructural changes in organs during various diseases. Electron microscopy extends and supplements the data of light microscopy and plays an important role in detection of the pathogen in infectious process.

MATERIALS AND METHODS

Rickettsiosis was modeled in random-bred albino mice (n=20) by injection of Astrakhan scrub typhus pathogen (*R. astrakhani* AR-1 strain). Control group consisted of 10 intact animals. The pathogen was injected intraperitoneally (10^5 minimum infective doses). Electron microscopy of the liver and spleen was carried out in control and experimental animals on days 4, 6, and 8 postinfection. Material for electron microscopy was prepared by the standard method and examined under a JEM-100 C electron microscope.

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RESULTS

Invasion of rickettsia into organs is associated with the formation of granulomas. The granuloma includes mainly lymphocytes surrounded by hepatocytes and Kupffer cells. Individual rickettsia were found in the extracellular space and Kupffer cells. The formation of granulomas is associated with destructive processes in hepatocytes manifesting mainly by metabolic changes. Appearance of individual clarified foci in the hyaloplasm of swelled hepatocytes attested to disorders in water-salt metabolism. Sings of other metabolic disorders were also seen in hepatocytes. Decreased number of glycogen granules attested to inhibition of glycogenolysis and glyconeogenesis. Dilation and degranulation of the granular endoplasmatic reticulum (GER) can be interpreted as morphological signs of protein metabolism disturbances. Cisterns of the Golgi complex are dilated, and the number of glycogen granules in hepatocytes decreased. Rickettsia at different stages of development were seen at the hepatocyte periphery adjacent to granuloma cells. Swelling of mitochondria paralleled by changes in their cristae attested to impairment of the energy metabolism in hepatocytes. These changes persisted to day 4 postinfection.

On days 6-8 after infection we observed activation of detoxification and repair processes: numerous

0007-4888/02/1344-0374$27.00

cisterns of agranular endoplasmatic reticulum (AER) appeared and the number of ribosomes in the GER membranes increased. Hepatocytes contained many glycogen granules, mitochondria were more active, and the number of mitochondrial cristae increased. The decrease of granulomas was paralleled by rickettsia penetration into macrophages and endotheliocytes. We did not found rickettsia in hepatocytes, but admit the possibility of their invasion.

Degradation of rickettsia observed mainly on day 8 postinfection was realized in cytophagosomes and cytolysophagosomes of Kupffer cells and blood capillary endotheliocytes. In large macrophages phagosomes of different size captured rickettsia and gradually digested them. This process took long time and depended on activity of repair processes in hepatocytes.

In the spleen rickettsia invaded extracellular spaces and cells belonging to different populations. We detected rickettsia in red pulp lymphocytes, endotheliocytes of blood and lymph capillaries, and macrophages. This can be explained by higher permeability of splenocyte membranes compared to hepatocyte membranes. Invasion of the antigen sharply activated the protective function of the spleen. Activation of phagocytosis was observed in immunocompetent cells, i.e. in macrophages and blood and lymph capillary endotheliocytes. Lysosomes, cytophagosomes, cytolysophagosomes accumulated in these cells captured rickettsia.

Hence, the infectious process in Astrakhan scrub typhus by its pathological and submicroscopic characteristics, mechanisms of action on hepatocytes and splenocytes is similar to rickettsioses described previously (tick-borne fevers), but has some peculiarities intrinsic of this particular disease.

Electron microscopy of the liver showed groups of rickettsia in the extracellular spaces and in liver macrophages. Granulomas in the liver were located near the capsule and were presented mainly by lymphocytes, plasmacytes, and macrophages; eosinophils, fibroblasts, and monocytes were sometimes seen. Groups of rickettsia were sometimes seen near granulomas. Ultrastructural changes were found on hepatocyte membrane. It seemed that rickettsia formed protrusions and invaginations of the hepatocyte plasmalemma. Disorders in carbohydrate metabolism manifested in sharp decrease and disappearance of glycogen granules. Disorders of other types of metabolism (water-salt, lipid, and protein) were seen in some hepatocytes; energy balance was impaired. Changes in hepatocyte organelles confirmed these disorders. Kupffer cells contained individual rickettsia and their groups.

Hence, we observed parallel changes in cell populations of the liver and spleen . The most important role in the mechanisms of invasion, dislocation, translocation, and degradation of rickettsia is played by cells with defense functions.

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