NOTE

Amyloidosis in Rabbits Infected with *Trypanosoma evansi*

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Amyloidosis was observed in 3 out of 6 male rabbits experimentally infected with *Trypanosoma evansi*. Amyloid deposit was seen in the splenic perifollicular spaces, hepatic sinusoids or renal glomerular tufts. Lymphoid and plasma cell clusters were seen in the spleen and lymph nodes with persistent high levels of serum IgM.—**Key words:** Amyloidosis, Trypanosomiasis.

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The virulence and pathogenicity of trypanosomes have been extensively studied using rabbits [1], and clinical signs in this species of animals are known to be similar to those in cattle, goats, sheep, and dogs in infected with brucel subgrup of trypanosomes. On the histopathology of the infections in rabbits, however, a few papers have be published especially of *Trypanosoma evansi* (*T. evansi*) infection [2]. This report describes a marked amyloid deposition in the spleen, kidney and liver of the rabbits experimentally infected with *T. evansi*.

Six male rabbits weighing about 2 kg were inoculated intramuscularly at the buttock with *T. evansi*, strain Tanshui. Each animal received $10^7$ to $10^8$ organisms in 0.2 ml of dilution of blood of mice, which had been injected with a frozen stock of *T. evansi*. Two to three weeks after inoculation, reddish swelling appeared in the scrotum of all rabbits producing an erosion. The skin lesions were produced latter at the ears, external nares, eyelids, prepuce and limbs. No parasitemia was detectable by examination of a drops of blood from the auricular vein, but it was intermittent and moderate even at moribund stage. Animals died 26 to 70 days after inoculation, manifesting anorexia and emaciation.

Postmortem examination revealed skin lesions at various sites, swelling of lymph nodes, and systemic congestion. The extensive changes were seen in the skin of the nose, ears, eyelids and toes. They were granulomatous lesions with hemorrhage, edema and infiltration of neutrophils and mononuclear cells at the subcutaneous tissue. In the testis there were severe atrophy of seminiferous tubules and infiltration of mononuclear cells.

Splenomegaly was seen in three of six rabbits. The cut surface of the affected spleen showed large white nodules (Fig. 1), and the liver was white and mottled (Case. 3). There were jelly clot formation in the heart (Cases. 1 and 3) and swelling of kidney (Case. 6).

The most remarkable histological changes were seen in the spleen. Small lymphocytes in the follicles decreased in number, with increase of large lymphocytes and reticular cells. The outer zones of follicles and the perifollicular spaces were replaced either wholly (Cases. 1 and 3) or partially (Case. 6), by eosinophilic hyaline materials (Fig. 2), which were positive for PAS and Congo red and gave a white fluorescence with thioflavin.
T under ultra-violet. Also the green polarization color was prominent on Congo red stained section (Fig. 3). Electron microscopy of the formalin-fixed tissues revealed that these
materials were composed of extracellular fibrils (Fig. 4). In the marginal zones of the splenic follicles with amyloid deposition there were several capillaries, a few plasma cells and degenerated lymphocytes.

There were clusters of large pironinophilic cells or plasma cells in the red pulp of the spleen and the paracortical areas and medullary cords of lymph nodes of most cases. Lymph nodes had dilated sinuses with multinucleated giant cells and proliferated macrophages. In the liver, moderate swelling of Kupffer cells and infiltration of plasma cells in Glisson’s sheath were seen in 4 rabbits. Amyloid deposition was remarkable on the walls of hepatic sinusoids and slightly on the renal glomerular tufts in one case (Fig. 5). In the heart, there was infiltration of a few lymphocytes and plasma cells in perivascular and intermuscular spaces of 2 rabbits.

The concentrations of serum IgG and IgM of 3 rabbits (Cases 4, 5 and 6) were determined by the single radial immunodiffusion technique at intervals of two to three days (Fig. 6). The IgG concentration increased gradually by 24 days, remaining at a high level until death. The IgM concentration showed a rapid increase 10 days after inoculation, reaching a maximum (500 to 1,000 percent of the preinoculation value) around 20 days and remaining at high levels in two cases.

Amyloid deposition was described in the splenic lymph nodules and renal glomeruli of the rabbits infected with *T. equiperdum*, and IgG and IgM were demonstrated by immuno-
fluorescence [3]. Deposition was more prominent and extensive in the present cases of rabbit while showing a similar pattern of distribution. Secondary or induced amyloidosis associated with leishmaniasis has been reported also in hamster [4] and dog [5].

Pathogenesis of amyloidosis remains unclear whereas there have been some analytical evidences of amyloid fibrils [6]. Recently a new concept of the immunoregulatory function was proposed that macrophage activation associated with T-cell suppression and B-cell proliferation might play an essential role in amyloidogenesis [7]. A persistent high level of IgM in trypanosomiasis with proliferation of plasma cells and large pironinophilic cells in the spleen and lymph nodes as described above has been reported by many investigators [8, 9]. Immunosuppression on heterologous antigens in this disease has also been described by some investigators [10, 11]. In immunological responses to trypanosomes antigenic variation that serial changes in the surface antigenicity in the host body take place against host’s antibody seem to be of impotance [8, 12]. It can be presumed that trypanosomiasis is associated with amyloidosis in some disorders of the immune mechanism.

The edematous and granulomatous lesions in the skin and genital organs of the present cases appeared to be similar to those demonstrated previously in rabbits infected with T. evansi [13], T. equiperdum [3], and T. brucei [1, 14]. Interstitial myocarditis was described in cattle, sheep, dogs and rodents infected with various species of trypanosomes, and it might be attributable to changes in vascular permeability due to antigen-antibody complex [1, 15-17].
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REFERENCES


要約

Trypanosoma evansi 感染家兎におけるアミロイド症について（短報）：柳田昌樹・礒田政直（日本獣医畜産大学獣医学部病理学教室）——Trypanosoma evansi 活水株 10⁶~10⁸ を筋肉内接種した雄家兎 6 例のうち 3 例に、腎臓、脳髄質の著明なアミロイド沈着が認められ、原虫感染に続発したアミロイド症と考えられた。そのうちの 1 例では、肝臓機能および腎尿管系機能障害にもアミロイド沈着が認められた。脾およびリンパ節における形質細胞、大型ビロン体好性細胞の増加と、血中 IgM の持続的高値がみられた。