Eosinophilic Granulomas Caused by Adult Setarial Worms in the Bovine Urinary Bladder

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Abstract. A pathologic study was performed on parasitic lesions found in the urinary bladder of cattle. Grossly, these lesions were curved, linear and sclerotic. Microscopically, they were nodular, granulomatous lesions with parasites at their center, presenting features characteristic of exudative inflammation with marked infiltration of eosinophils, in relatively fresh cases. In contrast, they were characterized by the infiltration of giant cells and phagocytes, as well as by the follicular proliferation of lymphocytes, in long-standing cases.

The parasite found in the tissue of the urinary bladder bore morphological resemblance in many respects to *Setaria digitata* isolated from the abdominal cavity of cattle in a district where intra-abdominal infection with this worm showed an incidence as high as 55%. The worms isolated from lesions in the urinary bladder of two of the infected cattle were identified as *Setaria digitata*.

These results indicate that the lesions were caused by adult worms of *Setaria digitata* originally harbored in the abdominal cavity and accidentally entering the wall of the urinary bladder.

Few reports have been published on the development of lesions due to parasitic invasion in the bovine urinary bladder [6]. The authors investigated tumors of the urinary bladder over a period from 1969 to 1972. In the course of this investigation they found the deleterious effects of the filarial worm *Setaria digitata* upon the urinary bladder in thirty-six cattle. Inasmuch as they considered that changes caused by these effects could not be belittled as those of a disease of the uropoietic system in cattle, they carried out the present investigation. This communication deals with the findings of bovine vesical nematodiasis and discussion on the pathogenesis of the disorder.

Materials and Methods

Thirty-six specimens of the urinary bladder with lesions due to parasitic invasion were obtained from slaughtered cattle over a period from October, 1969 to August, 1972. After gross pathological examination at necropsy, representative sections of the vesical tissues were fixed in a 10% neutral formalin solution and Bouin's solution, embedded in paraffin, cut into serial thin sections, and stained with hematoxylin and eosin (HE), with periodic acid-Schiff (PAS) stains, or by the argentation technique of Watanabe.

Identification of parasites was accomplished by examining the prepared slides under the light microscope, as well as under the stereomicroscope. Microscopic examination was also made on preparations cleared with glycerin-alcohol solution. Surveys were carried out to investigate the incidence and distribution of intraperitoneal filarial infection in the bovine population of the district involved in the infection. Serial and intermittent

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cross sections of filarial worms harbored in the abdominal cavity of a cow were also prepared. Their microscopic features were compared with those of worms found in vesical lesions of the same cow.

Results

1. Gross pathological findings (Figs. 1, 2 and 3)

Grossly, lesions of *Setaria digitata* parasitism were demonstrated in most instances as tortuous or funicular, circumscribed, indurated foci in such areas as the serosa, muscularis, and submucosa of the bladder and adjoining ligaments. Some of the offending helminths penetrated the vesical wall longitudinally with their cephalic ends protruded into the vesical cavity. In five cases the urinary bladder had only white eminences, which were similar to the gross lesions of setarial infection when examined by the microscope. Most of the lesions were solitary and accompanied occasionally by petechiae or hemorrhagic spots. Edematous swelling was prominent in areas surrounding lesions situated in the submucosa. Whitish helminths up to 9.0 cm in length were recovered from the center of each lesion in three cases. It was impossible to find setarial worms having intruded into any other organ or the abdominal wall.

2. Histopathological findings

Microscopically, the lesions were nodular and granulomatous with filarial worms harbored at the center (Figs. 4 and 5). Relatively fresh lesions were characterized by a marked infiltration of eosinophilic leukocytes and destructive inflammatory changes (Fig. 8). Lesions were found most frequently in an area extending from the serosa to the muscularis. The infiltration of eosinophilic leukocytes was demonstrated primarily in an area with helminths at its center and later mostly in areas around degenerated blood vessels (Fig. 11). It was

accompanied by the minimal perivascular mobilization of lymphocytes and plasma cells.

Frequently noted was the formation of acidophilic club-like bodies in the outermost layer of the lesion with parasites at center (Fig. 7). These parasites were degenerated, disintegrated, and often associated with the infiltration of macrophages and giant cells against foreign body (Figs. 6 and 7).

In the lesions of cases which seemed to be fairly advanced, the reactive infiltration of eosinophils showed a trend to diminish in intensity. It was accompanied by nodular granulomatous changes with marked enlargement and proliferation of histiocytic cells and pronounced infiltration of lymphocytes, plasma cells and fibroblasts around residual or calcified helminths. Lymphocytic proliferation was particularly conspicuous, presenting a nodular or follicular feature (follicular hyperplasia). In longstanding lesions, numerous lymph follicle-like structures were found around the parasite, presenting a microscopic structure of lymph node. An abscess was formed evidently at the center of the lesion in two cases. These parasitic lesions tended generally to extend from the serosa to the mucosa, frequently associated with changes characteristic of cystitis.

3. Parasitological findings

The worms isolated from relatively fresh lesions in two cases had the morphological characteristics of *Setaria digitata*, though slightly degenerated. Especially, their cephalic portion made it possible to identify them as this parasite (Figs. 14 and 15).

They were white nematodes about 9.0 cm in length and approximately 700 μ in diameter. Their cephalic end was tapering and had two pairs of odontoid processes. Their external surface was covered entirely

with a smooth, cuticular structure and apparently had a dorsal and a ventral line.

The worms had remarkably well developed female reproductive organs. Their uterus contained abundant microfilariae 250 to 300 μ in length. Histological preparations of vesical tissues showing the cross sections of worms revealed that the parasites had been disintegrated or calcified to various degrees with morphological features fully characteristic of the Phylum Nematoda, especially of some species of the Superfamily Filariodae (Fig. 9).

Worms 400 to 700 μ in diameter had a keratinous circular structure, as the outermost layer or the external cuticle, supported by the hypodermis, within which were radially arranged folds of muscle layer surrounding the body cavity. In the body cavity were an alimentary canal and reproductive organs with tubular structures. There were two circumscribed, distinctly thickened portions of the external cuticle in positions opposite to each other, representing the dorsal and ventral lines characteristic of the Phylum Nematoda. In six of the cases studied, numerous larvae about 260 μ in length with a close morphological resemblance to microfilariae were contained in the reproductive organs (Fig. 10).

Histological examination revealed that the lesions in the urinary bladder had been induced by invasion of the parasites through the serous membrane. To clarify the pathogenesis of these vesical lesions, a survey was conducted on filarial infection in the abdominal cavity of cattle in the district mentioned above. As a result, a total of 148 worms were discovered in 58 (55%) of 105 slaughtered animals surveyed. All of them were identified as *Setaria digitata* (Fig. 12). Histological, intermittent cross sections of these worms were prepared and examined microscopically in comparison with the

foregoing sections of parasites in vesical tissues. The resultant findings made it possible to confirm that there was a similarity in many of the morphological respects described above between the parasites harbored in vesical tissues and those in the abdominal cavity (Fig. 13).

Discussion

As one of the disorders due to setarial infection in ruminants, lumbar paralysis is widely recognized to be caused by accidental wandering of larvae in the cerebrospinal parenchyma [1-5, 7]. Nevertheless, it appears that few reports have been made on the deleterious effects of setarial infection upon other viscera than the brain and spinal cord. Exceptionally, vesical lesions have been described by Ohbayashi [6] in only one bovine case. It is clear from the findings in the thirty-six cases reported herein that the development of granulomatous lesions and cystitis in cattle due to accidental wandering of *Setaria* into the urinary bladder cannot be overlooked.

Microscopically, the vesical lesions were characterized by the presence of the parasite surrounded by infiltrating eosinophilic leukocytes and proliferated follicular lymphocytes. The histological features of exudative inflammation associated with a marked infiltration of eosinophils were seen during the incipient stage. They were virtually consistent with the findings described by Ohbayashi [6]. Nevertheless, the majority of lesions presented microscopical features characteristic of proliferative inflammatory reactions of long standing, showing a diminishing trend of eosinophils and a prominent follicular proliferation of lymphocytes. These results suggest that there may have been an immunological relationship between the host tissues and the offending parasites.

With respect to the pathogenesis of the granulomatous lesion of the urinary bladder, the histological findings of the present investigation indicate the significant role of the intrusion of *Setaria digitata* into the vesical serosa. The incidence of filarial infection in the abdominal cavity was as high as 55% among the 105 slaughtered cattle examined in this investigation. All the worms detected were identified as *Setaria digitata*. These results suggest the possibility of parasitic intrusion into the vesical wall.

Problems still remain to be solved as to the affinity of intraperitoneal *Setaria digitata* for the urinary bladder. It would be reasonable to assume that the active physiological movement (contraction and dilatation) of the urinary bladder may probably have not a little influence upon the organotropic attribute of the parasite.

Parasitic granulomatous lesions were observed in the urinary bladder in the present investigation. They were presumed to have been caused by accidental wandering of adult worms of *Setaria digitata* directly into the vesical wall. Parasitic granuloma may be regarded as a new entity of diseases of the uropoietic system of cattle. The results of the present investigation seem to offer a new problem on the pathogenicity of *Setaria digitata*.

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Explanation of Figures

- Fig. 1. An indurated, linear lesion with tortuosity in the submucosa of the apex of urinary bladder. Edema and hemorrhage are evident in areas surrounding the lesion.
- Figs. 2 and 3. A tortuous, linear lesion in the serosa of urinary bladder. Note the sharp demarcation of the lesion in vesical tissue.
- Fig. 4. A lesion located in the submucosa. It is nodular and granulomatous with prominent cellular infiltration. Associated with the lesion is edema of the tunica propria. Hematoxylin and eosin staining (HE). Low-power magnification.
- Fig. 5. The same lesion as above. A cross section of the worm is shown at the center of the lesion located in the serosa. HE. Low-power magnification.
- Fig. 6. A cross section of the parasite in a lesion presumed to be relatively fresh. Note the entire structure of the worm which is relatively well preserved. The external cuticle contains muscle layers. Ovary and uterus are affected with calcification to some extent. An intense infiltration of inflammatory cells and phagocytes is seen in an area surrounding the parasite. HE. $\times 280$.
- Fig. 7. A dead, calcified worm surrounded by inflammatory cells, phagocytes, and a few giant cells. Acidophilic club-like bodies are frequently seen along the margin of the dead worm. HE. $\times 280$.
- Fig. 8. A lesion induced in the initial stage of parasitic intrusion. A marked infiltration of eosinophils and hemorrhage are seen around the worm. The cross section of the parasite resembles that shown in Fig. 13 in many morphological features. HE. $\times 280$.
- Fig. 9. A cross section of nematode showing a relatively well preserved original structure. Inside the calcified external cuticle are seen the muscle layer and tubular structures of the alimentary canal and reproductive organs. HE. $\times 280$.
- Fig. 10. Numerous larvae 250 to 280 μ in length contained in the parasite. HE. $\times 280$.
- Fig. 11. Marked focal infiltration with eosinophils of the muscularis and interstice of the vesical wall. Infiltration with eosinophils is demonstrable in the initial stage of parasitic intrusion. HE. $\times 280$.
- Fig. 12. Adult *Setaria digitata* isolated from the abdominal cavity. Upper three worms are females 8.8 cm in average length and 745 μ in average diameter. The lower worm is a male 4.7 cm in length and 423 μ in diameter.
- Fig. 13. A cross section of *Setaria digitata* isolated from the abdominal cavity of cattle. HE. $\times 112$.
- Fig. 14. Cephalic portion of a female worm in cleared preparation. It has a dully rounded cephalic margin with a mouth crown at its tip, along with two pairs of odontoid processes.
- Fig. 15. Caudal end of a male worm. Three pairs each of small projections are arranged anterior and posterior to the anus, respectively. A few small projections are scattered on the median line of the cauda. A pair of conical projections are noted near the caudal end.