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Feminization and reduction of testicular weight in mouse sparganosis

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Abstract: After infection of male mice with the plerocercoids (spargana) of *Spirometra mansoni*, serum levels of estrogen and testicular weight were analyzed by enzyme-linked immunosorbent assay (ELISA) and weighing machine, respectively. The serum level of estrogen increased progressively in infected mice compared with normal controls, whereas the testicular weight of infected mice decreased significantly ($P < 0.05$). These results suggest that certain substances from spargana change the steroid hormone metabolisms in the host by unknown pathways, and chronic infection may contribute to change of the function of steroid hormone target organ, i.e., testis, in male mice.

Key words: *Spirometra mansoni*, sparganum, plerocercoid, estrogen, testis

Human sparganosis is a disease caused by ingestion of the plerocercoid of *Spirometra mansoni* in the snakes (Cho et al., 1975). After infection in humans, the sparganum is able to avoid host immune responses during their long life migration period due to its excretory-secretory proteases (Kong et al., 1994). The surface and excretory-secretory molecules are the key modulators or targets of the host immune system (Kong et al., 1994, 1997). Therefore, excretory-secretory proteases of spargana might have immunoendocrinological effects on the host. Examples of reciprocal endocrinological interactions between the parasite and the host, including man, have been found. For example, the administration of secretory products from *Taenia taeniformis* metacestodes into rats inhibits testosterone production in the rat testis (Rikihisa et al., 1985) and *T. taeniformis* infection alters reproduction in the infected female rat host (Lin et al., 1990).

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In this study, we hypothesized that the sparganum induced sex hormone changes leading to feminization of the male host, and its target organ, i.e., testis, may be affected. Larval spargana were collected from the snakes caught in the Republic of Korea. A total of 10 male BALB/c mice (Daehan Biolink, Daejon, Korea) were purchased and grouped into non-infected normal control and infected mice. One sparganum was infected to each mouse and blood was serially collected from the tail. Steroid hormone levels in the mouse sera were measured by estradiol EIA kit (Cayman Chemical Company, Ann Arbor, Missouri, USA) according to manufacturer's instruction. Finally, at 12 weeks after infection, mice were sacrificed and both side testes were weighed. Data are expressed as the mean and standard deviation and analyzed for statistical significance by the Student t-test. A P-value of < 0.05 was considered significant.

The serum level of estradiol increased in infected mice, whereas the testicular weight significantly decreased at 12 weeks in infected mice ($P < 0.05$; Table

Table 1. Changes of estrogen level and testicular weight in mouse sparganosis

		Pre-infection	2 weeks PI[a)]	4 weeks PI	8 weeks PI	12 weeks PI
Serum estrogen	Normal	13.8 ± 5.0	16.7 ± 3.4	11.2 ± 4.9	11.0 ± 6.2	10.8 ± 6.8
(pg/ml)	Infected	13.5 ± 4.3	17.0 ± 3.3	16.5 ± 3.9	16.2 ± 5.5	14.8 ± 3.8
Testicular weight	Normal	0.19 ± 0.01	ND[b)]	ND	ND	0.20 ± 0.01
(g)	Infected	0.20 ± 0.02[c)]	ND	ND	ND	0.14 ± 0.01[c)]

[a)]Post-infection.
[b)]Not done.
[c)]Significantly lower ($P < 0.05$) at 12 weeks PI compared with pre-infection.

1). Examples of changes of steroid hormones have been reported in normal immune responses and autoimmune diseases. Therefore, this result suggests that the reproductive endocrine system may interact with the host immune responses. In male mice, it is well known that infection of *Taenia crassiceps* cysticerci triggers a feminization process, which is characterized by significantly reduced testosterone and increased estradiol serum levels (Larralde et al, 1995). Concomitantly, infected male mice progressively lost their sexual behavior and none of the infected males showed any sexual response toward female mice at 16 weeks of infection and complete restoration of the sexual behavior of infected males was obtained after an administration of testosterone (Morales et al., 1996). In the present study, we observed variations of testicular weight instead of the sexual behaviors of sparganum-infected mice. Recently, the loach (*Rutilus rutilus*) infected with a pseudophyllidean tapeworm, *Ligula intestinalis*, showed approximately 50% less gonadotropin (LH) contents than non-infected fish and its negative effects on gonadal development in infected fish (Carter et al., 2005). Therefore, the present results suggest that the sparganum, i.e., a larval stage of pseudophyllidean tapeworm, may interact with the brain-pituitary-gonadal axis and affect gonadal development of the mouse host.

The endocrine system of the host's gender is of great consequence for the rate of reproduction of some parasites. For example, *T. crassiceps*-infected females carry larger parasite loads than males in early infection, but males also become massively parasitized in very chronic infections (Sciutto et al., 1991). Some findings are suggestive of estrogen-mediated immunoendocrinological modulation in favor of Th2-mediated immune responses (humoral responses) and depression of Th1 type immunity (cellular responses) in *T. crassiceps* infection (Terrazas et al, 1994). Another finding of a weight gain phenomenon in mouse sparganosis has been well known (Shiwaku et al., 1982) since the first publication (Mueller, 1963). Although strict calorie intake was not checked in this study, male mice infected with the sparganum showed an increase in body weight significantly (data not shown) than normal controls.

The results of the present study may be an example of hormonal relationship between the host and the parasite, which may allow the sparganum to survive using the host's more complete endocrine system. In return, the sparganum may provide the male host with an additional quantity of estrogen in chronically infected mice. There should be further studies on the control mechanisms of steroid hormones, including pituitary-gonadal axis, in mouse sparganosis.

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