Hormonal milieu of the new murine EAO model

Yo Tokunaga and Hiroyoshi Tanaka

Department of Urology, Kawasaki Medical School, 577, Matsushima, Kurashiki City, Okayama 701-01, Japan

Introduction

Experimental autoimmune orchitis (EAO) is well known to be both a prototype organ-specific autoimmune diseases like experimental autoimmune encephalomyelitis (EAE), thyroiditis (EAT) and uveitis (EAU), and also a major animal model of human immunological male infertility. In 1991, Itoh, Hiramine and Hojyo succeeded in inducing EAO against most C3H/He mice sensitized by two subcutaneous injections of live syngeneic testicular germ cells (TC) without using any immunological adjuvant (a new murine EAO model)1).

Since there have been no reports regarding a hormonal milieu of this new murine EAO model, we decided to study the serum levels of luteinizing hormone (LH), follicle stimulating hormone (FSH) and testosterone in relation to the extent of histopathological involvement of the testes.

Materials and Methods

Groups of from 10 to 12 male C3H/He mice aged from 8 to 10 weeks were subcutaneously sensitized with $1 \times 10^7$ TC twice at two-week intervals in each examination. The testes of the mice were removed for histological examinations just before the first injection (Day 0), on the 7th day after the first injection (Day 7), just before the second injection (Day 14), and on the 7th (Day 21), 14th (Day 28), 21st (Day 35), 24th (Day 40), 46th (Day 60), 76th (Day 90) and 106th days after the second injection (Day 120).

Blood sampling from the axillary artery for the investigation of the hormone levels was performed in each mouse on Day 0, Day 7, Day 14, Day 21, Day 28, Day 35, Day 40, Day 60, Day 90 and Day 120. The serum levels of LH, FSH and testosterone were measured by ELISA kits for rats.

Results and Discussion

The pathological changes of orchitis were completed on Day 40 in all mice although some severities of hypospermatogenesis were found in each mouse. The earliest changes in the testes were mainly observed in the rete testis and around the seminiferous tubules as the infiltration of lymphocytes and macrophages with some
polymorphonuclear leukocytes into the stroma. Together with progression of the lesions, the infiltrating cells entered the seminiferous tubules through the basement membrane. Finally germ cells as well as the infiltrating cells disappeared from the testis; i.e., the testis became azoospermic with only Sertoli cells present.

There were not remarkable changes in the serum levels of LH, FSH and testosterone until Day 35; i.e., before completion of EAO. However, serum FSH levels were elevated on Day 40 and its after relating to completion of EAO and the severities of pathological changes of the testes while serum LH and testosterone remained at almost basal levels (Fig. 1).

One of the pathogenetic factors of clinical idiopathic hypo- and aspermatogenesis has been thought to be an autoimmune disease because of the similarities in pathological changes between EAO and the lesions of specimens from in idiopathic infertile males. Additionally, in this study, we also proved that endocrinological changes in mice with EAO and patients with idiopathic testicular disease are similar.

This new EAO model induced against C3H/He mice could be a useful animal model for elucidating the pathogenesis of idiopathic male infertility.

---

![Graphs showing hormone levels](image)

**Fig. 1** Serum hormone levels in TC-immunized C3H/He mice

---

**References**