The Role of Prolactin in the Pathogenesis of Autoimmune Disease

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Abstract

Prolactin has emerged in recent years as a major regulator of both the maturation and the function of lymphocytes. Prolactin abnormalities, which include elevated serum levels, decreased bioactivity, abnormal circadian rhythm, and exaggerated secretion after stimulation by TRH, are associated with various autoimmune conditions in humans. Some animal experiments and observations in humans indicate that prolactin has an important role in the pathogenesis of autoimmune disease. There are several mechanisms through which prolactin could promote the development of autoimmunity. It is concluded that prolactin abnormalities alone are not likely to cause autoimmunity, but rather additional regulatory defects are perhaps also required for disease to develop.

Prolactin and Autoimmune Disease

Pathogenesis of autoimmunity has also been considered at length, with similar conclusions [126]. It is likely that the development of autoimmune disease involves T cells of the helper type, because B cells and killer/suppressor T cells all require T-cell help for autoreactivity. Thus, control of self-nonspecific discrimination is largely due to helper T lymphocytes. It is well recognized that bacteria and viruses have the capacity to induce autoimmune disease; drugs and toxins are also capable of inducing autoimmunity. These facts point to the importance of environmental agents in the pathogenesis of autoimmune disease. The role of cytokines in the development of autoimmunity is currently being investigated. Despite these considerations, the precise mechanisms for the breakdown of self-tolerance are not known for any autoimmune disease [126].

Recent observations indicate that prolactin (PRL) has an important role in the maintenance of immunocompetence and that abnormalities of PRL secretion contribute to the development of autoimmunity. The role of PRL in normal immune function and its possible contribution to the development of autoimmune diseases are presented and discussed herein.

Prolactin and Immune Function

Prolactin and Bone Marrow Function

Blood and plasma volumes, total erythrocyte levels, and hemoglobin are increased significantly above control values in lactating rats. Plasma from pregnant or lactating mice stimulated erythropoiesis in polycythemic mouse recipients [70]. Pretreatment of normal or pregnant mice with PRL stimulated erythropoiesis and increased plasma volume [71,72]. Placental lactogen also had some erythropoietic activity that could be antagonized by estrogen [73].

Normochromic normocytic anemia, leukopenia, and thrombocytopenia coupled with impaired DNA and RNA synthesis developed in the bone marrow of hypophysectomized (Hypox) rats. All these abnormalities could be corrected by syngeneic pituitary grafts (SPG) placed under the kidney capsule or by treatment with ovine or bovine PRL or growth hormone (GH) or human placental lactogen (HPL) [17,19,100]. Hypophysectomized rats had 10–20% lactogenic hormone activity in their serum when compared with control animals, as established by the Nb2 lymphoma proliferation assay. Daily treatment of Hypox animals with a rabbit anti-rat PRL serum decreased further their serum lactogenic activity, which was associated with the development of severe anemia; death occurred within 8 weeks. In contrast, serum lactogenic hormone levels gradually increased in untreated Hypox animals starting the 7th week after pituitary removal; these levels increased up to approximately 50% of control levels by week 9. At this point, anemia was stabilized. Incorporation of H-thymidine by rat bone marrow cells was stimulated in vitro by rat and ovine PRL and GH and by HPL [101].

Bovine PRL increased the mitotic activity and inhibited histologically demonstrable secretory activity of the bursa of Fabricius in chickens [25]. Administration of bovine PRL to male white leghorn chickens for 5 consecutive days tended to decrease the weight of the bursa of Fabricius [127].

Prolactin and the Thymus

Smith [130] observed in 1930 that the thymus gland of Hypox rats regressed in weight to less than half that of control animals in long-term survivors. In contrast, rats with partial Hypox showed an absolute weight loss no greater than the control animals. Because pituitary remnants were subsequently found to secrete only PRL in significant quantities, this article can be regarded as the first to indicate the role of PRL in thymic physiology.

Ectopic pituitary transplants induced an increase in thymus weight and in the number of thymocytes in Ames dwarf mice. The weight of the thymus in grafted animals remained lower than in normal mice, but the number of thymocytes was normal [51].

Involution of the thymus could be reversed in Hypox rats by transplantation of SPG under the kidney capsule, whereas body growth was only modestly stimulated by such grafts. If normal animals were grafted the same way, their thymuses grew significantly bigger than those of controls.