A surprising and dramatic neuroendocrine-immune phenotype of mice deficient in Growth Hormone-Releasing Hormone (GHRH)

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In the framework of close interactions between the immune and neuroendocrine systems, Growth Hormone (GH) has been proposed to exert significant effects on the immune system, but there is not yet a consensus about GH immunomodulatory properties. These studies investigated the immune and anti-infectious response of dwarf Ghrh−/− mice presenting a severe deficiency of the GHRH/GH/IGF-1 axis. In basal conditions, thymic parameters and T-cell responses of Ghrh−/− mice were not severely affected but a constant B-cell lymphopaenia was observed. Thus, we investigated vaccine and anti-infectious responses of Ghrh−/− mice toward Streptococcus pneumonia, a B-dependent pathogen, Ghrh−/− mice were unable to trigger production of specific IgM and IgG against serotype 1 pneumococcal polysaccharide (PPS) after vaccination with either native PPS (Pnx23) or protein-PPS conjugate (Prev-13) vaccines. These vaccines both include the serotype 1 (our S.pneumoniae strain) and provide an effective protection in mice. A short GH supplementation to Ghrh−/− mice (1 daily injection of 1 mg/kg GH for 4 weeks) restored IgM and IgG response to Pnx23 vaccine but not to Prev-13. This suggests that GH could exert distinct impacts upon spenic areas. Furthermore, after intranasal instillation of a non-lethal dose (defined by the full clearance by WT C57BL/6 mice after 24h) of serotype 1 S.pneumoniae, Ghrh−/− mice exhibited a dramatic susceptibility. This was proved by a marked time-dependent increase in pulmonary bacterial, a septicemia already 24h after infection and a survival limit of 72h. We also observed a dramatic decrease in lung B- and T-cell populations and an increase in proportion of inflammatory macrophages. By contrast, wild-type and heterozygote mice completely cleared S.pneumoniae infection after 24h. In conclusion, our data show without ambiguity that the somatotrope GHRH/GH/IGF-1 axis plays an important and unsuspected role in defense against S.Pneumoniae.