



Original article

ACTA FAC. MED. NAISS. 2005; 22 (4): 191-194

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HISTOPATHOLOGICAL CHANGES IN THE SPLEEN OF RATS TREATED WITH MONOSODIUM GLUTAMATE

SUMMARY

Neonatal treatment of animals with monosodium glutamate (MSG) induces lesions of the arcuate, paraventricular and ventromedian nuclei of the hypothalamus. The aim of the study was to investigate the effect of MSG on the spleen of rats. Damage to these structures leads to functional disruption in the hypothalamic-pituitary-adrenocortical (HPA) axis. White Wister rats were used. The experimental group comprised 10 rats that underwent subcutaneous treatment with MSG (4mg MSG per g/b.w.) on the 2nd, 4th, 6th, 8th, and 10th day of postnatal life. The control group consisted of 10 animals, as well. Four months after the treatment with MSG, the animals were sacrificed. Paraffin sections of the spleen tissue were stained using HE method. Macroscopically, the experimental animals displayed the atrophy of the spleen. Pathohistological changes in the spleen manifested as the atrophy of the white pulp. Germinal centers were missing. Follicles with preserved germinal centers were rare. In the red pulp of the spleen, there were morphologic elements of chronic delay, abundance of hemosiderophages and cell elements of hematopoiesis, especially megakaryocytes.

Key words: monosodium glutamate, spleen

INTRODUCTION

Glutamate is a well-known and significant excitatory neurotransmitter in the central nervous system. The administration of monosodium glutamate (MSG) to experimental animals during first postnatal days induces selective lesions in the brain. Of all brain regions, the hypothalamus and its arcuate (1), ventromedian (2) and paraventricular (3) nuclei are most susceptible to neurotoxic effects of MSG. These nuclei are sites for synthesis of numerous stimulatory and inhibitory hormones, the most numerous of which are releasing hormones of adenopituitary tropic hormones. The lesions of these structures are essentially endocrine metabolic

disturbances in character (4-6) which manifest in adult life.

Damage to the neurocytes of the hypothalamic nuclei leads to functional disturbance in the homeostasis of the hypothalamic-pituitary-adrenocortical (HPA) axis (7, 8). Literature in the field shows contradictory data about the accurate mechanism (8-9) underlying functional disruptions in the HPA axis. The results related to plasma ACTH levels stretch from those suggesting decreased values (8) through those indicating normal (9) up to increased (10) values. On the other side, the majority of authors (8-10) find the elevated values of plasma corticosterone in MSG-treated animals. The cause of plasma corticosterone increased levels, despite

unaltered or even lower ACTH values, is seen as a consequence of decreased corticosterone clearance (11), increased sensitivity of the adrenal cortex to ACTH (8) in MSG-treated animals, or secretion of secretagogues other than ACTH (8).

The elevated level of plasma glucocorticoids in MSG-treated animals leads to Cushing-type obesity, osteoporosis, steroid diabetes, atrophy of the testicles, and bilateral diffuse-symmetric adrenocorticotrophic hyperplasia.

In addition to playing a significant role in the metabolism, glucocorticoids, due to reduced synthesis of RNA and increased protein catabolism in the lymphatic tissue, induce lymphopenia and a decrease in the immune function of the lymphatic tissue (12).

Our study was motivated by a small number of data and inconsistent findings on the condition of the lymphoreticular system of the spleen in MSG-treated rats.

AIMS

Provided that glucocorticoids induce lymphopenia, as well as that the results on the condition of the lymphoreticular system of the spleen in MSG-treated Wister rats are rather vague and contradictory, the aim of the study was to determine the condition of the lymphoreticular system of the spleen in Wister rats after MSG administration.

MATERIAL AND METHODS

The study was done on white, adult, male and female Wister rats, body mass 150-200g, 9-12 weeks old, divided into two groups: experimental and control. Each group comprised 10 rats (5 male rats and 5 female rats).

The experimental rats underwent subcutaneous treatment with MSG at 4mg dose g/b.w on the 2nd, 4th, 6th, 8th, and 10th day of postnatal life. The control animals were not treated. Both experimental and control rats were sacrificed four months after MSG treatment. Paraffin sections of the spleen tissue were stained using HE method.

RESULTS

Microscopically, the control group showed the spleen tissue of normal composition (figure 1).

Pathohistologically, the experimental animals displayed the atrophy of the white pulp and the absence of germinal centers (figure 2).

Rare follicles with preserved germinal center were present (figure 3). In the red pulp of the spleen,

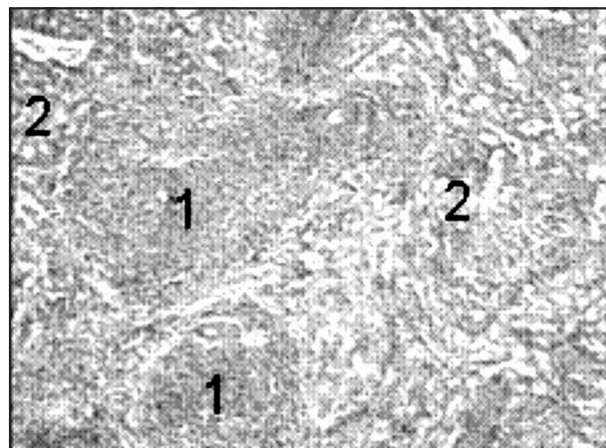


Figure 1. Normal spleen structure – control group (HEx20)
Microscopic presentation of the normal spleen parenchyma:
1 – lymphatic follicles of the spleen
2 – red spleen pulp

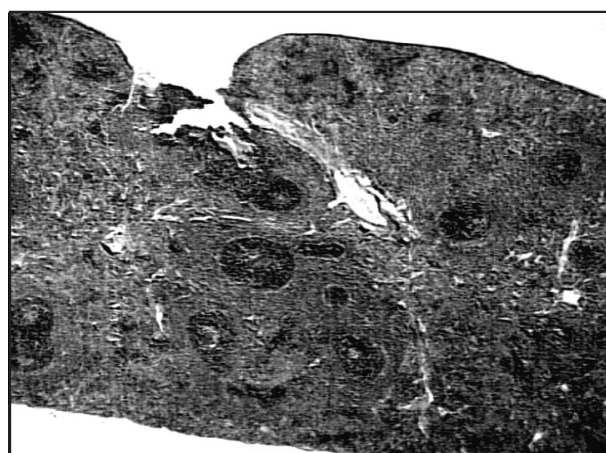


Figure 2. Atrophy of the white spleen pulp – experimental group (HEx10)

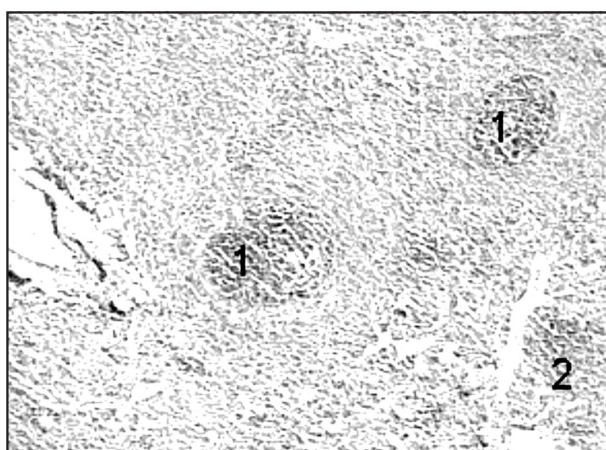


Figure 3. Atrophy of white spleen pulp – experimental group (HEx20)
In the spleen, we can see lymphatic follicles of decreased volume and cellularity, with domination of the elements of the red spleen pulp, with different degree of lymphatic follicles' atrophy of:
1 – lesser degree
2 – higher degree

there were morphologic elements of chronic delay (congestive sinusoids of the spleen), abundance of hemosiderophages (figure 4), as well as the presence of cell elements of hematopoiesis, primarily megakaryocytes (figure 5).

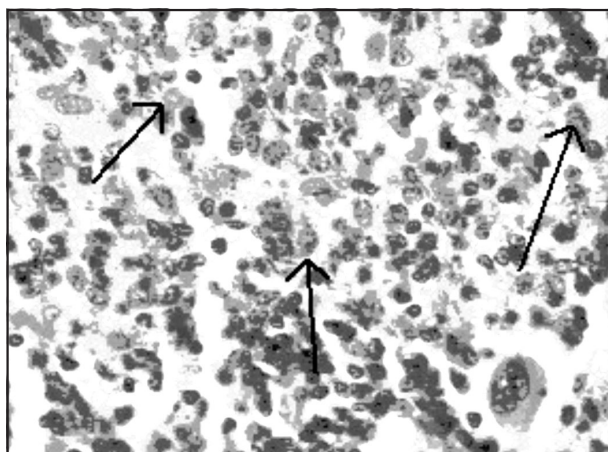


Figure 4. Hemosiderophages (indicated by arrow) in the white spleen pulp – experimental group (HE_x40)

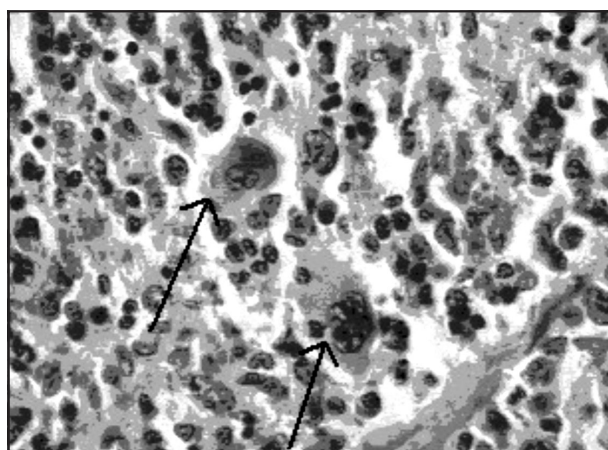


Figure 5. Megakaryocytes (indicated by arrow) in the red spleen pulp – experimental group (HE_x40)

DISCUSSION

The administration of MSG to animals in early neonatal period induces lesions of the neurocytes of the hypothalamic arcuate (1), ventromedian (2), and paraventricular (3) nuclei. Glutamate leads to reversible changes in the permeability of the blood-brain barrier (13, 14), especially in the hypothalamic area, thus leading to neurotoxic lesions of its nuclei followed by changes in the content of

neuropeptides and neurotransmitters. As these nuclei play the major role in the neuroendocrine regulation (15, 16), their lesions result in disturbed functional activity of the HPA axis (7, 8). Data concerning plasma ACTH levels are contradictory (8-10). Glucocorticoids play a significant role in both metabolic and immune events.

The experiments on the activity of the hypothalamic-pituitary-adrenocortical axis in MSG-treated animals have revealed the increased number of neurons secreting corticotropin-releasing hormone (CRH) in the paraventricular nucleus of the hypothalamus, and the increased number of ACTH-secreting adenopituitary cells and the glucocorticoid-secreting cells in the adrenal fasciculate area. The tissue of the thymus shows atrophy and decreased lymphocyte proliferation (13). These findings are followed by the elevated plasma CRF and ACTH levels. These results suggest that the HPA axial hyper-function is associated with cell-mediated immunodeficiency (10).

Glucocorticoids lead to suppression of the immune response by decreasing RNA synthesis and increasing protein catabolism in the lymphatic tissue (15). It is for this reason that patients with Gushing syndrome (induced either by adrenal tumor or tumor of basophilic adenopituitary cells) are susceptible to opportune candidiasis, cytomegalic and other virus infections. The results we obtained on the atrophy of a lymphoreticular organ such as the spleen, T and B-lymphocytes, and reticular cells of the red pulp are explanatory of 'infections' geneses. The finding of megakaryocytes in the spleen tissue of MSG-treated animals may be interpreted as a compensatory mechanism of the spleen atrophy.

In order for the pathogenesis of elevated ACTH secretion to be comprehended, an analysis is necessary at the level of peptidergic fibers that, in physiological conditions, synthesize somatostatin-inhibiting releasing factor (SIRF) displaying an inhibitory effect on the function of basophilic adenopituitary cells.

CONCLUSION

Based on the obtained results, the conclusion may be drawn that the administration of monosodium glutamate to animals leads to the atrophy of the spleen, cells of both white and red pulp, which explains the immunosuppressive effects of glucocorticoids.

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HISTOPATOLOŠKE PROMENE U SLEZINI PACOVA TRETIRANIH MONOSODIJUM GLUTAMATOM

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Injekciono tretiranje životinja u neonatalnom periodu, monosodijum glutamatom (MSG), dovodi do nastanka lezija hipotalamusnih jedara: arkuatnog, paraventrikularnog i ventromedijalnog. Ovaj rad je za cilj imao ispitivanje uticaja MSG na slezinu pacova. Oštećenja ovih struktura uzrok su poremećene funkcije hipotalamusno-hipofizno-adrenokortikalne osovine (HHA osovine).

U radu su korišćeni pacovi Wistar soja. Eksperimentalna grupa brojala je 20 pacova i tretirana je subkutano MSG-om (4 mg MSG/g/TT) 2, 4, 6, 8. i 10. dana postnatalnog perioda. Kontrolnu grupu činilo je 10 životinja. Posle četvoromesečnog tretiranja MSG-om, životinje su žrtvovane. Parafinski preseki tkiva slezine bojeni su HE metodom.

Makroskopski se zapaža atrofija slezine kod životinja eksperimentalne grupe u odnosu na kontrolu. Histopatološke promene slezine ogledaju se u atrofiji bele pulpe. Germinativni centri nedostaju. Retki su folikuli sa očuvanim germinativnim centrom. U crvenoj pulpi slezine postoje morfološki elementi hroničnog zastoja, obilje hemosiderofaga kao i ćelijskih elemenata hematopoeze, pre svega megakariocita.

Ključne reči: monosodijum glutamat, slezina