Increased Serum High Mobility Group Box 1 (HMGB1) Concentration and the Altered Expression of HMGB1 and Its Receptor Advanced Glycation Endproducts in Pemphigus

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Dear Editor:

Pemphigus is an autoimmune mucocutaneous blistering disease induced by antibodies bind to desmoglein (DSG) 3 and 1. Nevertheless, people's understanding towards molecular mechanisms underlying the progression of the disease is incomplete. High mobility group box 1 (HMGB1), a ubiquitous nuclear protein expressed in almost all cell types, could be translated to cytoplasm and released extracellularly during sterile inflammation and infection. Extracellular HMGB1 contributes to inflammatory reaction and tissue damage through its receptor advanced glycation endproducts (RAGE). Moreover, neutralizing HMGB1 can attenuate inflammation and tissue damage in many types of inflammatory conditions including arthritis, colitis, sepsis and ischaemia reperfusion¹. Thus, serum levels of HMGB1 and tissue expression of HMGB1 and its receptor RAGE in patients with pemphigus were investigated herein.

This study consisted of 27 patients with pemphigus, 22 with bullous pemphigoid and 32 age- and gender-matched healthy subjects. All patients were not on drugs 15 days before this study. Pemphigus patients were treated with systemic corticosteroids and intravenous immunoglobulin therapy. Their serum samples, collected before and after treatment, were examined by enzyme-linked immunosorbent assay (ELISA; RapidBio Laboratories, Calabasas, CA, USA) under instructions of the manufacturer. Skin expression of HMGB1 and RAGE were observed from 15 pa-

tients with pemphigus, 12 with bullous pemphigoid, as well as 15 age- and gender-matched healthy individuals. Immunohistochemistry were used to detect the expression of HMGB1 and its receptor RAGE using antibodies against HMGB1 (clone EPR3507; Epitomics, Burlingame, CA, USA), RAGE (Boster Biological Technology Co., Ltd., Wuhan, China) and horseradish peroxidase-conjugated secondary antibodies.

As shown in Fig. 1A pemphigus patients had significantly higher serum HMGB1 levels than bullous pemphigoid patients, and healthy controls. As presented in Fig. 1B, serum HMGB1 levels in 16 pemphigus patients before treatment were significantly higher than those after treatment ($p=0.008$). As shown in Fig. 2, HMGB1 expression was found principally. Skin expression HMGB1 from healthy individuals and Bullous pemphigoid was nearly entirely confined to nucleus. In contrast, plentiful cytoplasmic of HMGB1 was detected in the epidermis of lesional skin in pemphigus patients. Besides, the skin expression of RAGE was negative in controls, strong positive in pemphigus patients and weak positive in bullous pemphigoid patients.

As we know, pro-inflammatory cytokines or cell apoptosis is involved in HMGB1 release. In the pathogenesis of pemphigus, apoptosis promotes the separation of epidermal cells, which causes acantholysis of matrix cells, together with the stimulation from proinflammatory factors, abnormal expression of HMGB1 can be inferred^{2,3}. Our previous work showed the existence of cytoplasmic ex-

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Fig. 1. Serum levels of high mobility group box 1 (HMGB1) were determined by enzyme-linked immunosorbent assay. (A) Serum levels of HMGB1 were obtained from 27 patients with pemphigus, 22 with bullous pemphigoid and 32 control subjects. Serum HMGB1 levels in patients with pemphigus were significantly higher than those in control subjects. p -values are based on the Mann-Whitney U test. (B) Wilcoxon signed ranks test for paired data showed that serum HMGB1 levels of 16 patients with pemphigus before treatment were significantly higher than those after treatment.

Fig. 2. Tissue samples were obtained from 15 patients with pemphigus, 12 patients with bullous pemphigoid and 15 control subjects. The expression of high mobility group box 1 (HMGB1) and receptor advanced glycation endproducts (RAGE) in the skin was detected by immunohistochemistry. The skin expression of RAGE was negative in controls, was strong positive in pemphigus patients and weak positive in bullous pemphigoid patients. Inset: HMGB1 expressed in cytoplasm of patients with pemphigus. Scale bars = 50 μ m.

pression of HMGB1 in lesional skin of psoriasis⁴. In this work, we indicated that HMGB1 serum levels were obviously increased in pemphigus patients. Furthermore, cytoplasmic expression of HMGB1 and overexpression of it

receptor RAGE in the epidermis observed in pemphigus skin lesions. Therefore, we suggest that HMGB1/RAGE interaction may contribute to inflammatory reaction and tissue damage in pathogenesis of pemphigus. Further study is

undergone to explore the function of HMGB1 in the pathogenesis of pemphigus, and achieve a new therapy method by inhibiting their interaction.

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Cutaneous Implantation Metastasis of Papillary Thyroid Carcinoma Following Fine Needle Aspiration Biopsy

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Dear Editor:

Thyroid carcinoma is the most common endocrine malignancy and the incidence has increased continuously¹. Thyroid fine-needle aspiration biopsy (FNAB) is a reliable, safe, and cost-effective screening test and recommended study for evaluation of thyroid nodules^{2,3}. Post-FNAB local pain and minor hematomas are the most common complications, while serious complications, such as infection, recurrent laryngeal nerve palsy, hemangioma, and tumor implantation seem to be rare³.

A 34-year-old woman presented with an asymptomatic, solitary, bean sized bluish nodule on the right anterior neck for 6 months. Five years ago, thyroid ultrasound ex-

amination revealed a solitary nodule on the right thyroid lobe. Ultrasound-guided FNAB performed on the thyroid nodule and she underwent right lobectomy with regional neck dissection. Pathological findings showed that the tumor was a papillary adenocarcinoma of the thyroid. After surgery, she regularly visited the hospital for follow-up and last visit revealed nonspecific findings.

A subdermal nodule was noted about 3 cm above the operation scar line, at the site where aspiration needle had been inserted (Fig. 1). We removed the nodule with elliptical excision. Pathologic findings showed a well demarcated nodule consisting of many tumor cells with multiple follicular structures. Nuclear features demonstrated apparent ground

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