

CLINICOPATHOLOGICAL STUDIES OF EOSINOPHILIC LYMPHOGRANULOMA

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Objective: To research the formative mechanism of eosinophilic lymphogranuloma (ELG), investigate its essence, provide morphologic base for treatment. **Methods:** The biopsies and surgical specimens of 41 cases were studied with the light microscope, fluorescein microscope, electron microscope and immunohistochemical methods. In these cases, 10 cases levels of serum IgE were measured, it was high level, and 11 cases cured with radiotherapy. **Results:** The lesions mainly included proliferation of both lymph tissues and post-capillary venules and formed many new scattered lymph follicles. Marked hyperplasia of plasmocytes and mast cells and diffusible infiltration of eosinophilic granulocytes were observed in tissues. The eosinophilic granulocytes were obviously degranulated. When stained with fluorescein isothiocyanate (FITC) labeled antiserum IgE, the cells showed yellow-green fluorescence, which showed reticular shape in the germinal center of lymph follicles. The swollen tumor-like masses could disappear with radiotherapy, and the eosinophilic granulocytes count in circulation and level of serum IgE reduced to normal. **Conclusion:** The serum IgE is high lever and it is positive reaction in the tissues strongly. It is accord with allergic granuloma. The lymphocytes are allergenic amboceptor cells, the x-ray can kill them and stop allergenic agent, the illness was recovered.

Key words: Granuloma, Kimura's disease, IgE, Allergia.

The etiology of eosinophilic lymphogranuloma (ELG), also called Kimura's disease, is obscure.

Adults and young makes from the mongoloid race are usually involved. The lesion has a predilection for soft tissues in the subcutis around the ears, parotids, elbows and cervical lymph nodes as a tumor-like mass. The illness may last over ten years. In order to study its the clinical and histopathologic character and formative mechanism of lesions, investigate its essence and provide morphologic base for treatment, 41 cases were examined and reported in this paper.

MATERIALS AND METHODS

Clinical Materials

Biopsies and surgical specimens of 41 ELG patients were drawn from amongst the samples collected from 140000 cases between 1960 and 1995. The ELG detectable rate was, therefore, 0.029%. 37 occurred in men, and 4 in women. Among the 41 cases of ELG, the average age of the patients was 28.61 years. Clinical measurement of mass volume was about 2.8 to 10 cm in diameter. The tumourlike masses of 20 cases were found around ears, the masses of 12 cases were in parotid gland (Figure 1), 8 cases elbows were involved, cervical lymph nodes of 7 cases were involved. Among masses 6 cases were found in several site of body; 35 patients (85.36%) presented skin itching around the mass; twenty-one cases 51.2% were associated with urticaria. Classification index of eosinophilic granulocytes in the peripheral blood were greatly increased in every patient, varying from 0.1 to 0.9 international unit. In ten cases, the levels of serum

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IgE were measured separately and were 0.10, 1.31, 2.78, 3.47, 4.05, 1.77, 2.10, 3.41, 2.19, 3.40 mg/L. In 11 cases the masses disappeared with deep x-ray local radiation therapy. The total radiation dose was 3000 cGy: 3 times weekly 150 to 200 cGy exposure. There was no recurrence in all of the patients which follow-up survey for 13 to 33 years. The classification index of the eosinophilic granulocytes in circulation and level of serum IgE were reduced to normal.

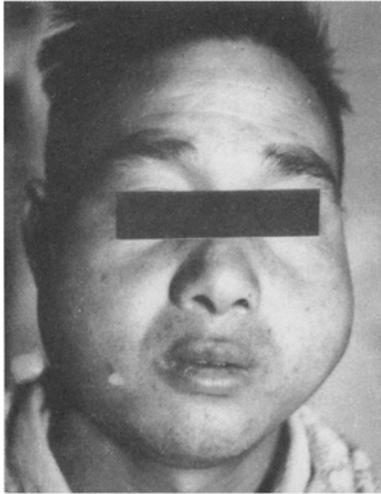


Fig. 1. Eosinophilic lymphogranuloma at the left parotid

Experimental Methods

The paraffin sections of specimens stained with haematoxylin eosin and methyl green- pyronine and periodic acid schiff. The fluorescence microscopy: Paraffin sections were digested with trypsin and stained with sheep anti-human conjugated with fluorescein isothocyanate (FITC) and with direct method. The T-lymphocytes were stained by CD3 and B-lymphocytes were stained by CD20 according to immunohistochemical streptavidin (SP) conjugated method. Control slides: Ten cases of slices of controls, phosphate buffered saline replaced the first antibody. The same immunohistochemical methods used as above. The fresh specimens of 10 cases were examined under the electron microscope.

RESULTS

The lymph tissue of the disease showed obvious

benign hyperplasia and a large number of new lymph follicles had formed, there is no lymphoid sinus. The follicles varied in size and their distribution was no regular (Figure 2). The B-lymphocytes were situated in the germinal center of lymph follicles, T-lymphocytes round its periphery, and T and B lymphocytes were disseminated between the lymph follicles. Diffusible infiltration of most eosinophilic granulocytes was observed in the tissues. Rejuvenization formed a large number of prolymphocytes, proplasmocytes, plasmocytes and some immunoblasts. The pyronine positive reaction was shown in the cytoplasm of these cells. Hyperplasia of mast cells was also found, their cytoplasm granules stained purplish red with thionine were seen. Post capillary venules proliferative as branch-like vessels and were accompanied proliferative fibroblasts, sometimes, the wall of small blood vessels became loose and edematous and it was infiltrated by plasma. The blood vessels were reduced in old lesions, the fibrosis ultimately resulting in scarring.



Fig. 2. Lymphadenosis formed new follicles HE × 40

Under electron- microscopy, mitochondria and ribosomes of hyperplastic cells increased. Rough- endoplasmic reticulum was extremely abundant in the cytoplasm of the plasmocytes. The eosinophilic granules in the cytoplasm of the eosinophilic granulocytes showed obvious degranulation. Their acidophilic granules were broken or dissolved, gradually becoming vesicles of different sizes (Figure 3).

Fluorescence microscopy, fluorescence appears yellow-green colour, the nuclei have no fluorescence. The fluorescence showed in the cytoplasm of the prolymphocytes, lymphocytes, proplasmocytes and eosinophilic granulocytes (Figure 4). The fluorescence IgE was seen also in germinal centers of the lymph

follicles. The distribution of fluorescence conjugated with C3 and IgE were identical. The fluorescence did not appear in the connective tissue, walls of blood vessels and remaining ducts of the parotids. The control slides showed no fluorescence.

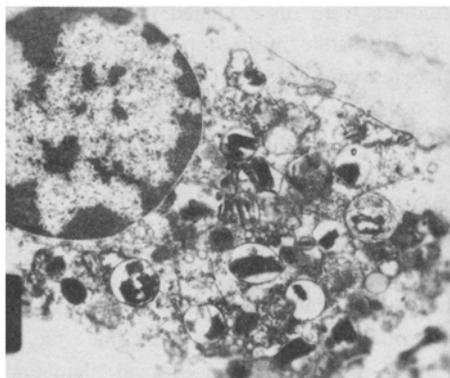


Fig. 3. Degranulation in the cytoplasm of eosinophilic granulocyte electron microscopy $\times 1300$

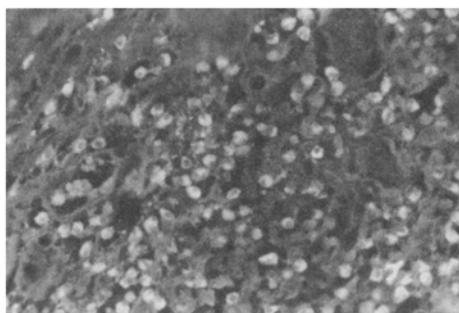


Fig. 4. Yellow-green fluorescence of IgE in the parotid gland. No fluorescence in the connective tissue and walls of blood vessels and remaining ducts, FITC $\times 200$

DISCUSSION

In 1976, Tabenaka et al.¹ found that the level of IgE antibodies against candida albicans in the patients' serum was increased and the disease was considered to be caused by the antigen of soluble substances of the fungi absorbed through oral membranes. In 1981, Ishikawa et al.² pointed out that the disease was probably the rarity of Type 1 hypersensitivity. In 1988, we³ suggested that local lesions of this disease were allergic granuloma, which showed immunohistological

features and there was a positive IgE reaction strongly. It always has illness owing to some allergic factors entering to the body with allergic constitution. In 1992, the works being similar to ours were also reported by Motoi and his colleagues.⁴ An important problem is to explain the mechanism of formative lesions and to provide morphological base for treatment.

The histological of feature of the ELG was mainly lymphocytic proliferation which formed tumor-like masses. These lymphocytes produced antibodies and released lymphokine factors in the process. The T-lymphocytes assist the B-lymphocytes to differentiate into proplasmocytes, plasmocytes, and to produce antibodies. The increased rough endoplasmic reticulum in the cytoplasm of immunoglobulin and these cells presented more active antibodies. They were stained by the antiserum of immunoglobulin labeled by FITC and emitted yellow-green fluorescence.

The IgE level rose in the serum of the patient. The IgE is a special immunoglobulin in allergies which combines with an Fc-receptor of the mast cell. These receptors have a very high affinity for IgE. The hyperplastic mast cells in the lesion tissue were stimulated by antigen and then released bioactive substances consisting of histamine, chronic reaction substances and chemotactic factors for eosinophilic granulocytes. These substances take part in the binding of the Fc-receptor in the mast cells surface to the Fc-portion of IgE. A series of enzyme reactions occurs so that hypersensitive inflammation is evoked and results in cutaneous pruritus of the peripheral local tumor-like mass, urticaria of the whole body, eosinophilia, and plasma infiltration of blood vessel walls. The chemotactic factor of eosinophilic granulocytes leads to infiltration of the lesion tissue by eosinophilic granulocytes. The degranulation of the eosinophilic granulocytes releases histaminase which dissolves the histamine, and aromatic sulphatase which dissolves the substances of chronic reaction. Proliferating capillaries act as a channel for carrying away allergic substances, diminish local inflammation.

Tarada, et al.⁵ suggested that mechanism of eosinophilia was due to interleukin-5 that was produced and lymph tissues after simulation with candida antigen. If it is indeed, the patent's oral membrane is usually maintained protection and clean, and the illness can be prevention.

The lymphocytes are allergenic amboceptor cells in the ELG-patient. The lymphocytes can be injured by x-ray so masses disappeared after radiotherapy. The

lymphocytes died and stopped allergenic agent, the illness recovered health.

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