Histiocytosis-X with Chronic Weeping Ulcers in the Anogenital Areas

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This is a report of a 26-year-old female with histiocytosis-X showing chronic, mildly pruritic and painful weeping ulcers on the labia majora and perianal area for 6 years. She had shown amenorrhea for 7 years and polyuria and polydypsia for 5 years. She also had a history of simple goiter, otitis media, and spontaneous pneumothorax.

Lesions with a honeycomb appearance on both lower lung fields were noted on chest X-ray, and computed tomography of the brain revealed thickening of the pituitary stalk. Diabetes insipidus was demonstrated by water deprivation test. A biopsy specimen from the perianal lesions showed an infiltration composed almost entirely of histiocytes with kidney-shaped nuclei and abundant cytoplasm. They were proved as Langerhans' cells on electron microscopy.

She showed a good response to external radiation therapy (total 2000 rad) to the anogenital and pituitary areas. The skin lesion recurred in 6 months, but cleared again by the same dose of radiation. (Ann Dermatol 2:(2) 128-131 1990)

Key Words: Histiocytosis-X, Anogenital area, Radiation therapy

Histiocytosis-X is a group of closely related diseases characterized by a benign or malignant granulomatous hyperplasia of Langerhans' cells, with involvement of the skin, bones, lungs, nervous system, and other internal organs.[1]

Herein we report a case of histiocytosis-X presenting with chronic, weeping anogenital ulcers and symptoms of diabetes insipidus (DI) successfully treated with radiation therapy.

REPORT OF A CASE

A 26-year-old woman with chronic, weeping lesions on the vulva and perianal area for 6 years was seen at Kyungpook National University Hospital in May 1988. She had suffered from a variety of related medical problems including amenorrhea of 7 years' duration, polyuria and polydypsia for 5 years, and dyspnea on exertion after spontaneous pneumothorax, which had developed in 1986. She had a past history of simple goiter (1982) and of otitis media (1985). At her first visit to our department in 1985, the patient showed several shallow ulcers on the anogenital region and was treated, under the diagnosis of chronic dermatitis, with systemic and topical steroids, and antibiotics which relieved the skin problem only partially and temporarily.

Physical examination revealed a well developed and well nourished woman with a skin problem. There were variously sized, multiple weeping ulcers on the labia majora and perianal area (Fig. 1). Inguinal lymph nodes were not palpable.

Complete blood cell count, urinalysis, VDRL, stool examination, liver function test, and OKT4/OKT8 ratio in peripheral blood were within normal limits or negative. Endocrinological studies including thyroid function test and levels of FSH, LH and prolactin were normal. Electrocardiogram,

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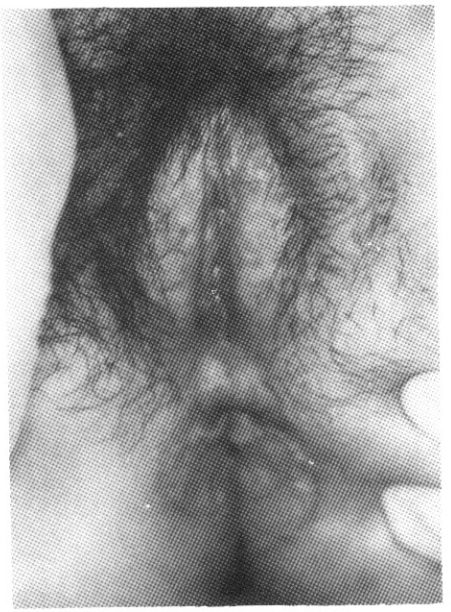

Fig. 1. Variously sized, multiple weeping ulcers on the labia majora and perianal area.

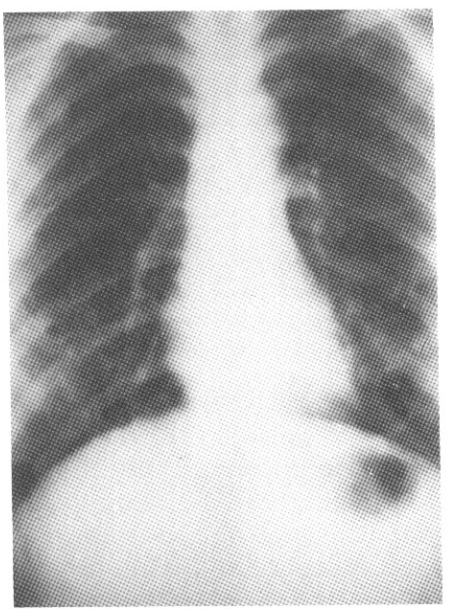

Fig. 2. A lesion with a honeycomb appearrance in both lower lung fields.

bone X-ray, and scannings of bones, liver, and thyroid showed no abnormal findings. A honeycomb appearance in both lower lung fields was detected by chest X-ray (Fig. 2), interstitial lung fibrosis finding by pulmonary function test, and thickening of the pituitary stalk by brain computed tomography (Fig. 3), respectively. Water deprivation test revealed diabetes insipidus findings.

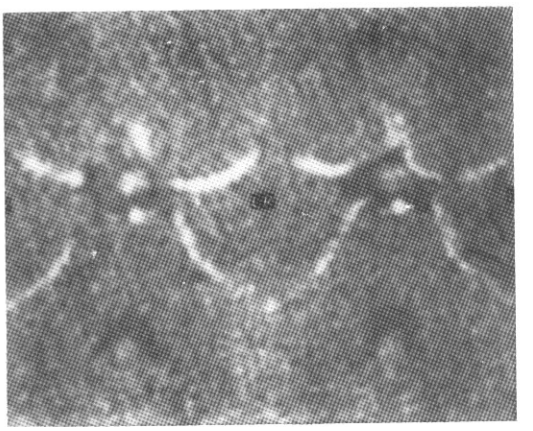

Fig. 3. Computer tomograpy revealed the thickening of the pituitary stalk.

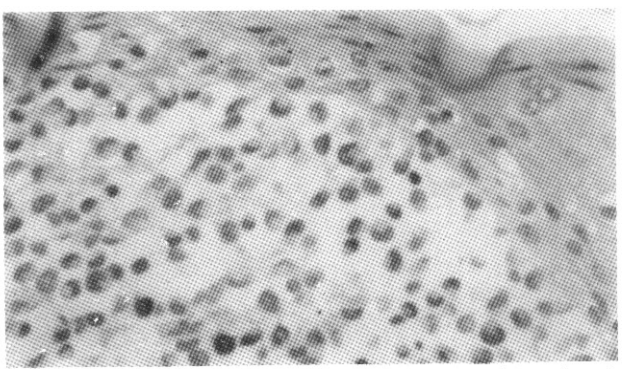

Fig. 4. Many histiocytes with kidney-shaped nuclei and multiple mitoses were seen at high magnification (H & E stain, × 400).

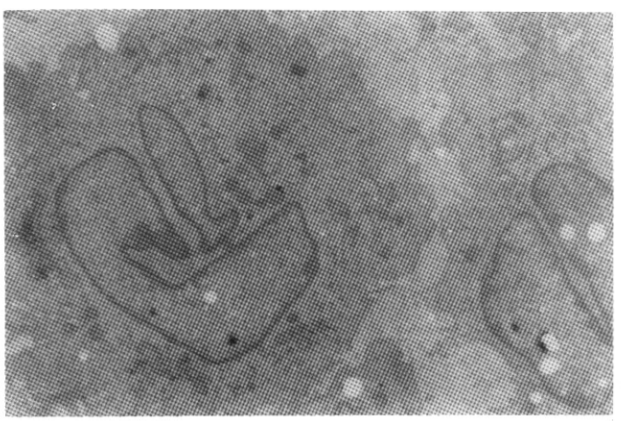

Fig. 5. Kidney-shaped, indented nucleus and abundant cytoplasm of a histiocyte on EM.

A biopsy specimen from her perianal lesion showed destruction and erosion of the epidermis with an inflammatory infiltrate composed mainly of histiocytes, lymphocytes, and eosinophils mixed with other inflammatory cells. Histiocytes with kidney-shaped nuclei, abundant, well demarcat-

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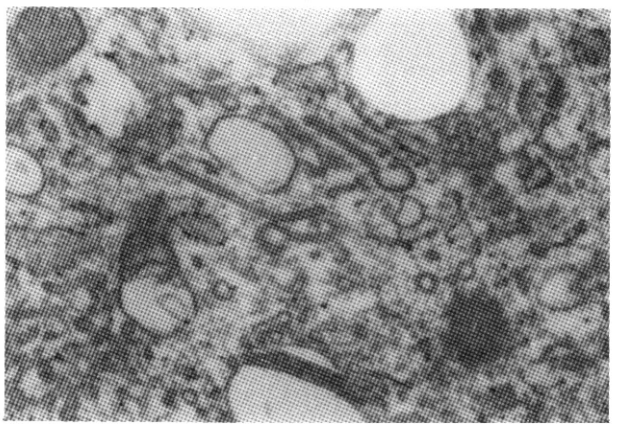

Fig. 6. Multiple tennis racquet-shaped Langerhans' granules consisting of vesicles and rods on EM.

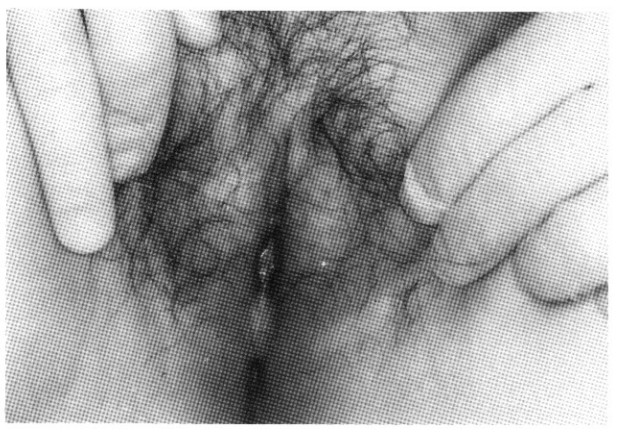

Fig. 7. Remarkable improvement of vulva lesion after external radiation therapy composed of 2000rads.

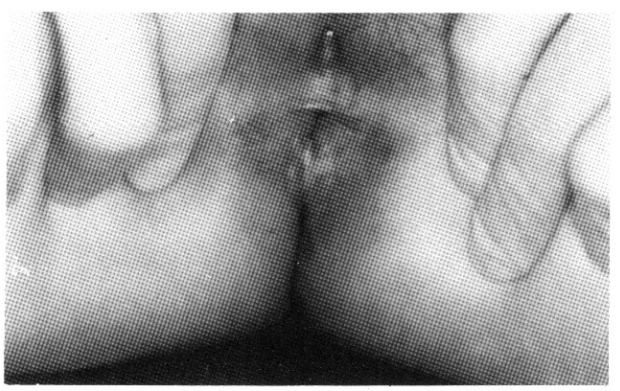

Fig. 8. Remarkable improvement of anal lesion after the same therapy

cated cytoplasm, and multiple mitoses were seen at high magnification (×400) (Fig. 4).

Final diagnosis was confirmed as histiocytosis-X through electron microscopic findings which showed histiocytes with indented nuclei (Fig. 5) and tennis racquet-shaped Langerhans' granules consisting of vesicles and rods (Fig. 6).

She was first treated with systemic prednisolone (40-60mg/day) for 10 days without any improvement, and then external radiation therapy composed of 2000 rads (in ten-200 rad fractions) was applied to her anogenital area with a good response. The lesions, however, recurred in 6 months and again cleared with the same dose of radiation (Fig. 7, 8). Also, 2000 rads (in five-200 rad fractions X2) to the pituitary gland relieved DI symptoms.

DISCUSSION

The etiology of histiocytosis-X remains unkown at present. However, recent studies suggest some immunologic abnormalities, including T-lymphocyte suppressor cell deficiency,[2] and dysgammaglobulinemia and delayed hypersensitivity.

The skin is a major organ of involvement with histiocytosis-X. The cutaneous lesion may be acute or chronic, focal or generalized, and related to the activity of the histiocytic cells. If proliferation of histiocytes is rapid and uncontrolled, infiltration of the skin will be extensive and necrosis of the epidermis may occur with crusting and ulceration. Nodules and papules will result if the histiocytic activity is controlled at a low level of proliferation with focal accumulation of histiocytes. [5]

The cutaneous manifestations were classified by Altman and Winkelman[4] as 1) diffuse, papular, or scaling seborrheic eruptions, 2) petechial, purpuric eruptions, 3) xanthomas, 4) bronzing of the skin, and 5) granulomatous ulcerative lesions.

Ulceration of the skin is a rare, persistent and chronic process usually involving oropharyngeal, axillary, anogenital and intergluteal regions. Histiocytosis-X of the vulva was first reported by Lane and Smith[6] in 1939 in a six-year-old patient with erythematous crusted patches on the vulva and scalp as well as exophthalmos and multiple skeletal lesions. In our case, chronic, persistent, oozing granulomatous ulcerations were noted. The severity of the disease depends upon the organ systems involved which are mainly the liver, spleen, lung, bone, lymph nodes, teeth, pituitary gland, and skin. The

physical examination and past history also revealed symptoms and signs thought to be related with involvement of multiple organ systems. These were simple goiter, otitis media, spontaneous pneumothorax, pulmonary lesions with a honeycomb appearance, interstitial lung fibrosis, thickening of the pituitary stalk, DI symptoms, and amenorrhea.

Therapeutic alternatives include symptomatic, surgical or radiation therapy, as well as local or systemic steroids and chemotherapy. More recently, immunotherapy has been used.[7] The chemotherapeutic agents most commonly used for systemic histiocytosis-X include prednisolone, vinblastine, and 6-mercaptopurine alone or in various combinations.[7] In our case, poor responsiveness to prednisolone led us to treat with radiation therapy. She responded excellently to all courses of radiation. However, the lesions used to recur several months after completion of each therapy. This tendency was consistent with the clinical observations made by Borglin et al.[8]

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