# A Case of Langerhans Cell Histiocytosis in an Adult

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**Langerhans cell histiocytosis(LCH) is a reactive disease in which abnormal Langerhans cells accumulate in various body sites and cause damage to affected organs. LCH usually occurs in children but can also affect adults although rarely. LCH in a case of 65-year-old man initially involved the lymph nodes(left supraclavicular and right inguinal area) and pelvic bone, and eight months later cutaneous involvement was noted. The skin lesions were waxy papules with crust on the anterior chest. The histologic examination of a biopsy specimen from the waxy papules showed that the dense infiltrate, predominantly of histiocytes, was present in the dermis. Immunohistochemistry for S-100 protein showed positive staining and electron microscopy disclosed Birbeck granules, which is characteristic findings of Langerhans cells.**
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*Key Words* : Langerhans cell histiocytosis, Old age, Lymph nodes

Langerhans cell histiocytosis(LCH) consists of closely related diseases characterized by proliferation of Langerhans cells with involvement of the skin, bones, lungs, nervous system, and other internal organs.

LCH is primarily a disease of childhood, but adulthood onset has also been reported[1,2]. Letterer-Siwe disease, the acute disseminated form, begins within 6 months of a patient's life in one third of the cases and before 2 years of age in most of the other cases. Hand-Schüller-Christian disease, the chronic multisystemic form, occurs between the second and sixth decade of life in 70% of cases and before the age of 30 in 91%. In less than 4% dose it occur after the fifth decade[3]. Eosinophilic granuloma, the localized form, occurs between the third and fifth decades. However, onset after the seventh decade has been reported[4-6].

In our case of LCH, the lymph nodes and bones were initially involved due to old age. Despite systemic chemotherapy and radiotherapy, eight months later, suprasternal lymph nodes involvment and waxy papules on the left anterior chest developed, and the patient died 12 months after the initial diagnosis.

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## REPORT OF A CASE

A 65-year-old man was attended the department of Dermatology in July 1993, complaining of multiple papules on the left anterior chest. Examination revealed skin colored, waxy papules on an erythematous base(Fig. 1). One month later the waxy papules become enlarged with a crust formation. Physical examination revealed irregular, firm, fixed mild tender masses on the left supraclavicular(2x2x2cm) and right inguinal area (5x5x3cm). There was no hepatomegaly and splenomegaly. The lungs were clear to auscultation and percussion. The following studies were normal or negative : complete blood cell count, urinalysis, VDRL, liver function test, thyroid function test, EKG, chest and skull roentgenograms, barium examination of the gastrointestinal tract, and scan of liver and spleen. Fasting blood sug-

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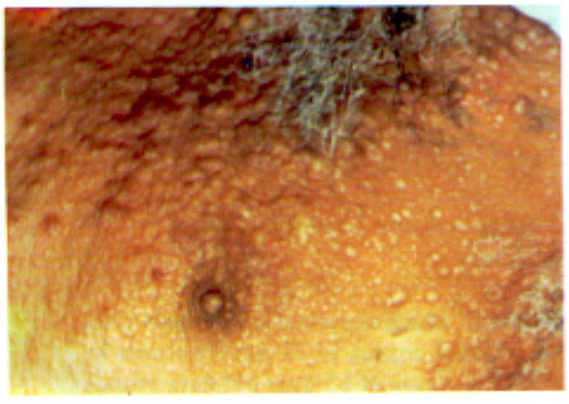

Fig. 1. Various sized waxy papules on an erythematous base on the left anterior chest.

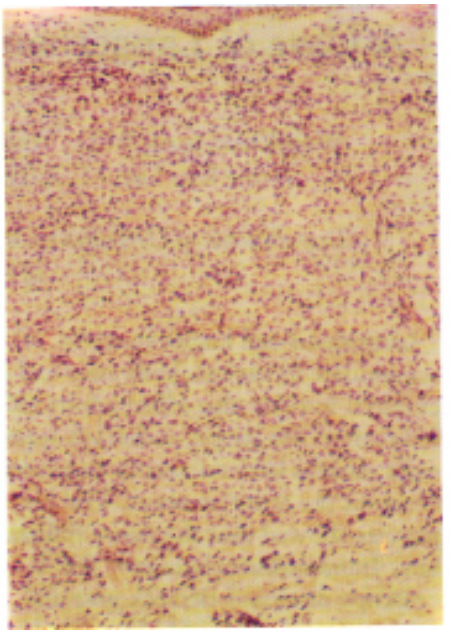

Fig. 2. There were extensive aggregates of histocytes in the dermis(H & E stain, ×100).

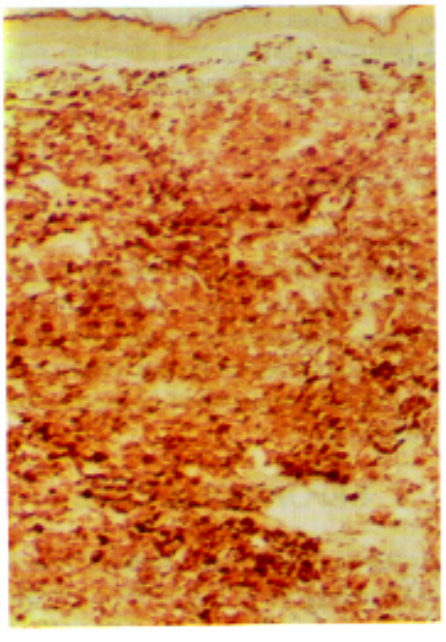

Fig. 3. Immunoperoxidase staining with anti S-100 antibody demonstrates strong reaction in histiocytes (S100, ×100).

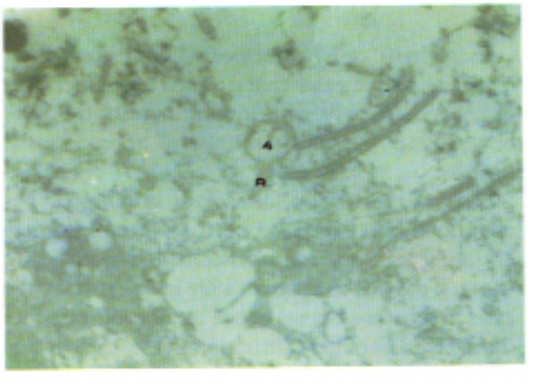

Fig. 4. Electron microsopy showing Birbeck granules consisting of a vesicle(A) and a rod(R).

ar was 200.4mg/dl(normal range, 70-110mg/dl), alkaline phosphatase 141.7IU/L(normal range, 39-117IU/L), CEA 6.77ng/ml(normal range, below 2.5ng/ml). Roentgenographic studies, including tomograms of the cervical, abdomen, and pelvis, showed bony destruction in the right iliac wing, and lymph nodes enlargement in the left transverse cervical chain, retroperitoneal space, and right inguinal region.

A biopsy specimen from a waxy papule revealed dense infiltration in the dermis. The infiltrate showed extensive aggregates of histiocytes. In addition, some lymphocytes and foam cells were found. The histiocytes appeared as large, round cells with abundant, slightly eosinophilic cytoplasm. The nuclei were eccentric in location and indented or reniform. The epidermis was thin and flat. The infiltrate had not invaded the epidermis(Fig. 2). Immunohistochemistry for S-100 protein showed positive staining(Fig. 3) and electronmicroscopy disclosed typical cytoplasmic racket-shaped Birbeck granules(Fig. 4).

Eight months ago the patient was admitted to the department of oncology for evaluation of masses on left supraclavicular and right inguinal area. The cytologic features of fine needle aspiration showed a large number of polygonal cells with abundant pale blue cytoplasmic and elongate nuclei with longitudinal groove. Mitotic figures were absent. Hematoxylin-eosin-stained from the left supraclavicular and right inguinal lymph node showed massive sinusoidal infiltrate of benign-appearing histiocytes. The histiocytes had fairly abundant, pale, eosinophilic cytoplasm and vesicular nuclei with indentation of nuclear membranes, which resulted in the characteristic reniform, grooved vesicular nuclei. Mitosis and phagocytic activity were absent. Immunohistochemical stains for S-100 protein showed positive. Electronmicrographs demonstrated intracytoplasmic tubular inclusions identical to Langerhans cell granules. After the diagnostic tests had been carried out, treatment with CVB(cisplantin, vinblastin, bleomycin in combination), CHOP(cyclophosphamide, PDL, oncovin, adriamycin in combination), and PROMACE-CYTABOM (cystarabine, bleomycin, vincrisitin, MTx, Leucovorin in combination), was given for 8 months, and the patient received 2500 rads of radiotherapy in 10 weeks, but this failed to achieve any significant resolution of the lymph node enlagement. He died 12 months after the diagnosis.

## DISCUSSION

LCH is a proliferation of Langerhans cells that usually occurs in children. Because LCH rarely occurs in old age, the diagnosis might frequently be missed by clinicians. The cause is unknown. However, recent studies suggest some immunologic abnormalities, including T-lymphocyte suppressor deficiency, and dysgammaglobulinemia and a failure of DTH(delayed type hypersensitivity) senstization.

LCH is characterized clinically by various combinations of systemic and cutaneous manifestations[7,8]. Letterer-Siwe disease is usually the most severe and often terminates fatally within several years of onset[1,9]. Hand-Schüller-Christian disease is the slowly progressive form and its classical triad consists of bone defects(especially the skull), exophthalmos, and diabetes insipidus. The initial manifestations are frequently diabetes inspidus, chronic otitis media, or skin involvement. Bone lesions are the most frequent manifestations(80% of the case), whereas hepatomegaly and lymphadenopathy are rare[1,3,9-12]. Eosinophilic granuloma is the monosymptomatic form and cutaneous lesions are rare. The course is chronic, but the prognosis is good because the disease responds well to treatment. Lymph nodes involvement may be the first sign of the disease. There is usually a single bone lesion which may go undetected unless there is a spontaneous fracture. About two-thirds of lymph node lesions are solitary and one-third are associated with evidence of skeletal involvement, usually in close proximity to the involved nodal group[9-12]. This classification is currently generally accepted despite the frequent clinical and histologic overlap of the syndromes, which may be difficult to classify.

Adults with LCH may have different clinical and histologic findings than children. The eruption commomly involves the seborrheic areas of the body(trunk, groin, axilla, scalp) in children and adults[13,14]. Although these areas are rich in adnexal structures, adnexal involvement in children with LCH has only rarely been mentioned in the literature[10,13]. In contrast, the periadnexal infiltrate has usually been in adults[5]. Xanthoma[13], granuloma annulare-like appearance[6], and localized skin ulcers[10] have been reported in adults. The histologic examination of the skin biopsy specimen from our patient showed that the infiltrate was found in the dermis, but periadnexal infiltrate could not be seen. The infiltrate was composed predominantly of histiocytes surrounded by some lymphocyte and foam cells. Mitotic figures were absent. Immunohistochemistry for S-100 protein showed positive staining and electronmicroscopy allowed a definite diagnosis as the classic Birbeck granules were identified.

The cytologic pattern of LCH appears to be characteristic and, when coupled with immunohistochemical and electronmicroscopic study of material obtained by aspiration may be diagnostic[15-17]. But, Leyfield[17] had reported that aspiration cytologic diagnosis may not be appropriate for the initial diagnosis of LCH but may be useful in establishing the extent or recurrence of the disease.

Previous studies attempted to determine a patient`s prognosis. Some authors have reported

that histologic appearances can differentiate the more benign types of illness from the more malignent, the former having mixtures of eosinophils and histiocytes and the latter having diffuse histiocyte infiltration[18]. In contrast, most studies found that the prognosis was dependent on the extent of organ involvement, not histologic features[9]. Recent studies of patients with LCH have shown that the intensity of PCNA(proliferating cell nuclear antigen) staining correlates with prognosis and is more prominent in aggressive disease. Because PCNA staining occurs during several stages of the cell cycle, positive staining more accurately correlates with a growing cell papulation than with the mitotic rate[5].

Therapeutic alternatives include symptomatic, surgical or radiation therapy, as well as local or systemic steroids and chemotherapy. More recently, immunotherapy has been used. Common therapy regimens for multisystem disease include prednisone, vinblastine, 6-mercaptopurine, epipodophyllotoxin etoposide, or methotrexate given as single agents or in combination for 3 to 6 months. Cyclophospamide, chlorambucil, and anthracyclins needs to be given with great caution in non responding patients as salvage therapy because of their potential carcinogenic properties[19-23].

In our case, poor responsiveness to systemic chemotherapy(cisplantin, vinblastin, bleomycin, cyclophosphamide, adriamycin, PDL, oncovin, cystarabine, vincrisitine, MTx, Leucovorin in various combination), led us to treat the patient with radiation therapy, but without any improvement. Our patient died 12 months after diagnosis despite aggressive chemotherapy and radiotherapy.

Our case of LCH is unusual, because LCH rarely occurs in adults. We think that our patient was eosinophilic granuloma which(initially involved the lymph nodes and bone without any skull defect, exophthalmos, and diabetes inspidus). Although previous reports of eosinophilic granuloma have described infrequent cutaneous involvement and a benign course, our case showed cutaneous involvement and poor prognosis.

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