

light induces excretion of higher amounts of 5-S-cysteinyl-dopa in Caucasians (10). The present investigation demonstrates the need for further analysis of genetic influence on the 5-S-cysteinyl-dopa excretion, and illustrates the importance of 5-S-cysteinyl-dopa as a melanocyte metabolite also in humans born dark.

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A Study of Sézary Cells in Peripheral Blood and Skin Lesions

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Abstract. A patient with Sézary syndrome is presented. By phase contrast and scanning electron microscopy Sézary cells were demonstrated in peripheral blood and in skin tissue. Investigation of atypical mononuclear cells seen in the peripheral blood showed that these cells lack receptors for sheep erythrocytes, C3 and Fcγ. Similarly, an examination of dermal mononuclear cell infiltrates showed that most of the cells lack receptors for sheep erythrocytes, C3 and Fcγ.

Key words: Lymphoma; Sézary cell; Surface Markers

The Sézary syndrome is characterized by exfoliative erythroderma, severe pruritus and atypical mononuclear cells in the peripheral blood, so-called Sézary cells, which were originally considered to be giant histiocytes (5). However, in 1971 Crossen et al. (2), presented evidence for the lymphocytic origin of these cells. The cells are characterized by convoluted cerebriform nuclei, variability in size (large and small variants), and a prominent network of cytoplasmic fibrils (9). Furthermore, it has been shown that the Sézary cell has properties similar to the T-lymphocyte (9, 10).

In the case presented, Sézary cells with unusual mitogenic responsiveness and surface properties are reported.

CASE REPORT

An 81-year-old man was admitted to the Department of Dermatology with generalized eczema. The disease

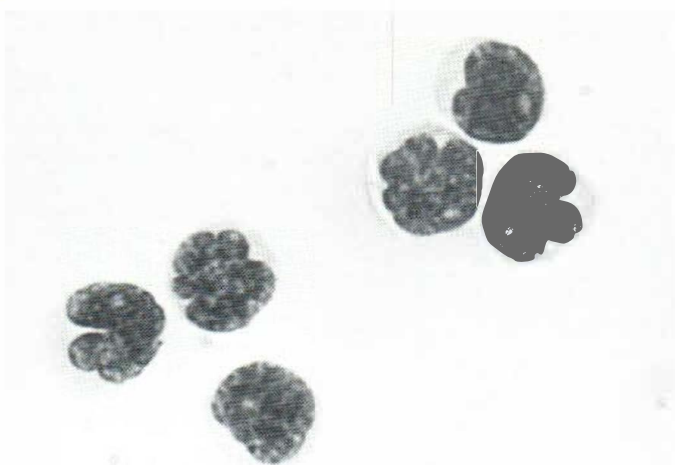


Fig. 1. Peripheral blood smear. Lymphocytes with irregular, cleft nuclei. Stained with May-Grünwald-Giemsa, $\times 1360$.

started 12 years ago with eczematous eruptions on the hands, followed by similar lesions on the face and neck, gradually developing into a generalized erythroderma. During the 2 to 3 years prior to admission, the patient suffered from a severe pruritus, but his general health remained unaffected.

On admission, the skin was erythematous, excoriated and hyperpigmented. He presented a total alopecia, bilateral ectropium, chronic conjunctivitis and blepharitis. There were slightly enlarged non-tender and non-adherent lymph nodes in the cervical, axillary and inguinal regions. The liver was palpable just below the right costal margin and the spleen was palpable about 6 cm below the left costal margin.

Laboratory Data

Hemoglobin 11.9 g/dl, red blood count 3.9×10^{12} l, sedimentation rate 21/30 mm/h, white blood count 21.3×10^9 l with a lymphocytosis of 74%. Seventy per cent of the

lymphocytes had an irregular, cleft nucleus (Fig. 1). Bone marrow showed normal myelopoiesis and erythropoiesis. Serum electrolytes, uric acid, alkaline phosphatase, γ -glutamyltransferase, alanin aminotransferase, bilirubin, fasting blood sugar, Waaler's reaction and the serum levels for immunoglobulin, C3, C4 and C1-esterase inhibitor were all within normal limits. The antinuclear factor was not demonstrated. Several cultures for acid-fast bacilli of the urine were repeatedly negative. Retrograde lymphangiography showed slightly enlarged lymph nodes along the arteriae iliaca and the aorta. Scintigraphic examination showed an enlarged spleen, but the liver was found normal.

Histological Examination

Several biopsies taken from different lesions of the skin exhibited a rather uniform picture. The epithelium showed acanthosis, elongation of the rete ridges and occasional exocytosis of lymphocytes into the epidermis. Focal in-



Fig. 2. Skin section. Acanthosis, elongation of the rete ridges and focal infiltrates of lymphocytes in the upper dermis. Stained with hematoxylin-eosin, $\times 72$.

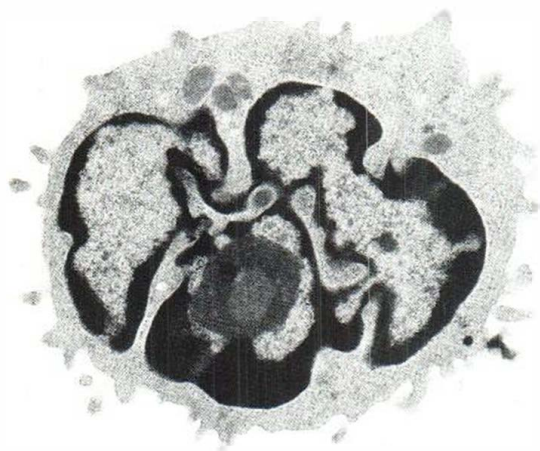


Fig. 3. Electron micrograph of Sézary cell showing highly convoluted nuclei and chromatin condensation at nuclear membrane. Nucleocytoplasmic ratio is high. $\times 13\,520$.

filtrates of lymphocytes were found in the upper dermis and perivascularly (Fig. 2). No enlarged or atypical cells were seen.

Study of Mononuclear Cells in Peripheral Blood and in Skin Biopsy Specimens

Mononuclear cells were separated from heparinized blood by the Ficoll-Isopaque centrifugation gradient (Lymphoprep, Nyegaard & Co., Oslo). Phase contrast and electron microscopy showed that the mononuclear cell suspension contained Sézary cells (Figs. 3 and 4). Fourteen per cent of the cells formed rosettes with 2-aminoethylisothio-uronium bromide (AET)-treated sheep erythrocytes (4) (normal mean 72%). Fc γ and C3 receptor-bearing cells were detected by the rosette assay previously described (3, 6). Receptors for Fc were found on 13% of the cells (normal mean 24%) and receptors for C3 were found on 6% (normal mean 25%). Direct immunofluorescence using a polyvalent fluorescein isothiocyanate-conjugated rabbit antihuman immunoglobulin serum (Dako immunoglobulins A/S, Copenhagen) showed that less than 1% of the cells had membrane-bound immunoglobulins. The mononuclear cells did not adhere to glass, nor phagocytize latex particles, whereas monocytes from normal blood donors do. Similar results were obtained when cells cultured overnight at 37°C in Eagle's medium supplemented with 10% foetal calf serum. L-glutamine and gentamycin (50 μ g/ml) were tested. The cells either did not respond at all or else showed only a weak response to an *in vitro* stimulation with mitogens (PHA, PWM and Con A), using the technique described by Steel & Creasy (8). Scanning and transmission electron microscopy of biopsy specimens from skin lesions showed that the majority of the mononuclear

cells in the upper dermis were the same morphologically as Sézary cells.

Cryostat sections of lesional skin tissue specimens were examined for receptors for AET-treated E (T-lymphocytes) and for the complement components C3b (B-lymphocytes and macrophages) and C3d (B-lymphocytes). The indicator cells were applied using a closed chamber techniques as described previously (7). The results were estimated by the capacity of the mononuclear cells to absorb the different indicator cells. Some cells absorbed EAC3b (Fig. 5), and only a few absorbed EAC3d and E.

DISCUSSION

The diagnosis of Sézary syndrome in our patient was based on the clinical picture and also on the presence of atypical mononuclear cells in the peripheral blood (10). The lack of surface immunoglobulin receptors for C3 and Fc γ and the lack of phagocytic and adhesive properties are consistent with the findings that Sézary cells are not of a B-lymphocytic or monocytic origin. This accords with data reported by others (9). Most investigators have found that the Sézary cells form rosettes with sheep erythrocytes and are stimulated by mitogens *in vitro* (9). Consequently, the disease is considered to be a T-cell neoplasia. This does not agree with the findings in our patient. Here the Sézary cells did not form rosettes with sheep erythrocytes nor did the cells respond to stimulation by mitogens. These

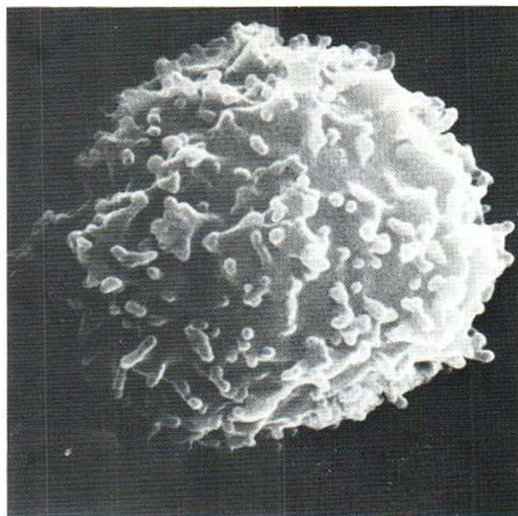


Fig. 4. Scanning electron micrograph of Sézary cell covered with short microvilli. $\times 16\,000$.

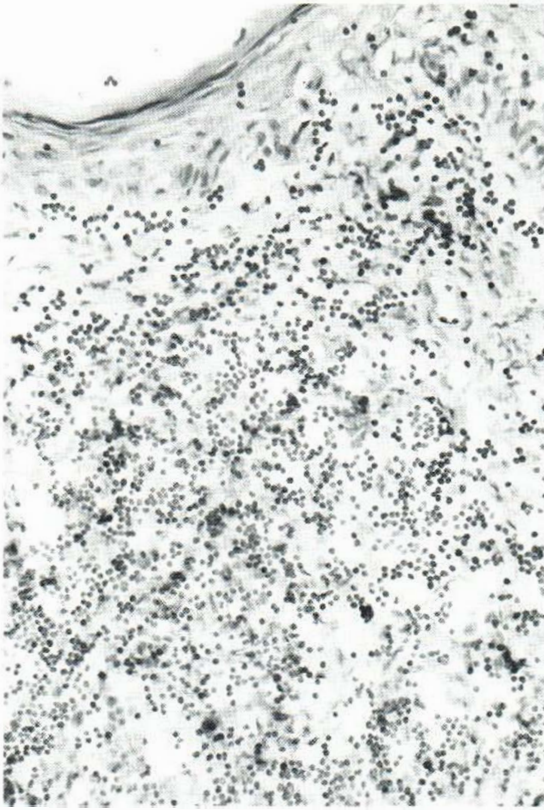


Fig. 5. Skin section showing adherence of EAC3b indicating macrophages and B-lymphocytes. Stained with benzidine and hematoxylin-eosin, $\times 250$.

data are in line with the results reported by Braylan et al. (1).

In the skin, the lymphocytic infiltration showed a focal distribution in the upper dermis in contrast to the usual, common band-like involvement. The majority of the mononuclear cells in the dermis lacked receptors for C3, Fc γ and sheep erythrocytes. Furthermore, electron microscopy showed these cells to be similar to the atypical mononuclear cells seen in the peripheral blood. These results suggest that the Sézary cells in the peripheral blood and in the dermis are of the same cell type. Although most investigators have presented evidence for the T-lymphocytic nature of the Sézary cell, findings made with our patient strongly suggest that Sézary cells have dissimilar characteristics from patient to patient. Presumably the Sézary cells proliferate from cell populations at various stages of cell maturation, resulting in Sézary cells with differing

characteristics, dependent on the stage of maturation.

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Antinuclear Antibodies during Puva Therapy

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Abstract. During PUVA therapy 7 patients out of 34 with severe psoriasis developed circulating antinuclear antibodies (ANA) (21%). Before treatment only 3 patients of 50 (6%) considered for PUVA had detectable ANA.