The Ultrastructure of an Abnormal Cell in Sézary’s Syndrome

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Sézary1 described a syndrome manifested by edematous and pigmented erythroderma, leonine facies, lymphadenopathy, and abnormal circulating cells. He considered these abnormal cells to be giant histiocytes which probably originated in the skin, then entered the circulating blood, creating a leukemic state.

In this report, the ultrastructural features of the Sézary cell in peripheral blood, lymph nodes, and skin from three patients with Sézary’s syndrome are described.

Materials and Methods

Materials

Skin, lymph nodes, and buffy coat preparations were examined with the light and electron microscope from three patients with Sézary’s syndrome. One patient was a 50 year old woman with a peripheral leukocyte count of 30,000/mm.³ and 50 to 75 per cent Sézary cells; the second was a 54 year old woman with a peripheral leukocyte count of 6,000/mm.³ and 10 to 20 per cent Sézary cells; the third was a 48 year old man with a peripheral leukocyte count of 16,000/mm.³ and 5 to 10 per cent Sézary cells.

Normal blood, blood from patients with chronic lymphocytic leukemia, a lymph node from a patient with Hodgkin’s disease, and skin from a variety of benign and neoplastic cutaneous lesions were studied as controls.

Methods

Tissue was fixed in 6 per cent phosphate-buffered glutaraldehyde for two hours, then post-fixed in 1 per cent phosphate-buffered osmium tetroxide, dehydrated in upgraded alcohols, and embedded in Epon. 1 μ, semithin sections for light microscopy were stained with Azure II. Thin sections for electron microscopy were stained for 15 min. at 60 C with 3.5 per cent aqueous uranyl acetate and for 1 min. at room temperature with lead citrate.2

Leukocyte pellets from peripheral blood were prepared by either of the following two methods:

1. Ten cc. of heparinized blood was pipetted into 1 cc. plastic tubes and centrifuged at 2,000 rpm for 10 min. Plasma was removed and a small cylinder of tube containing the buffy-coat was cut away with a razor blade and placed in the fixative. After one-half hour in glutaraldehyde, specimens had hardened so that they could be successfully separated from the plastic tube. After two hours in glutaraldehyde, the processing continued as described above.

2. The second method employed was that described by Anderson.3

Peripheral blood films were prepared by standard methods.

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Figs. 1–3.—Light micrograph. Peripheral blood films from patients with Sezary's syndrome. Characteristic Sézary cells are shown with nuclei which appear cerebri-form with overlapping clefts and folds. Wright's stain. Approximately 1,400 X.

Fig. 4.—Electron micrograph. Portion of a buffy coat pellet from a patient with Sézary's syndrome. Four characteristic Sézary cells are shown. A nucleolus (N) is present in two of the cells. Nuclei are strikingly irregular, serpentine, indented, and lobulated. The nuclear pattern is heterochromatic with nuclear particles concentrated at the nuclear membrane. Mitochondria can be seen in the cytoplasm. Uranyl and lead stained. Approximately 8,000 X.
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Fig. 5—Electron micrograph. A portion of a characteristic cell from the peripheral blood of a patient with Sézary's syndrome. The nucleus of this cell is drawn into narrow ribbons (arrows) consisting of single or double row of nuclear particles and nuclear membranes. Uranyl and lead stained. Approximately 30,000 X.

RESULTS

Blood

The Sézary cell is easily identifiable in peripheral blood films (Figs. 1–3). The nucleus appears cerebriform with overlapping folds and clefts. Occasionally, cytoplasmic vacuoles or granules are seen. By electron microscopy, the nucleus of the Sézary cell appears serpentine with lobulations and indentations, often interconnected by narrow bridges composed of rows of dense nuclear particles and nuclear membranes (Figs. 4 and 5). The nucleus appears heterochromatic with dense particles concentrated at the nuclear membrane. Nucleoli occur in some planes of section. The cytoplasm of these cells contain mitochondria, ribosomes, polysomes, and small amounts of endoplasmic reticulum. In addition, the cytoplasm may contain aggregates of glycogen particles (Fig. 6) and an occasional electron-dense granule (Fig. 7).

Sézary cells could be recognized using the light microscope in one micron, semi-thin, plastic-embedded specimens of buffy-coat preparations (Fig. 8).

Skin

Sézary cells, identical to those seen in the blood, could be recognized in the skin of all three patients. In the epidermis, Sézary cells were found singly or in large aggregates surrounded by elongated keratinocytes (Fig. 9) (Pautrier's microabscesses). In the dermis, plasma cells, lymphocytes, and histiocytes could be recognized along with Sézary cells.

Lymph Nodes

Sézary cells were found in axillary lymph nodes from all three patients (Fig. 10). Lymphocytes, plasma cells, reticulum cells, and histiocytes could also be recognized in these nodes.

A Sézary cell is diagrammatically represented in Figure 11.
Fig. 6.—Electron micrograph. Portion of a Sézary cell from the peripheral blood of a patient with Sézary's syndrome. An aggregate of glycogen granules is seen in the cytoplasm (arrow). Uranyl and lead stained. Approximately 20,000 X.

Fig. 7.—Electron micrograph. Portion of a characteristic Sézary cell from the peripheral blood of a patient with Sézary's syndrome. Mitochondria, ribosomes, polysomes, and a dense granule (G) are present in the cytoplasm. Uranyl and lead stained. Approximately 22,000 X.

Control Studies
No cells resembling Sézary cells were found in any of the control tissues examined.

Discussion
Sézary\(^1\) was the first to describe a syndrome manifested by erythroderma and characteristic circulating cells. He described these cells as having strikingly irregular nuclei . . . "a sprouting appearance . . . sending out finger-like processes," and found these cells in skin and lymph nodes as well as in the blood. The syndrome and its characteristic cell bear Sézary's name.

In this study, the electron microscope has been used to characterize the ultrastructural features of the Sézary cell in blood, skin, and lymph nodes. The nucleus is bizarre—lobulated, indented, and serpentine, often narrowed to a single row of nuclear particles, and resembles somewhat the nucleus of the histiocyte or macrophage which may have several deep indentations.\(^4\) However, the cytoplasm of the histiocyte and macrophage contain many large dense granules and phagocytic vacuoles which are not present in the Sézary cell.

The nucleus of the lymphocyte has a round contour or a single deep notch and can be easily distinguished from the Sézary cell. The nucleus of the monocyte may have several deep indentations, but it is not serpentine and does not have narrow nuclear bridges. Lobulations and interconnecting bridges of the
Fig. 8.—Light micrograph. Portion of a buffy coat pellet prepared from the peripheral blood of a patient with Sézary’s syndrome. (1 μ semi-thin, plastic section, Azure II stained.) Sézary cells with irregular, lobulated nuclei can be recognized (arrow). Approximately 1,200 X.

Fig. 9.—Electron micrograph. Pautrier’s microabscess in the epidermis of a patient with Sézary’s syndrome. Sézary cells (arrows) with indented, irregular nuclei lie within a dilated space surrounded by elongated keratinocytes (K). Uranyl and lead stained. Approximately 3,000 X.
neutrophil nucleus may be mistaken for the Sézary cell nucleus, but the characteristic cytoplasmic granules of the neutrophil are an unmistakable, identifying feature. Since knowledge at present is limited, the cell(s) of origin of the Sézary cell must be considered unknown.

No abnormalities could be recognized in the cytoplasm of the Sézary cell. PAS-positive, diastase-soluble granules\textsuperscript{5} and PAS-positive, diastase-resistant granules\textsuperscript{6} have been reported in Sézary cells. These may correspond respectively to the glycogen aggregates and electron-dense granules described above. However, granules do not seem to be a characteristic feature of the Sézary cell.

Tanaka and Brecher\textsuperscript{7} have also observed abnormal cells in Sézary patients, with ultrastructural features similar to those described here.

We have found cells similar to Sézary cells in tissues of patients with mycosis fungoides.\textsuperscript{8,9} However, in mycosis fungoides, nuclear irregularities are less bizarre and the cells are found less frequently. In view of many common features, it may be that Sézary's syndrome is a leukemic phase of mycosis fungoides.\textsuperscript{5,9}

None of the control tissues examined to date revealed an abnormal cell similar to that described here.

**Summary**

Sézary described a characteristic cell found in a syndrome which bears his name. This syndrome is manifested by erythroderma, lymphadenopathy, and
Fig. 11.—Schematic diagram of a Sézary cell. The nucleus has a circular outline, but is lobulated and cerebriform, composed of highly convoluted folds. On the “cutaway” surfaces, the sectioned nucleus appears serpentine, composed of irregular ribbon-like strands.

abnormal circulating cells. The electron microscope was used to study skin, lymph nodes, and blood from three Sézary patients and all demonstrated characteristic cells. The nucleus of this Sézary cell was strikingly irregular, indentated, lobulated, and serpentine, often narrowed to a single row of nuclear particles. The cytoplasm exhibited no abnormalities. No abnormal cells similar to those described have been found in any control tissues studied.

SUMMARIO IN INTERLINGUA

Sézary ha describite un cellulas characteristic trovate in un syndrome que porta su nomine. Iste syndrome se manifesta per erythroderma, lymphadenopathia, e cellulas anormal in le circulation. Le microscopio electronic esseva usate in studiar le pelle, nodos lymphatic, e sanguine ab tres patientes con le syndrome de Sézary, e omne le tres habeva ille characteristic cellulas. Le nucleo del cellula de Sézary in iste casos esseva frappantemente irregular, indentate, lobulat, e serpentiniforme, frequentemente restringite a un sol serie de partículas nucleari. Le cytoplasma exhibiva nulle anormalitates. Nulle anormal cellulas simile al describites esseva trovate in ulle del tissus de controlo studiate.

REFERENCES


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