Ropalocytosis in acute leukemia

L. Skinnider

Department of Pathology, University of Saskatchewan, University Hospital, Saskatoon (Saskatchewan, Canada S7N OW8), 29 November 1976

Summary. Unusual club-shaped processes have been seen in the lymphoblasts in the peripheral blood of case of untreated acute leukemia. These arose from a single area of the cell surface and appeared identical to the morphologic change seen in ropalocytosis in red cells. Red cells in the peripheral blood were also affected.

Ropalocytosis is the name given to the formation of numerous branched and unbranched club-shaped processes in red cells and their precursors and has been found in a variety of conditions[1–4]. It has not been reported as occurring in other haemopoietic cells. Recently during the ultrastructural study of the peripheral blood obtained before treatment of a 10 year old child with acute lymphoblastic leukemia, a similar abnormality was noted in the leukemic blast cells.

Materials and methods. The material was obtained from the peripheral blood of the child prior to treatment. The peripheral blood count was 24,000/mm^3 with 90% blasts. There was nothing unusual in the presentation or course of the leukemia except that lymph node enlargement was more prominent than the average. For light microscopy Wright-Giemsa stain was used. For ultrastructural studies the cells from leucocyte rich plasma were fixed directly in ice-cold 2% gluteraldehyde, postfixed in 2% osmium tetroxide buffered with cacodylate, then dehydrated in increasing concentrations of alcohol, cleared in propylene oxide and embedded in epoxy resin. Ultrathin sections were stained with uranyl acetate and lead hydroxide and examined with the electron microscope (Zeiss EM 9-S).

Results and discussion. Small foci of club-shaped processes were seen in the leukemic blast cells (figure 1). The percentage of affected cells as judged by the 1 μm sections and the electron microscope appeared to be about 5–10% but as the affected areas are quite focal actual percentage may be greater. There was never more than one such focus to a single cell and only a small area of the cell surface seemed so affected. The processes usually contained cytoplasm but in some vacuole formation was seen at the bulbous ends (figure 2). Some erythrocytes and reticulocytes were also affected (figure 3).

The significance of these morphological changes is obscure but review of certain previous observations and study of the effects of the cytochalasins on mammalian cells suggest that an alteration in the microfilament structure of the cell may be implicated. Our own observations (unpublished) and illustrations in the reports of others[5–7] show that club-shaped processes of similar morphology are sometimes seen in cells exposed to cytochalasin B or cytochalasin D. The description of 'complex, knobbed structures presenting a flower like configuration'[7] indicates the similarity between these changes and the ones found in the leukemic blasts in this case. Similar appearances to ropalocytosis have been seen in red cells after denucleation[8] and presumably for denucleation to occur in a cell some temporary alteration of the microfilaments network might be expected. It is interesting to note that the cytochalasins themselves cause nuclear extrusion[9], suggesting a possible common link in the formation of

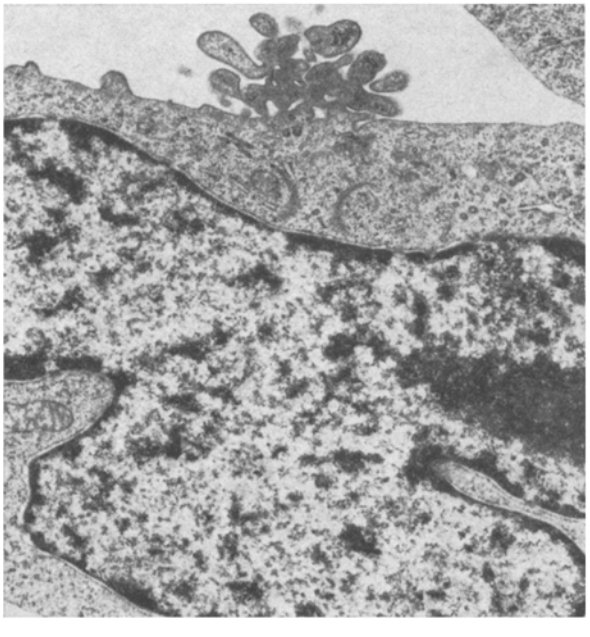

Fig. 1. Small focus of club-shaped processes arizing from the surface of a lymphoblast from the peripheral blood. ×12,000.

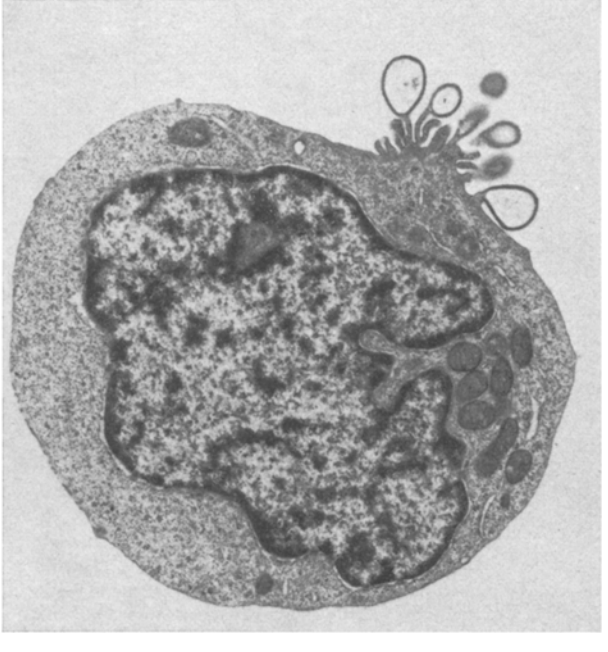

Fig. 2. Lymphoblast from peripheral blood with vacuole formation in the club-shaped processes. ×10,000.

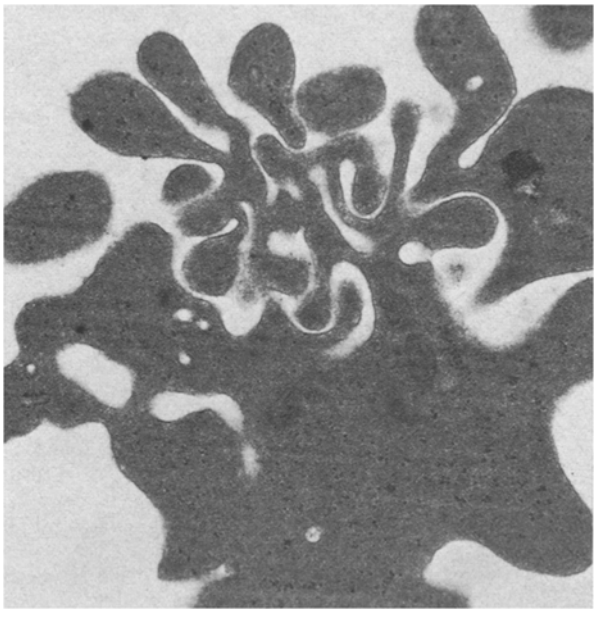

Fig. 3. Marked degree of ropalocytosis in reticulocyte in the peripheral blood. ×20,000.

ropalocytosis in erythrocytes and in cells exposed to the cytochalasins. The fact that this phenomenon has been found in leukemic blasts is more difficult to explain. There was no known exposure to drugs or chemicals prior to obtaining the specimen but some agent in the blood cannot be absolutely excluded. The occurrence of the clear vacuoles in the extremities of the processes is also intriguing. Formation of 'blisters' on cell surfaces is known to occur in malignant cells spontaneously or on exposure to certain agents[10] and formation and release of membrane bound vacuoles has been noted in lymphoblasts exposed to the vinca alkaloids[11], but one cannot say from the static photographs in our case whether the vacuoles have formed in the processes or whether active discharge is taking place.

Whatever the cause may be, it is evidently not the result of degeneration of the cell as both the nuclei and organelles show no evidence of damage. Nor can ropalocytosis be an artefact of fixation in gluteraldehyde as it has been seen in red cells with osmium fixation[2]. The cause may lie in the fact that cell surface alterations occur in malignant transformation and the formation of these club-shaped processes may be an expression of changes occurring in neoplastic cells making them more susceptible to unknown agents in the environment.

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Allergic reactions, cyclic AMP and histamine release[1]

P. Stahl Skov, A. Geisler, R. Klysner and S. Norn

Department of Pharmacology, University of Copenhagen, 20, Juliane Maries Vej, DK-2100 Copenhagen Ø (Denmark), 30 July 1976

Summary. Both isobutylmethylxanthine and theophylline increased the level of cyclic AMP in the mast cell. Theophylline reduced the allergic histamine release, whereas isobutylmethylxynthine caused a pronounced potentiation of the histamine release. This indicates that the hypothesis of an inverse relationship between the level of cyclic AMP in mast cells and histamine release is too simple.

Cyclic AMP is assumed to modulate the release of allergic mediators, i.e. histamine and SRS-A (slow reacting substance of anaphylaxis) from mast cells and basophils in the allergic response. It is claimed that increase and decrease in the level of cAMP in these target cells would suppress and enhance, respectively, the release of histamine and SRS-A. This hypothesis is based on comparisons between the influence of drugs on cAMP level and release of allergic mediators in mast cells, peripheral leukocytes and lung tissue[2-6]. Thus, anti-allergic drugs increase the level of cAMP and concomitantly reduce the release of histamine and SRS-A. Different mechanisms are involved in the augmentation of the level of cAMP: beta-adrenergic agents (e.g. isoproterenol) increase cAMP formation by stimulating beta-adrenergic receptors and methylxanthines (theophylline, aminophylline) inhibit the breakdown of cAMP. Propranolol may promote attacks in asthmatic patients. In fact, this drug shows the reverse effects: a reduced cAMP level by blocking beta-adrenergic receptors and an increased release of allergic mediators[6]. However, this hypothesis of drug-induced alterations of histamine and SRS-A release by changes in cAMP level is as yet unproved.

1 This work was supported by grants from the Danish Medical Research Council (Grant No. 512-5270) and from Lundbeckfonden.
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