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The Acanthocyte-Echinocyte Differential

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Abstract

Acanthocytes are a distinct structural (and functional) entity compared to echinocytes. The differential, however, is not always clear. A summary of morphologic characteristics to make a clear distinction is provided, using the blood of a rare neurologic disease with acanthocytic transformation of red blood cells.

Key words: Acanthocytes; Echinocytes; Chorea-acanthocytosis (ChAc); Neuroacanthocytosis (NA)

Chorea-acanthocytosis (ChAc) is a progressive neurodegenerative disorder correlated with a deformation of the red blood cells (RBCs) called acanthocytosis (from *acantho-* "thorn", "spur cell"). ChAc is part of a clinical syndrome group called *Neuroacanthocytosis syndromes* (NA), first described in 1960 as "Levine-Critchley syndrome" [1]. ChAc is an autosomal recessive choreo-athetoid movement disorder with orofacial dyskinesia and dementia, while the second common clinical disorder of the same group, the *McLeod syndrome* (MLS), is an a X-linked chronic haemolysis with chorea, peripheral neuropathy and myopathy. Other subtypes of the NA include: *pantothenate kinase associated neurodegeneration* (PKAN), *Huntington's disease-like 2* (HDL 2) and the variant *hypoprebetalipoproteinemia acanthocytosis retinitis pigmentosa pallidal degeneration syndrome* (HARP) [2, 3].

Neuroanatomical changes are present in form of extensive neuronal loss and gliosis of the caudatum, the corpus striatum and the pallidum and peripheral axonal neuropathy [4, 5]. The concomitant neuronal degeneration and erythrocyte membrane abnormality may have a common proteic source [6], distinct from the lipidic source of acanthocytes of other aetiologies (M. Anderson, abetalipoproteinaemia, hypobetalipoproteinemia, alcoholic liver cirrhosis, anorexia nervosa) [7]. These abnormalities may reside on defects of the band 3 protein, involved in the regulation of the intracellular pH in neurons and major proteic component in the membrane of erythrocytes. This defect leads to disturbances in various membrane functions: anion transport, anchoring with cytoskeleton, enzyme binding, age-related vesiculation and immune signalling for removal of the old erythrocytes from the circulation [8].

Microscope images of peripheral blood smears, especially scanning electron microscopic ones, are reported as useful tools in investigating NA, while only genetic testing can confirm its diagnosis [4, 9, 10]. Our scanning electron microscopic investigation makes it possible to objectify the morphology of RBC in ChAc in detail, in fact the abnormality of the acanthocytic-transformed erythrocytes is very pronounced, sometimes grotesque. This is an indication that acanthocytes are a distinct structural (and functional) entity compared to echinocytes (from *echino-* "porcupine", "burr cell") [11], a differential which sometimes has been confused.

Summarizing, acanthocytes are deformed red blood cells characterized by few, irregularly distributed spikes ("spiculae") in a blood smear where also echinocytes are present in great quantity. Echinocytes, to the other hand, are characterized by many spiculae regularly distributed on the membrane surface of the erythrocyte, mainly in blood smear without acanthocytes [7]. We could observe the presence of grotesque membrane abnormalities in acanthocytes compared to echinocytes, where the forms of the spiculae are limited to different degrees of the spiny character. Acanthocytic forms, in fact, are determined by a structural pathologic membrane defect [6, 7], whereas echinocytic forms can be caused and reversed by pH-, osmolarity-, biochemical- and even electrical variations [12–15].

This short communication aims to make the readers aware of the potential trap which echinocytes can cause when looking for acanthocytes. This is particularly true in the case of ChAc, which diagnosis, however, relies on clinical investigations and genetic testing, in particular when light- and electron microscopy are not available.

Methods

EDTA-blood sample from an advanced genetically proven Chorea-acanthocytosis (ChAc) clinical case with severe choreo-athetoid movement disorders, orofacial dyskinesia and dementia is fixed in 2.5% glutaraldehyd and stored at room temperature for 24 h in Sörensen solution. After three washing procedure (centrifugation in bidest. H_2O), the solution is dehydrated in increasing concentrations of acetone (20, 40, 60, 80, 95 and 100%; 10 min each), placed on Poly-l-lysine coated 6 mm coverslips and air dried for 2 h. Platin coating was performed with a Balzers SCD 004 sputter coater and visualized with a Scanning Electron Microscope Jeol JSM 840, with 15,0 kV accelerating voltage, magnification 1400x (fig. 1), 6000x (fig. 3) and 35000x (fig. 4), 13000 (fig. 5c), 7500x (fig. 6c). The light-microscopic images (fig. 2, 5a,b, 6a,b) were recorded with a Zeiss Axiovert 200 M, camera Sony DSC-S85, standard preparation and stain [15] from EDTA blood. Control blood was derived from an hepatocellular carcinoma suffering patient.

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Literature

1 Danek A. Neuroacanthocytosis Syndromes, Springer Verlag, 2005: 5–7.
2 Walker RH, Saiki S, Danek A. Neuroacanthocytosis Syndromes, A Current Overview. Neuroacanthocytosis Syndromes II, Springer Verlag, 2008: 3–4.
3 Ichiba M, Nakamura M, Sano A. Neuroacanthocytosis update, Brain Nerve. 2008;60(6):635–41.
4 Hardie RJ, Pullon HW, Harding AE, et al. Neuroacanthocytosis. A clinical, haematological and pathological study of 19 cases. Brain. 1991;114(1A):13–49.
5 Huppertz HJ, Kröll-Seger J, Danek A, et al. Automatic striatal volumetry allows for identification of patients with chorea-acanthocytosis at single subject level. J Neural Transm. 2008;115(10):1393–400.
6 Bosman GJ, Horstink MW, de Grip WJ. Erythrocyte membrane abnormalities in neuroacanthocytosis. Evidence for a neuron-erythrocyte axis. Neuroacanthocytosis Syndromes, Springer Verlag, 2005: 153–60.
7 Perrin J, Georges A, Morali A, et al. Acanthocytes et hypercholesterolemia. Ann Biolo Clin. 2008;66(5):56972.
8 Bosman GJ, De Franceschi L. Neuroacanthocytosis-related changes in erythrocyte membrane organization and function. Neuroacanthocytosis Syndromes II, Springer Verlag, 2008: 133–42.
9 Marson AM, Bucciantini E, Gentile E, Geda C. Neuroacanthocytosis: clinical, radiological and neurophysiological findings in an Italian family, Neurol Sci. 2003;24(3):188–9.
10 Galey WR, Evan AP, Van Nice PS, et al. Morphology and physiology of the McLeod erythrocyte. I. Scanning electron microscopy and electrolyte and water transport properties. Vox Sang. 1978;34(3):152–61.
11 Lichtman M, Bentler E, Kipps TJ, et al. Williams Hematology, 7th ed., McGraw-Hill, 2005:369–82.
12 Reinhart WH, Chien S. Red Cell Rheology in Stomatocyte-Echinocyte Transformation: Roles of Cell Geometry and Cell Shape. Blood. 1986;4:1110–8.
13 Wong P. A Basis of Echinocytosis and Stomatocytosis in the Disc-sphere Transformations of the Erythrocyte, J Theor Biol. 1999;196(3):343–61.
14 Mrowietz C, Hiebl B, Franke RP, et al. Reversibility of Echinocyte Formation after Contact of erythrocytes with various Radiographic Contrast Media. Clin Hemorheol Microcirc. 2008;39(1-4):281–6.
15 Schwarz S, Deuticke B, Haest CW. Passive Transmembrane Redistributions of Phospholipids as a Determinant of Erythrocyte Shape Change. Studies on Electroporated Cells. Mol Membr Biol. 1999;16(3):247–55.
16 O'Connor BH. A Color Atlas and Instruction Manual of Peripheral Blood Cell Morphology, William & Wilkins, 1984: 3–5.

Figure 1

Chorea-acanthocytosis: acanthocytic (A) and echinocytic (E) deformation of RBCs.

Figure 2

ChAc: peripheral blood smear: differentiating echino-/acanthocytes.

Figure 3

ChAc: schizocyte (S), acanthocytes (A) and echinocytes (E) in concomitance.

Figure 4

ChAc: Gross deformation of RBC membrane in acanthocyte.

Figure 5

Echinocyte in control blood: numerous spiculae regularly distributed in living specimen (DIC 945x) (**5a**), standard staining (BF 1000x oil) (**5b**), and Scanning Electron Microscope (**5c**).

Figure 6

Acanthocyte in ChAc: fewer irregularly distributed spiculae, in living specimen (DIC 945x) (**6a**), standard staining (BF 1000x oil) (**6b**), and Scanning Electron Microscope (**6c**).

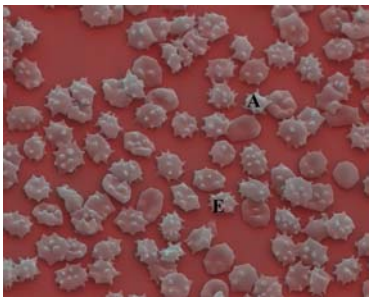

Figure 1

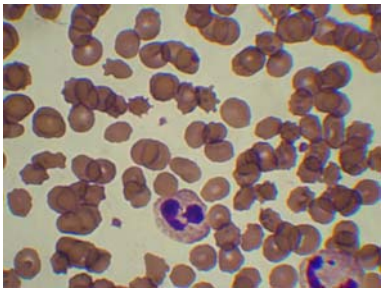

Figure2

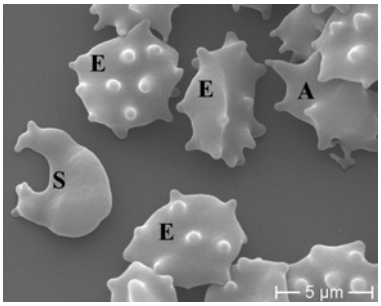

Figure 3

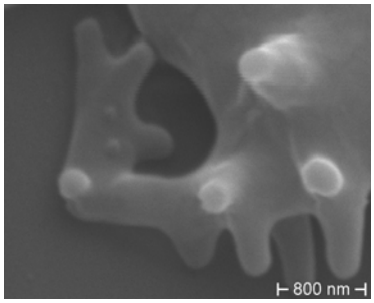

Figure 4

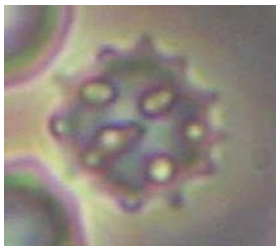

Figure 5a

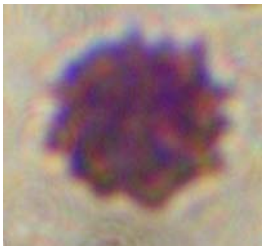

Figure 5b

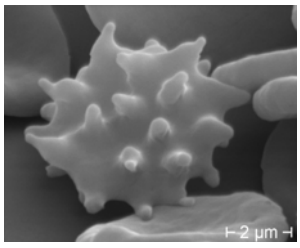

Figure 5c

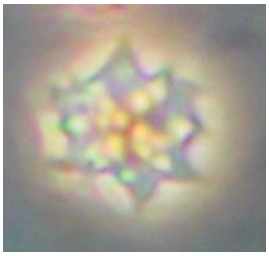

Figure 6a

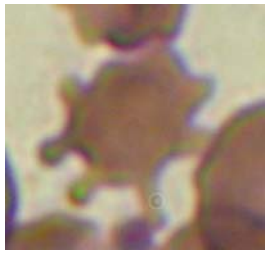

Figure 6b

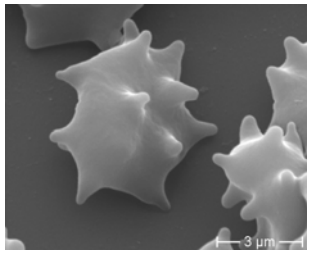

Figure 6c