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The acanthocyte-echinocyte differential

The Example of Chorea-Acanthocytosis

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Summary

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 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 *hypobetalipoproteinemia 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 characterised by few, irregularly distributed spikes (“spiculae”) in a blood smear where also echinocytes are present in great quantity. Echinocytes, to the other hand, are

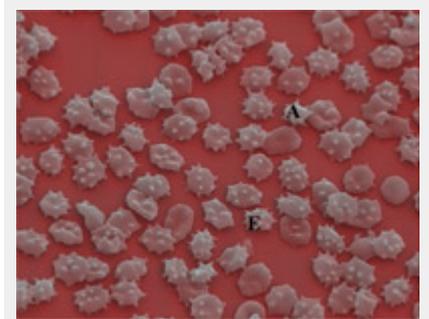


Figure 1

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

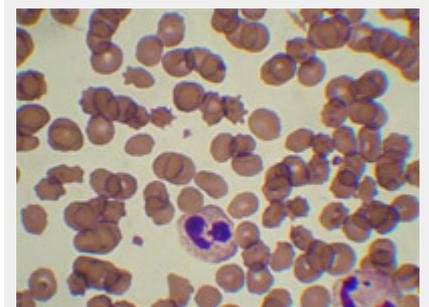


Figure 2

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

characterised 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 Sørensen solution. After three washing procedure (centrifugation in bidest. H₂O), 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 visualised with a Scanning Electron Microscope Jeol JSM 840, with 15.0 kV accelerating voltage, magnification 1400 × (fig. 1), 6000 × (fig. 3) and 35 000 × (fig. 4), 13 000 (fig. 5c), 7500 × (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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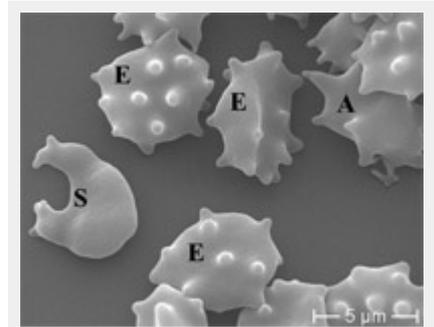


Figure 3

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

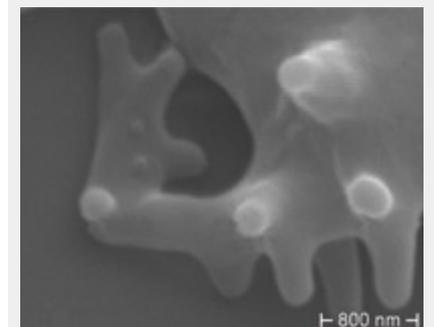


Figure 4

ChAc: Gross deformation of RBC membrane in acanthocyte.

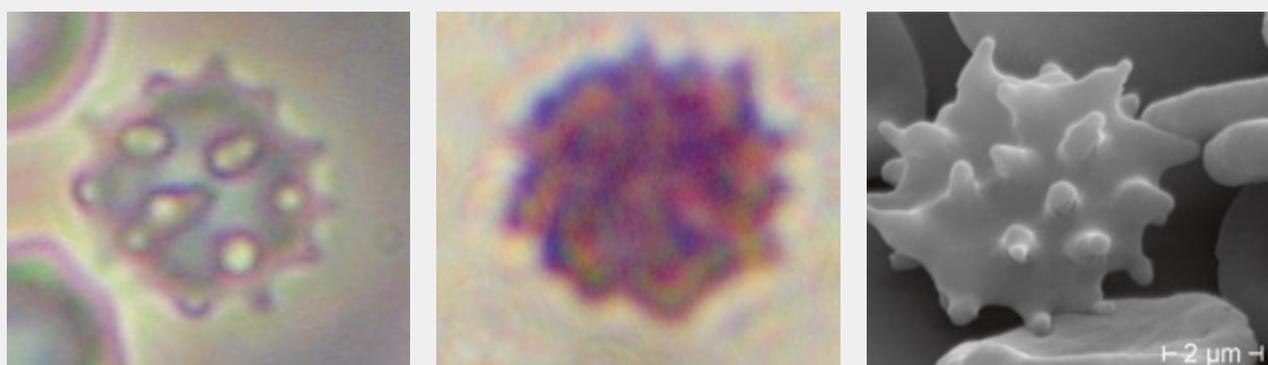


Figure 5

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

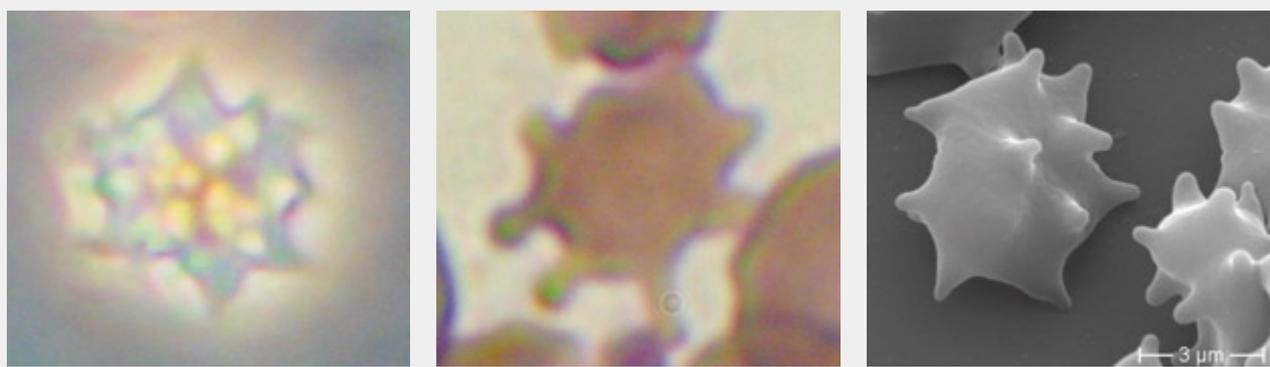


Figure 6

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

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