

Do Acanthocytes Appear Late During the Course of Chorea-Acanthocytosis?: Case Report

Kore-Akantositöz Seyrinde Akantositler Geç Dönemde Ortaya Çıkar mı?

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ABSTRACT Chorea-acanthocytosis is a rare disease presenting with chorea, dystonia, tics, amyotrophy, areflexia, dementia and oro-lingual self-mutilation. The presence of acanthocytes in blood smear and elevated creatin kinase levels are the most common laboratory findings. However, there are instances of late-appearing acanthocytes or of choreaacanthocytosis without acanthocytes. We report a 52-year-old patient with a 12-year history of chorea and orofacial dyskinesia. On neurological examination, he had facial, perioral and lingual hyperkinesias as well as dystonic trunk movements with severe limb chorea. Magnetic resonance imaging of the brain showed bilateral atrophy of the caudate nuclei. Peripheral blood smear, which failed to show any abnormality on all repeated evaluations, revealed abundant acanthocytes. Based on this, the patient was diagnosed with choreaacanthocytosis with late appearance of acantocytes in the course of the disease. In this paper, we underlined the significance of examination for acanthocytosis with special techniques to increase the diagnostic yield.

Key Words: Chorea; dystonia; dyskinesias; acanthocytes

ÖZET Kore-akantositöz, kore, distoni, tik, amiyotrofi, demans ve oro-lingual self-mutilasyonla seyreden nadir bir hastalıktır. Periferik yaymada akantositler ve kreatin kinaz düzeylerinde artış en sık bildirilen laboratuvar bulgularıdır. Ancak, bazı olgularda akantositler geç dönemlerde ortaya çıkabilir veya hiç görülmeyebilir. Bu makalede, yaklaşık 12 yıldan beri kore ve orofasiyal diskinezisi olan 52 yaşında bir hasta sunulmuştur. Hastanın nörolojik muayenesinde fasiyal, perioaral ve lingual hiperkinezinin yanı sıra trunkal distoni ile birlikte ağır kore saptandı. Manyetik rezonans görüntülemesinde bilateral kaudat nükleus atrofi izlendi. Daha önceki tüm değerlendirmelerde herhangi bir anormallik olmayan periferik yaymada bol miktarda akantosit gözlemlendi. Bu bulguyla hastaya, akantositlerin hastalığın geç döneminde ortaya çıktığı kore-akantositöz tanısı konuldu. Bu yazıda, doğru tanı olasılığını artırmak için akantosit incelemesinde özel tekniklerin önemi vurgulanmıştır.

Anahtar Kelimeler: Kore; distoni; diskinezi; akantositler; koreik bozukluklar

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Acanthocytosis, spiky erythrocytes, may be seen in various disorders. Since its first discovery in abetalipoproteinemia, its occurrence has been reported in several other hereditary and acquired disorders, including chorea-acanthocytosis, McLeod Syndrome, Huntington disease like-2, Bassen-Kornzweig Disease, pantothenate kinase-associated neurodegeneration (PKAN), lipoprotein disorders, malnutrition, cancer, thyroid disease, cirrhosis, uremia, psoriasis, vitamin E deficiency, anorexia nervosa

and hypothyroidism.^{1,2} Among these, neuroacanthocytosis is a rare neurodegenerative disease that is characterized by chorea, dystonia, tics, amyotrophy, areflexia, dementia and oro-lingual self-mutilation. The presence of acanthocytes in blood smear and elevation of creatin kinase levels are the most common laboratory findings. Here we report a case of chorea-acanthocytosis in which acanthocytosis was observed late in the course of the disease.

CASE REPORT

The patient was a 52-year-old male of nonconsanguineous parents. The clinical onset of the syndrome was reported at the age of 40 years with aggressiveness and abnormal movements on his face such as orofacial dyskinesia with tongue and lip biting, and spitting. Persistent choreic movements of the trunk and limbs appeared later. His family history was unremarkable for any movement disorder. Within years, he was evaluated in different hospitals; however, in all of those admissions, repeated peripheral blood smears, compared with positive controls, failed to show any abnormality. The number of CAG trinucleotide repeats, which is a predictor of Huntington disease, was within nor-

mal limits. He was admitted to our service with recurrent episodes of dysphagia and severely increased movement disorders. Within time facial, perioral and periorbital as well as lingual hyperkinesias occurred, speech was unintelligible, and frequent trunk and limb movements of a dystonic and choreic nature made the patient unable to stand or walk unaided. Both arms and legs showed some reduction in muscle strength with hypotonia and decreased deep tendon reflexes. Neuropsychological examination was impossible because of severe dysarthria and debilitating movement disorders.

Laboratory work-up revealed a mildly elevated serum creatine kinase level (240 U/L, N= 29-200 U/L). Serum ceruloplasmin, lupus anticoagulant, vitamin E, thyroid function tests, and lipoprotein electrophoresis were within normal ranges. There were no abnormal findings in the expression of Kell blood group antigen. Electrocardiogram showed no abnormality. There was bilateral, moderate atrophy of the head of the caudate nuclei on magnetic resonance imaging of the brain (Figure 1a). Nerve conduction studies showed compound muscle action potentials of slightly reduced amplitude on stimu-

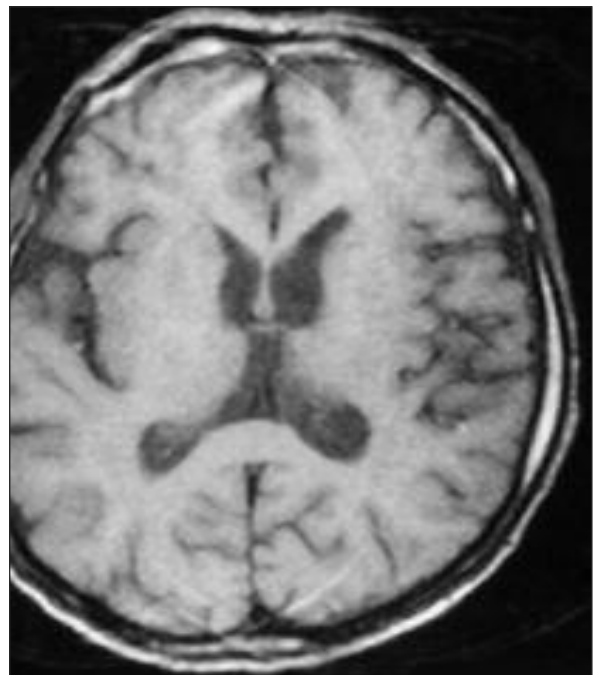
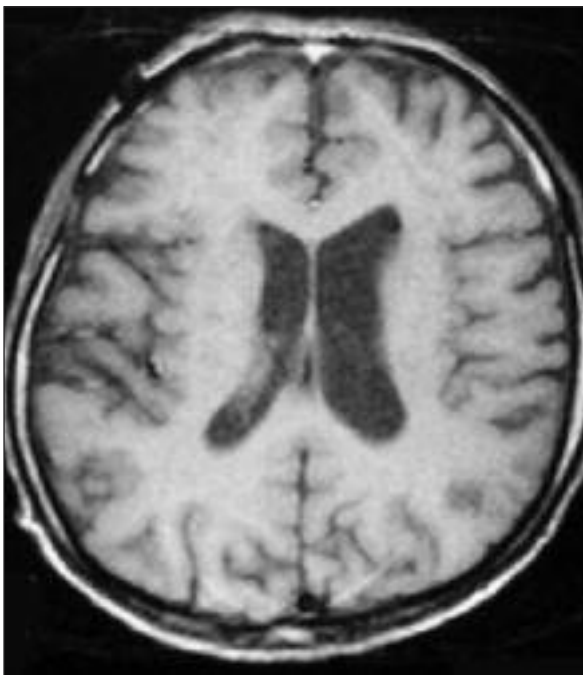


FIGURE 1a: Brain MRI T1-weighted images showing atrophy of the caudate nucleus bilaterally.

lation of the peroneal and tibial nerves, with normal conduction velocities. Slightly reduced sensory action potentials in both sural nerves, with normal conduction velocities, were also found. Peripheral blood smear, which was negative on all previous evaluations revealed the presence of acanthocytes, which accounted for approximately 50-60% of erythrocytes (Figure 1b). Peripheral blood smears of the two healthy sons of the patient yielded no acanthocytosis. Given the diagnosis of chorea-acanthocytosis, the patient was commenced on quetiapine 300 mg/day, which provided moderate relief in dysphagia and chorea.

DISCUSSION

In this paper, we reported an unusual case of chorea-acanthocytosis in which acanthocytes appeared late during the course of the disease. Considering the clinical signs, MRI, electrophysiological evaluations and the presence of acanthocytes in blood smear, the patient had neuroacanthocytosis. Other, neurodegenerative syndromes associated with acanthocytosis were considered in the differential diagnosis and we excluded based on the results of laboratory studies. The molecular basis of chorea-acanthocytosis is the large VPS13A gene consisting of 73 exons on chromosome 9q21. VPS13A encodes chorein, a 360-kDa protein of unknown function that is absent or markedly reduced in tissue from chorea-acanthocytosis patients.³ Genetic analysis for VPS13A mutations was not available in our patient.

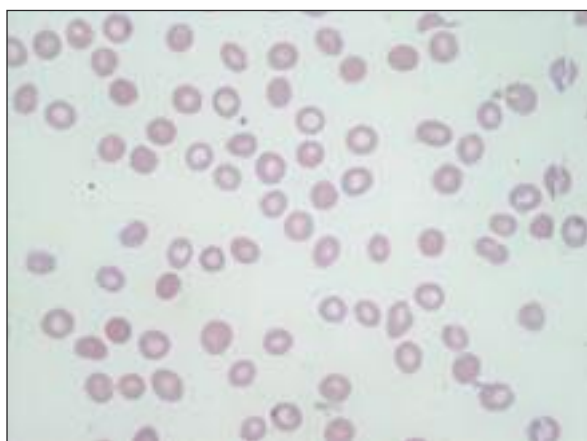


FIGURE 1b: Peripheral blood smear showing many acanthocytes (Wright-Giemsa X 1000).

Some instances of late-appearing acanthocytes or of neuroacanthocytosis without acanthocytes have been reported.⁴⁻⁶ However, some interpreted this with caution relating the phenomenon to the technical issues of acanthocyte determinations.^{3,7} When examining fresh blood for acanthocytes, it is important to avoid false positives, due to experimental artefacts or echinocytes, which may normally present (up to 3%) in adult peripheral blood. Thus, >3% of crenated forms is suggested to be considered pathological and repeated sampling is required.⁷ Incubation of erythrocytes in serial dilutions of saline or phosphate buffered saline was recommended to increase the diagnostic yield due to the observation by Feinberg et al that erythrocytes incubated in such conditions showed a marked (about 20%) tendency towards echinocytic-acanthocytic change.⁸ Storch et al, investigating only the red blood cells using diluted blood samples and wet blood preparations, observed pathological findings in all patients with undiagnosed hereditary neuroacanthocytosis and genetically confirmed chorea-acanthocytosis patients as well as all tested affected family members. Whereas, on standard dry blood smears of EDTA blood samples they showed normal values in 57% and 50% of all patients with hereditary neuroacanthocytosis and patients with genetically confirmed chorea-acanthocytosis, respectively. They suggested that the isotonic dilution of the blood sample and the wet preparation of the blood smear between two glass slides were superior to all other techniques with respect to test sensitivity. Indeed, all genetically confirmed patients/family members with chorea-acanthocytosis as well as all affected family members of atypical neuroacanthocytosis syndromes of their cohort were correctly identified. These patients showed high acanthocyte levels above 28% of total red blood cells.¹ The percentage of acanthocytes in the blood of chorea-acanthocytosis patients is highly variable, usually between 5% and 50% and does not seem to be correlated with the severity of the disease.⁷

In our patient, acanthocytosis was determined with examination of dry blood smears beyond the limits of any suspicion. Cases of chorea-acantho-

cytosis-like syndromes without acanthocytosis have been reported.^{8,9} Our case is of interest in that acanthocytes appeared only later during the course of the disease thus confirming the conclusion that the presence of acanthocytes is not mandatory for the diagnosis.⁹ In addition, the late

appearance of acanthocytes suggests the hypothesis that their presence might be controlled also by other factors partially different from those that underlie the neurological impairment.⁶ Based on our findings, the absence of acanthocytes should not exclude the diagnosis of choreacanthocytosis.

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