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Case Report Open Access

A Rare Case of Chorea-Acanthocytosis in India: Clinical Presentation, Diagnosis, and Management

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ABSTRACT

Chorea-acanthocytosis (ChAc) is a rare autosomal recessive neurodegenerative disorder classified under Neuroacanthocytosis syndromes. It is characterized by progressive neurological decline, psychiatric symptoms, and the presence of irregularly shaped red blood cells (acanthocytes) on peripheral blood smears. ChAc remains underdiagnosed due to its rarity and variable presentation. This case report describes a 44-year-old male from India, born of a consanguineous marriage, who presented with self-mutilating lip-biting or lingual dystonia, generalized chorea, and a history of seizures. The patient exhibited psychiatric symptoms including depression and agitation in addition to neurological features such as hypophonic speech, slowed saccades, and hypotonia. Initial diagnoses of tardive dyskinesia and generalized tonic-clonic seizures were revised following referral to neurology. Peripheral blood smears revealed acanthocytosis, and whole-exome sequencing confirmed a homozygous mutation in the VPS13A gene, leading to the diagnosis of ChAc. MRI findings included bilateral caudate and lentiform nucleus atrophy, with mild cerebral atrophy. The patient was treated symptoms were managed with antiepileptics, dopamine receptor antagonists, anticholinergics and vitamin supplementation, and vitamin supplementation, resulting in significant improvement in mandibular and lingual symptoms. Dental guards were provided to prevent further oral injury. This case highlights the importance of considering ChAc in patients presenting with neuropsychiatric and movement disorder symptoms, especially in the context of consanguinity. Early recognition and multidisciplinary management are crucial to improving quality of life. By documenting this rare case, we aim to enhance clinical awareness and facilitate early diagnosis of ChAc in resource-limited settings

KEYWORDS chorea-acanthocytosis (ChAc), neuroacanthocytosis syndromes, VPS13A gene mutation acanthocytes, basal ganglia atrophy, movement disorders

INTRODUCTION

Neuroacanthocytosis syndromes are rare, genetically inherited disorders marked by progressive neurodegeneration and the presence of irregularly shaped red blood cells called acanthocytes which can be seen on peripheral blood

smears (1). These syndromes are exceptionally uncommon, with an estimated prevalence ranging from fewer than 1 to 5 cases per 1,000,000 individuals (2). Due to their rarity and the variability in clinical manifestations, they are often misdiagnosed or overlooked, particularly in settings with limited access to advanced diagnostic tools (3). The clinical spectrum of neuroacanthocytosis syndromes typically involves degeneration of the basal ganglia, a region of the brain responsible for coordinating movement. This degeneration leads to a wide range of symptoms, including movement disorders, psychiatric abnormalities, and cognitive decline (4). While these symptoms form a common thread among patients with neuroacanthocytosis, their presentation can differ significantly, adding to the challenges of accurate diagnosis. Among the disorders grouped under neuroacanthocytosis syndromes, the most prevalent is Chorea-acanthocytosis (ChAc), followed by McLeod Syndrome (MLS), Huntington's disease-like 2 (HDL2), and the rarest, pantothenate kinase-associated neurodegeneration (PKAN). Additionally, metabolic disorders affecting lipoprotein metabolism, such as abetalipoproteinemia and hypobetalipoproteinemia, are sometimes included under this category, though they do not typically present with basal ganglia atrophy (5). This case study focuses on ChAc, a disorder caused by mutations in the VPS13A gene, which encodes the chorein protein. ChAc is a rare autosomal recessive condition associated with progressive neurodegeneration and diverse neurological and psychiatric manifestations (6). The underlying pathology involves abnormalities in the chorein protein, a critical component of the cell's vesicular transport and intracellular signalling mechanisms. These abnormalities disrupt neural and cellular functions, particularly in the basal ganglia, leading to the characteristic clinical features of ChAc (7).

One of the significant challenges associated with ChAc is its clinical heterogeneity (8). Patients often present with a combination of movement disorders, including chorea, characterized by involuntary, dance-like movements; dystonia, involving sustained muscle contractions and abnormal postures; and orofacial dyskinesias, which manifests as involuntary facial and mouth movements. Psychiatric symptoms such as depression, agitation, and impulsivity are also commonly observed, further complicating the diagnostic process (9). Additionally, patients may exhibit cognitive decline and seizures, which can mimic other neurological disorders, leading to delayed or incorrect diagnoses. The rarity of ChAc and the lack of awareness among clinicians further contribute to its underreporting (10). Given the clinical heterogeneity and diagnostic difficulties inherent to ChAc, we present a case that exemplifies these challenges: a 44-year-old male born of a consanguineous marriage, with a family history suggestive of a genetic disorder, as evidenced by his elder sibling who exhibited similar involuntary movements, orolingual dystonia, and psychiatric symptoms before passing away at the age of 40, likely due to the same condition. The patient in the present study presented with a range of symptoms, including involuntary movements, orolingual dystonia, and self-mutilating behaviors such as lip biting, which are characteristic of ChAc. Additionally, his clinical history included seizures and psychiatric disturbances, such as depression and irritability, underscoring the multifaceted nature of this disorder. Due to the limited clinical exposure to such rare conditions, the patient was initially misdiagnosed with other movement disorders, such as tardive dyskinesia, and generalized tonic-clonic seizures. However, further investigation, including peripheral blood smear analysis revealing acanthocytes and whole-exome sequencing confirming a homozygous mutation in the VPS13A gene, led to the correct diagnosis of ChAc (11). This case highlights the importance of combining detailed clinical evaluation with advanced diagnostic techniques, particularly genetic testing, in the diagnosis of rare neurodegenerative disorders (12). Reports like this provide valuable insights into the diagnostic and therapeutic challenges associated with ChAc and other neuroacanthocytosis syndromes. They underscore the need for heightened clinical awareness and the importance of considering such rare disorders in patients presenting with unexplained neuropsychiatric and movement-related symptoms, particularly in populations with higher rates of consanguinity. By documenting this case, we aim to contribute to the growing body of literature on ChAc, facilitating early recognition and appropriate management of this debilitating condition (13).

CASE REPORT

Medical history

A 44-year-old male patient presented to the outpatient department with complaints of lip biting causing self-mutilating behavior, involuntary tongue movements causing difficulty in swallowing and speech, and other abnormal involuntary bodily movements for the past one year. These symptoms were insidious in onset, gradually progressive, and lead to an inability to swallow. He had an emaciated look and appeared irritable. He had a one-year history of depression, weeping spells, restlessness, and agitation. Additionally, he had been diagnosed with generalized tonic-clonic seizures 3 years previously, and was treated for the last episode 1 year ago, after which the patient had stopped using antiepileptic medications. He had no prior history of psychological conditions or the use of antipsychotic medications. In view of his psychiatric symptomology, he was initially admitted to the hospital in the psychiatry department. The patient was originally diagnosed with Tardive Dyskinesia and Generalized Tonic Clonic Seizures with a query of motor tics. The patient was treated with tetrabenazine, vitamin B, and E supplements. This case was later referred to the Neurology department on account of abnormal involuntary movements of face and lip and a past history of seizures. On further inquiry, it was found the patient was born out of a consanguineous relationship and had an elder brother who had died of similar symptoms at the age of 40.

On neurological examination, the patient presented with hypophonic speech, orolingual dystonia, generalized chorea, a "rubber man" gait, and slowed saccades. Deep tendon reflexes were reduced to grade +1, and hypotonia was noted in the limbs. The sensory examination revealed diminished pinprick sensation in the fingers and toes. MRI findings indicated mild bilateral atrophy of the caudate and lentiform nuclei, along with ventricular prominence and bilateral cerebral atrophy (14). Additionally, a few hyperintense foci were observed on T2-weighted fluid-attenuated inversion recovery (FLAIR) sequences. EEG results were suggestive of generalized epileptiform discharges. Nerve conduction studies, which could have provided additional diagnostic clarity, were not performed due to financial constraints. Laboratory investigations revealed a normal hematological profile, but an elevated serum creatine phosphokinase (CPK) level of 7,166 U/L (normal range: 25–200 U/L). Lipid profile, hepatic, renal, and thyroid function tests were within normal limits. The patient tested negative for anti-HIV and syphilis antibodies. Peripheral blood smear analysis revealed normocytic, normochromic red blood cells with seven acanthocytes per high-power field, raising suspicion of neuroacanthocytosis. Whole-exome sequencing confirmed a homozygous mutation in the VPS13A gene located on exon 55, consistent with autosomal recessive inheritance, leading to a definitive diagnosis of ChAc (Figure 1). Treatment included antiepileptics (valproate), dopamine receptor antagonists (tetrabenazine), anticholinergics, and nutritional supplementation with vitamin E (400 mg BD) and vitamin B. Dental guards were provided to prevent further oral injuries. The patient showed improvement in oromandibular and lingual symptoms and was subsequently discharged. At the one-month follow-up, further assessments were performed to evaluate long-term progress.

The image is an axial T2-weighted MRI scan of the brain demonstrating features consistent with ChAc, a rare neurodegenerative disorder under the umbrella of neuroacanthocytosis syndromes. Prominent findings include atrophy of the bilateral caudate nuclei and lentiform nuclei, structures within the basal ganglia that are critical for coordinating movement and other motor functions. The atrophic changes result in the enlargement of the lateral ventricles, creating a characteristic appearance known as "boxcar ventricles." This is indicative of significant neurodegenerative processes affecting the basal ganglia. Additionally, the surrounding cerebral parenchyma shows mild

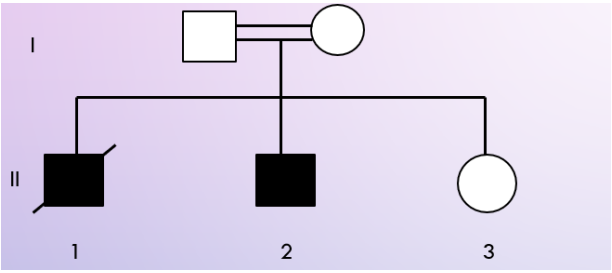

Figure 1. Pedigree chart showing an autosomal recessive inheritance pattern of Chorea-acanthocytosis. The proband (II-2) and a deceased sibling (II-1) are affected, with both parents (I-1 and I-2) being asymptomatic carriers.

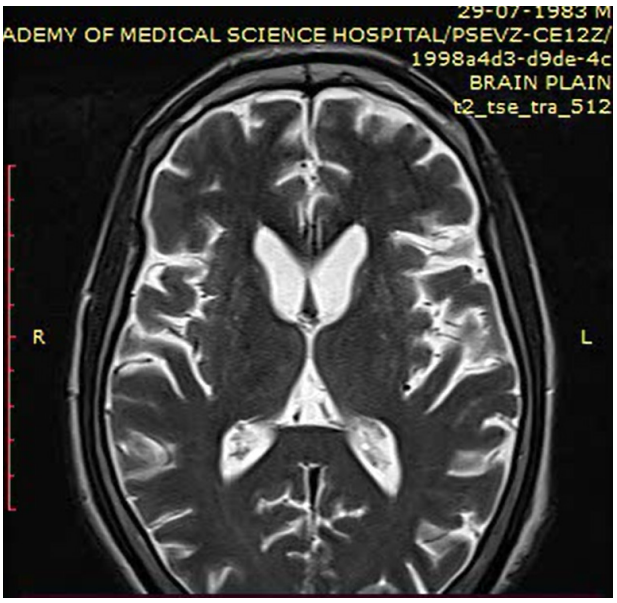

Figure 2. MRI brain (coronal T2-weighted image) showing mild bilateral caudate and lentiform nucleus atrophy with prominent ventricular system and cortical atrophy. These findings are consistent with neurodegenerative changes observed in Chorea-acanthocytosis (ChAc).

atrophy, as evidenced by widened sulci and fissures. The T2 hyperintensity in these regions may also suggest gliosis, a reactive process secondary to chronic degeneration.

These findings are typical of ChAc, where the degeneration of basal ganglia structures contributes to the clinical manifestations, including choreiform movements, dystonia, and psychiatric symptoms. The MRI provides critical diagnostic insights by correlating clinical symptoms with structural abnormalities, aiding in distinguishing ChAc from other similar disorders such as Huntington's disease. This neuroimaging evidence, when combined with genetic confirmation of VPS13A mutations, strengthens the diagnosis of ChAc and highlights the utility of MRI in assessing disease severity and progression (Figure 2).

This axial T2 FLAIR MRI image of the brain demonstrates characteristic findings of ChAc. The image shows atrophy of the bilateral caudate nuclei and lentiform nuclei, leading to the enlargement of the frontal horns of the lateral ventricles, often referred to as "boxcar ventricles." These findings are indicative of basal ganglia degeneration, a hallmark of neuroacanthocytosis syndromes. Additionally, mild cerebral atrophy is evident, as suggested by widened cortical sulci. The imaging findings are consistent with the

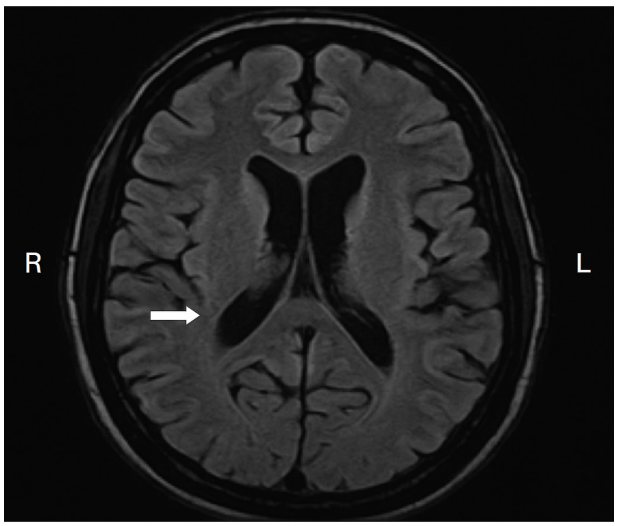

Figure 3. Axial T2-weighted FLAIR MRI showing bilateral caudate and putaminal atrophy with prominent lateral ventricles, consistent with neurodegenerative changes seen in Chorea-acanthocytosis

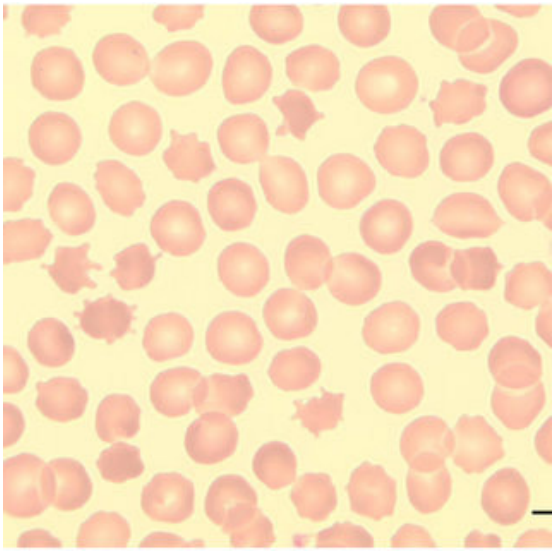

Figure 4. Peripheral blood smear showing acanthocytes (irregularly shaped, spiculated red blood cells) observed in a patient with Chorea-acanthocytosis (May-Grünwald-Giemsa stain; magnification x100; scale bar = 10 µm)

neurodegenerative processes underlying ChAc, which correlates with the patient's movement disorders and neuropsychiatric symptoms. MRI plays a vital role in supporting clinical and genetic diagnosis (Figure 3).

Figure 4 depicts a peripheral blood smear showing acanthocytes, which are misshapen red blood cells with spiculated, irregular projections. These abnormal cells are a hallmark finding in neuroacanthocytosis syndromes, including ChAc. Acanthocytes are formed due to disruptions in the lipid composition of the red blood cell membrane,

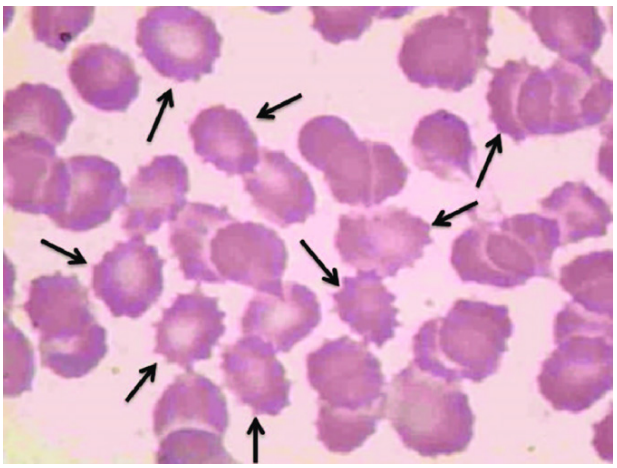

Figure 5. Peripheral blood smear showing acanthocytes, characterized by misshapen, spiculated red blood cells, indicated by arrows (magnification x100). These findings are diagnostic of neuroacanthocytosis syndromes, such as Chorea-acanthocytosis

which is often linked to underlying genetic mutations, such as those in the VPS13A gene. The presence of acanthocytes on a peripheral blood smear is a key diagnostic clue that, when correlated with clinical symptoms and genetic testing, confirms the diagnosis of ChAc or other related neuroacanthocytosis syndromes. This morphological abnormality plays a crucial role in distinguishing these conditions from other neurological disorders.

This image displays a peripheral blood smear showing acanthocytes, identified by their irregular, spiculated shapes (indicated by arrows). Acanthocytes are a distinctive feature of neuroacanthocytosis syndromes, including ChAc. These abnormal red blood cells result from disruptions in the lipid bilayer structure, often associated with mutations in the VPS13A gene. The presence of acanthocytes in a blood smear, coupled with neurological and psychiatric symptoms, strongly suggests a diagnosis of neuroacanthocytosis. Their detection is a critical diagnostic clue that, when paired with genetic and clinical evaluations, supports identifying conditions like ChAc. This figure emphasizes the role of peripheral smear analysis in diagnosing rare neurodegenerative disorders (Figure 5).

Figure 6 shows a patient with ChAc, demonstrating self-devised coping mechanisms to manage the symptoms of the disorder. The cloth placed in the patient's mouth is used to prevent further oral injuries caused by severe oromandibular

Figure 6. The patient devised a self-protective mechanism using a cloth placed in his mouth to prevent further oral injury caused by oromandibular dystonia and self-mutilating behaviors characteristic of Chorea-acanthocytosis

dystonia and self-mutilating behaviors, such as lip biting, which are hallmark features of ChAc. The patient's posture and facial expression reflect the physical and neurological toll of the disease, including involuntary movements and dystonic postures.

DISCUSSION

ChAc is a rare neurodegenerative disorder that is frequently misdiagnosed due to its heterogeneous presentation and lack of clinician familiarity, especially in resource-limited settings (15). In the presented case, a 44-year-old male with hallmark features such as self-mutilating behavior, orofacial dyskinesia, chorea, and psychiatric symptoms was initially misdiagnosed, highlighting the diagnostic complexities associated with ChAc (16). This case underscores the importance of a multidisciplinary approach. A comprehensive assessment that integrates clinical, radiological, hematological, and genetic evaluations was essential to establishing the definitive diagnosis. The presence of acanthocytes on a peripheral blood smear and the identification of a homozygous mutation in the VPS13A gene were critical in confirming ChAc. MRI findings of basal ganglia atrophy further supported the diagnosis, differentiating it

from similar disorders like Huntington's disease (17). Early and accurate diagnosis is essential for symptom management and improving quality of life. Importantly, expanding the availability of genetic testing in primary and rural healthcare settings could facilitate earlier recognition of such rare disorders, potentially preventing years of misdiagnosis and inappropriate treatment. While there is no definitive cure, symptomatic treatment with antiepileptics, dopamine antagonists, anticholinergics, and nutritional support showed considerable benefit in this case. Use of dental guards and patient-devised coping strategies, such as oral padding, also helped mitigate self-inflicted injuries resulting from oromandibular dystonia. Similar diagnostic challenges and therapeutic approaches have been documented in other isolated case reports and small cohort studies, which consistently emphasize the value of combining hematological, neuroimaging, and genetic findings to guide clinical management of ChAc (18). This case underscores the importance of recognizing neuroacanthocytosis syndromes in clinical settings, especially when patients present with neuropsychiatric and movement disorders in the context of consanguinity. Increased awareness and improved access to genetic testing are vital for earlier diagnosis and targeted management (19).

CONCLUSION

ChAc is a rare but devastating neurodegenerative disorder that often remains underdiagnosed due to its diverse clinical presentation and limited awareness among clinicians. This case report of a 44-year-old male born of consanguineous parentage illustrates the diagnostic challenges associated with ChAc, particularly in resource-limited settings. The patient exhibited hallmark features, including self-mutilating behaviors, orolingual dystonia, generalized chorea, and psychiatric symptoms. Despite initial misdiagnosis, the integration of clinical findings, blood smear analysis revealing acanthocytes, and genetic testing confirming a VPS13A gene mutation led to an accurate diagnosis. The findings underscore the critical role of multidisciplinary approaches in managing ChAc, combining neurological, psychiatric, and nutritional interventions. The use of antiepileptics, dopamine receptor antagonists, and nutritional supplementation improved the patient's quality of life, while preventive measures like dental guards mitigated self-injury risks. Imaging findings of basal ganglia atrophy and advanced genetic testing were pivotal in confirming the diagnosis, emphasizing the need for access to specialized diagnostic tools. This case report highlights the importance of considering ChAc in patients with unexplained neuropsychiatric symptoms, particularly in populations with higher rates of consanguinity. Increased awareness and documentation of such cases can facilitate early recognition and intervention, ultimately improving outcomes for affected individuals. Further research into the pathophysiology and targeted therapies for ChAc is essential to address its complex clinical spectrum. By contributing to the limited pool of documented cases, this case report aims to aid clinicians in identifying and managing this rare disorder more effectively.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

CONSENT FOR PUBLICATION

Patient/guardian consent was obtained for publication of this case report.

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