Feeding dystonia, chorea, psychosis, and self-mutilation in an African patient with neuroacanthocytosis syndrome

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A 34-year-old woman with a 2-year history of progressively worsening difficulties in walking, eating and swallowing, presented to our department. The patient's sister reported observing unusual behaviours over the past 6 months: she said her sister had been taking her meals to eat alone in the bathroom and had crafted a doll from leaves gathered from local trees, referring to it as her son (figure A). Additionally, she has been experiencing low mood and general cognitive decline, including memory and attention deficits, along with personality changes such as increased impulsivity and aggression. However, there were no signs of obsessive-compulsive behaviour.

The patient had no previous medical history and no family history of similar difficulties or any other neurodegenerative disorders. Her mother was alive and well at 62 years old, while her father died in his 70s from natural causes. She has three siblings: an older brother (38), a younger sister (31), and a younger brother (28), all of whom were in good health. There was no history of consanguinity in the past two generations. However, it was noteworthy that her parents share the same tribal origin, with their ancestries tracing back to the same village.

On examination, the patient was cachectic, drooling her saliva, and had multiple injuries and scars on her tongue, lower lips, and arms caused by self-biting (figure B); she had abnormal—primarily choreatic—movements of her trunk and oromandibular region, involuntary vocalisations, and vocal tics (video 1). She also had involuntary jaw opening and dystonia—particularly during feeding (video 2). The observed phenomenology was consistent with feeding dystonia. Limb examination showed mild bradykinesia, hypotonia, mild motor weakness, affecting both distal and proximal muscles (Motor Assessment Scale score: 4/5), and reduced reflexes in all extremities.

The observed motor weakness exhibits a myopathic pattern rather than motor impersistence. Her gait was ataxic.

Laboratory investigations found urea and electrolyte levels within normal range; liver enzymes were slightly elevated with alanine aminotransferase (ALT) at 43 U/L (normal range 4–36) and aspartate aminotransferase (AST) at 74 U/L (normal range 8–33). Thyroid function (TFT) was normal. Haemoglobin (Hb) concentration was within the normal range at 12·1 g/dL (normal 11·0–14·0). The serum creatinine kinase (CK) level was elevated at 1344 U/L (normal range 26–192), and lactate dehydrogenase (LDH) was raised at 269 UI/L (normal range 100–240). A blood smear showed that 15% of the red blood cells were acanthocytes (normal < 3%) (figure C). The elevated CK levels and myopathic weakness suggested that the increased LFTs are more likely due to muscle insult rather than direct liver damage.

An MRI brain showed bilateral atrophy in the caudate nucleus and subtle cortical atrophy in the frontal-parietal and occipital regions (figure D). Nerve conduction studies showed axonal neuropathy affecting both sensory and motor neurons. Whole exome sequencing showed the patient to be a compound heterozygous carrier of two novel pathogenic loss-of-function variants in the *VPS13A* gene, namely: NM_033305.3(VPS13A): c.2425C>T (p. Gln809*) and NM_033305.3(VPS13A): c.5072delA (p.Asp1691fs). No other pathogenic or likely pathogenic variants were found in any genes previously associated with adult-onset dystonia, chorea, or related movement disorders including *VPS13B, VPS13C, VPS13D, PANK2, ANGPTL3, APOB, ATN1, ATP7B, ELAC2, MTTP, HPRT1,* and *XK*. Furthermore, no pathogenic expansions were detected in the *HTT* or *JPH3* genes. Considering the findings together, we diagnosed VPS13A disease. Initially, we prescribed oral haloperidol with no response; she was switched to oral risperidone and tetrabenazine resulting in some improvement in both psychiatric and motor symptoms.

After 1 month, the patient was allowed home and followed up every 4 weeks as an outpatient. The patient's condition continued to deteriorate, with significant weight loss and worsening of both motor and psychiatric symptoms. At last review, she was receiving palliative care.

VPS13A disease—previously known as Chorea-acanthocytosis—is an autosomal recessive condition resulting from mutations in the *VPS13A* gene, which encodes a lipid transfer protein. Patients typically have progressive symptoms of chorea, oromandibular dyskinesia, Parkinsonism, neuropsychiatric issues, diminished or absent tendon deep reflexes and seizures. Symptoms usually begin around 30 years of age. Prognosis is poor, and the disease is ultimately fatal. Additional features indicative of VSP13A disease include elevated creatinine kinase levels, transaminitis, acanthocytocytosis, and caudate atrophy. The differential diagnoses include XK disease—also known as McLeod syndrome. Both VSP13A and XK disease fall under the

umbrella of neuroacanthocytosis syndrome: XK disease is an X-linked disorder predominantly affecting middle-aged men.

Huntington's disease, Huntington's disease-like 2, Wilson's disease, and other rare adult-onset choreatic disorders, including neuroferritinopathy, aceruloplasminaemia, and c9orf72-related disorders, should also be considered as other possible differential diagnoses. It is worth noting that recent evidence suggests globus pallidus internus deep brain stimulation (DBS) as a promising treatment option for patients with neuroacanthocytosis. However, its high cost and limited availability, particularly in low- and middle-income countries—especially in sub-Saharan Africa—significantly restrict its accessibility. To our knowledge, DBS services are currently available in only five of the 53 African countries: Egypt, Kenya, Morocco, Algeria, and South Africa, with no availability in sub-Saharan Africa.

In Africa, choreatic movement disorders—seen in our patient, which we believe is the first genetically confirmed case of VPS13A disease in a black patient from sub-Saharan Africa—are often underdiagnosed; many cases are referred to traditional healers and customary medicine.

Contributors

We all provided care for the patient and managed the case. We all reviewed and wrote the article. Written consent for publication was obtained from the patient.

Declaration of interests

MR declares a personal relationship with a senior editor at *The Lancet*. All remaining authors declare no conflicts of interest.

Figure Legends:

Figure (A) Photograph of a doll made from leaves which the patient said was her son.

Figure (B) Photograph shows bites on lips and tongue.

Figure (C) Blood smear shows 15% acanthocytosis (arrows).

Figure (D) MRI shows (arrow) atrophy in the caudate nucleus bilaterally, and subtle frontal-parietal region, and occipital part of the calvarium.

Multiple-choice question
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A 34-year-old woman with a 2-year history of progressively worsening difficulties in

walking, eating and swallowing, presented to our department. On examination, the patient was cachectic, drooling her saliva, and had multiple injuries and scars on her tongue, lower lips, and arms caused by self-biting (figure). She had abnormal movements—primarily choreatic—in her upper limbs and oromandibular region; involuntary vocalisation; and vocal tics. She also had involuntary jaw opening, forceful tongue protrusion and dystonia—prominent during feeding. Limb examination showed mild bradykinesia, hypotonia, mild motor weakness, and reduced reflexes in all extremities. Which of the following statements is false?

A) A raised creatinine kinase and acanthocytosis would be present
B) Biallelic mutations are likely to be detected in the *VPS13A* gene
C) Atrophy of the caudate would be seen on MRI
D) A history of a similar disorder would be reported in the patient's mother and paternal grandmother

Answer D) using images (B) and (C)