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An 11-month-old boy with transaminitis

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CASE PRESENTATION

An 11-month-old male infant had isolated transaminitis on lab investigations obtained during a viral illness with clear nasal discharge, mild cough, and fever. His alanine aminotransferase (ALT) was 203 IU/L (normal 13 to 45 IU/L) and aspartate aminotransferase (AST) was 224 IU/L (normal < 110 IU/L). He was otherwise well and returned to baseline health within a few days. Despite remaining asymptomatic, transaminitis persisted in the following months.

He was the product of a dizygotic twin gestation, born full-term by caesarean section. Both twins were healthy neonates. His parents were from East India and were nonconsanguineous.

Repeated examination over the next 6 months continued to be unremarkable: at 17 months, the child appeared well and had no jaundice. Abdomen was soft and nontender, with no organomegaly. Muscle bulk, tone, and reflexes were normal in all limbs. At 17 months, his weight was 14 kg (>95th percentile) and height was 82 cm (50th to 75th percentile). He met all developmental milestones; crawling at 7 months, pulling to stand at 9 months and walking independently between 12 and 14 months of age. No hepatic abnormalities were found on abdominal ultrasound or initial laboratory investigations of virology, metabolic screen, and autoimmune markers. Further neuromuscular investigation demonstrated an elevated creatine kinase (CK) of 5026 U/L (normal 20 to 200 U/L), gradually declining ALT (136 IU/L) and normal AST (104 IU/L). Further testing revealed the diagnosis.

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CASE DIAGNOSIS: MUSCULAR DYSTROPHY

The child's needle electromyography showed polyphasic potentials suggestive of a myopathic process. His genetic testing identified an in-frame deletion of exon 45 to 48 on the dystrophin gene, which has been associated with Becker's Muscular Dystrophy (BMD) (1); however, his young age precluded phenotypic expression determination. The child remained active with normal development of gross and fine motor skills. At age two, he developed calf pseudohypertrophy. At age six, he developed an ankle contracture. Further probing revealed a maternal uncle and first cousin once removed with lower extremity weakness in childhood and genetic confirmation of BMD. At age eight, he developed lower limb weakness requiring him to rest after walking a few blocks. To date, the child has had no myoglobinuria, behavioural issues, or cognitive impairment.

Dystrophinopathies are X-linked myopathies caused by a mutation in the dystrophin gene, leading to progressive muscle fibre degeneration. Clinical phenotype typically correlates with the amount and function of dystrophin protein. A spectrum of clinical severity exists: Duchenne muscular dystrophy (DMD) has the earliest onset and most debilitating symptoms, BMD has a later onset of milder sequelae and an intermediate phenotype comprises intermediary outliers (1–2). DMD has been associated with disruption of the translational reading frame, leading to near absence of dystrophin protein (2–3).

Classical DMD presents with delayed motor milestones in early childhood, with weakness of the proximal muscles and lower extremities. This leads to a waddling gait, and difficulty climbing stairs and standing from a squatting position (Gower's sign) (2). Other clinical features include flexor contractures as skeletal growth surpasses muscle growth, limb fractures from falls, progressive scoliosis, and cognitive impairment (2). Corticosteroid treatment for DMD contributes to short stature and vertebral fractures. Muscular weakness is rapidly progressive, causing wheelchair dependence by 12 years of age (2). Dilated cardiomyopathy (DCM) often occurs after 18 years of age. Most individuals die by 30 years of age, succumbing to respiratory failure and cardiomyopathy (1–2).

Comparatively, the age of onset in BMD ranges from 5 to 60 years of age and individuals are often ambulatory until at least 16 years (2). Cognitive impairment and contractures are less common. However, DCM is more prominent in BMD, as retained strength permits more exertion on myocardiocytes with malformed dystrophin (4). DCM is the most common cause of death in BMD, with variable lifespan (2).

Persistent elevation of transaminases should prompt investigation of muscular dystrophy with CK, especially in children with weakness or motor delay. Considering nonhepatic causes of transaminitis can avoid unnecessary and invasive tests. After obtaining an elevated CK level, differential diagnosis can include rhabdomyolysis, muscular dystrophies, spinal muscular atrophy, muscle trauma, recent immunization, viral myositis, and neuropathies. Diagnosis of dystrophinopathies can be elusive, given that milder forms present with a long preclinical phase and mild symptoms. Caregiver concerns, especially regarding motor development or weakness, should also trigger investigation for muscular dystrophy (Table 1). Further assessment for muscular dystrophy may include genetic testing, electromyography, muscle biopsy, and specialist referral. Genetic testing can inform future pregnancies and identify individuals eligible for novel genetic therapies.

Early treatment may improve outcomes and delay progression. In DMD, initiation of steroids can improve muscular strength and function. Cardiac monitoring is crucial to determine initiation of

Table 1. Common neuromuscular disorders and examples of prediagnosis concerns

Neuromuscular disorder	Examples of prediagnosis concerns
Becker muscular dystrophy	"His leg cramps interfere with his play"
	"He falls often and has problems standing up"
	"His muscles seem toned, but he doesn't have as much strength as other kids"
Duchenne muscular dystrophy	"He takes a while to walk and falls often"
	"His development seems slower than his brother"
	"He seems weaker than other children, he is not walking, and has behaviour problems"
Congenital muscular dystrophy	"She cannot crawl or raise her head. She does not move a lot and eats poorly"
	"He can't lift his head off my shoulder, drinks his bottle slowly and tires easily. He is floppy and lacks strength"
	"He is not meeting his milestones"
Spinal muscular atrophy	"She can't hold her head up or do tummy time"
	"He has hand tremors, falls down a lot, and walks funny"

Adapted from (5).

medical treatment for DCM, especially amongst female heterozygotes who may present with variable penetrance. Management should involve an interprofessional health care team, including psychosocial support, physiotherapy, and respiratory therapy.

We describe the case of an asymptomatic infant presenting with persistent transaminitis as an unusual presentation of Becker muscular dystrophy. Despite a lack of clinical symptoms, persistent transaminitis can be an important clue for further investigations to ensure early diagnosis, avoidance of unnecessary tests, and appropriate referral of individuals with muscular dystrophy.

CLINICAL PEARLS

1. Persistent elevation of ALT and AST is an important potential indicator of muscular dystrophy.
2. Muscular dystrophy may present with delayed motor milestones and weakness in the lower extremities and proximal muscles. A waddling gait and difficulty standing from a squatting position (Gower's Sign) may become apparent.
3. Muscular dystrophy, especially Becker's type, can be elusive given its long preclinical phase and mild symptoms.

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