Tangier disease in an adult: a case report

Doença de tangier em adulto: um relato de caso

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ABSTRACT

Background: This is a case report of a recently diagnosed patient with a rare and severe autosomal recessive disorder, Tangier Disease. **Objective**: To describe a rare case of Tangier Disease in an adult patient, highlighting clinical presentation, diagnostic findings, and implications for management. **Methods**: A detailed clinical evaluation was conducted on a 37-year-old woman diagnosed with Tangier Disease. Data collection included patient interviews, physical examinations, and review of laboratory, genetic, and imaging findings. Genetic analysis confirmed a homozygous mutation in the ABCA1 gene. **Results**: The patient presented with gastrointestinal symptoms, hepatosplenomegaly, and yellow-orange discoloration of the tonsils. Laboratory findings revealed severe hypoalphalipoproteinemia (HDL: 5mg/dL), hypertriglyceridemia, and anemia. Imaging showed hepatomegaly, chronic liver disease, and splenomegaly. Genetic testing confirmed Tangier Disease, a condition associated with extremely low HDL levels and systemic cholesterol deposition. Despite current therapeutic limitations, the case emphasizes the importance of genetic testing in rare lipid disorders. **Conclusions**: This case highlights the diagnostic challenges and therapeutic limitations of Tangier Disease. Increased awareness and further research are crucial for early identification, better management, and the development of targeted therapies to mitigate cardiovascular and systemic complications associated with this rare condition.

Keywords: Tangier disease; HDL; Hypertriglyceridemia; Genetic mutation; Case report.

RESUMO

Introdução: Trata-se de um relato de caso de uma paciente recentemente diagnosticada com uma desordem autossômica recessiva rara e grave, a Doença de Tangier. **Objetivo:** Descrever um caso raro de Doença de Tangier em uma paciente adulta, destacando a apresentação clínica, achados diagnósticos e implicações para o tratamento. **Métodos:** Foi realizada uma avaliação clínica detalhada em uma mulher de 37 anos diagnosticada com Doença de Tangier. A coleta de dados incluiu entrevistas com a paciente, exames físicos e revisão de achados laboratoriais, genéticos e de imagem. A análise genética confirmou uma mutação homozigótica no gene ABCA1. **Resultados:** A paciente apresentou sintomas gastrointestinais, hepatoesplenomegalia e coloração amarelo-alaranjada das tonsilas. Os exames laboratoriais revelaram hipoalfalipoproteinemia grave (HDL: 5mg/dL), hipertrigliceridemia e anemia. Os exames de imagem mostraram hepatomegalia, doença hepática crônica e esplenomegalia. O teste genético confirmou a Doença de Tangier, uma condição associada a níveis extremamente baixos de HDL e depósito sistêmico de colesterol. Apesar das limitações terapêuticas atuais, o caso destaca a importância do teste genético em desordens lipídicas raras. **Conclusões:** Este caso ressalta os desafios diagnósticos e as limitações terapêuticas da Doença de Tangier. Maior conscientização e pesquisas adicionais são cruciais para a identificação precoce, melhor manejo e desenvolvimento de terapias direcionadas para mitigar complicações cardiovasculares e sistêmicas associadas a esta condição rara.

Descritores: Doença de Tangier; HDL; Hipertrigliceridemia; Mutação genética; Relato de caso.

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INTRODUCTION

Tangier Disease is an autosomal recessive condition first described in 1961. It is extremely rare, with only approximately 100 cases reported globally from 1961 to 2023, affecting individuals across all racial groups[1,2,4]. The disease is caused by homozygous or compound heterozygous mutations in the ABCA1 gene, leading to the absence of high-density lipoprotein (HDL) particles and impaired cholesterol efflux to the extracellular medium[2,3].

Tangier Disease is characterized by extremely low or absent HDL and apolipoprotein AI (apoA-I) levels, accompanied by cholesterol accumulation in various tissues, predominantly within the reticuloendothelial system[1,2]. This leads to organomegaly and yellow-orange discoloration of affected organs, significantly increasing cardiovascular risk[1].

Due to its rarity, Tangier Disease is estimated to affect fewer than 1: 120.000.000 individuals. Its unfamiliarity among healthcare professionals often delays diagnosis and management[4].

CASE REPORT

A 37-year-old woman of mixed race presented with intermittent, nonspecific gastrointestinal symptoms, including diarrhea and nausea. Physical examination revealed hepatosplenomegaly, hypertriglyceridemia (313mg/dL), HDL levels of 5mg/dL, normocytic normochromic anemia with mild anisocytosis, and hepatic steatosis.

She was referred to an endocrinology clinic for evaluation of metabolic disturbances and weight management. The patient, a school secretary, denied alcohol or tobacco use, maintained a balanced diet, and reported a sedentary lifestyle. Her medical history included growth restriction in childhood due to a congenital atrial septal defect, corrected surgically at age 7 without complications, hyperhidrosis, and Plummer's disease, which remains under surveillance.

Family history revealed obesity in her 70-year-old mother and a history of Hepatitis C in her deceased father (59 years old). Her 40-year-old sister reported no medical conditions. Genetic testing of the family was declined.

On clinical evaluation, the patient appeared asymptomatic, with an elevated BMI of 27.17kg/m^2, hepatomegaly extending 5cm below the costal margin, splenomegaly extending 3cm below the costal margin, and yellow-orange tonsillar discoloration. Cardiopulmonary auscultation was unremarkable.

Laboratory results from April 2024 showed a total cholesterol of 52mg/dL, HDL of 5mg/dL, LDL of 14mg/dL, and triglycerides of 313mg/dL. Historical results included a total cholesterol of 51mg/dL in March 2023 and 105mg/dL in January 2021, with corresponding changes in HDL, LDL, and triglycerides. Imaging from a May 2023 abdominal MRI (Figures 1 and 2) revealed hepatomegaly with signs of chronic liver disease, mild fatty liver, iron overload, a hypervascular hepatic nodule (LI-RADS 3), multiple hepatic cysts, and homogeneous splenomegaly.

Genetic testing performed in May 2024 by Mendelics Laboratory confirmed a homozygous pathogenic variant in the ABCA1 gene (chr9;104,825.794, C>CA). Mutations in this gene are associated with Tangier Disease, with fewer than 100 reported cases worldwide[5].

DISCUSSION

Tangier Disease is an autosomal recessive condition with autosomal codominant traits for biochemical findings[1]. Parents heterozygous for the condition have a 25% chance of producing an affected homozygous offspring, a 50% chance of producing a heterozygous offspring, and a 25% chance of producing a normal offspring. A homozygous parent and a normal individual will produce 100% heterozygous offspring[1]. Genetic testing was declined by the family members of the reported patient.

Clinically, cholesterol deposition in the tonsils-manifesting as hypertrophy and yellow-orange discoloration-is a hallmark of Tangier Disease, commonly presenting in childhood or early adulthood. This finding was evident in the patient. Premature atherosclerosis makes affected individuals more susceptible to coronary artery disease and cerebrovascular events[1,3]. Cholesterol accumulation in the reticuloendothelial system results in hepatosplenomegaly, with splenic involvement potentially leading to thrombocytopenia[1]. Cholesterol deposition also occurs in lymph nodes, thymus, intestinal mucosa, and skin[2], with corneal accumulation causing opacities and visual disturbances[2].

Peripheral neuropathy, either transient or persistent, can involve cranial nerves and present as symptoms resembling syringomyelia[2,3].

Laboratory findings typically show HDL levels below 5mg/dL, apoA-I levels under 20mg/dL, and total plasma cholesterol below 150mg/dL[1]. Diagnostic criteria include HDL levels below 25mg/dL, apoA-I concentrations below 20mg/dL, clinical symptoms, and identification of a pathogenic ABCA1 mutation[2].

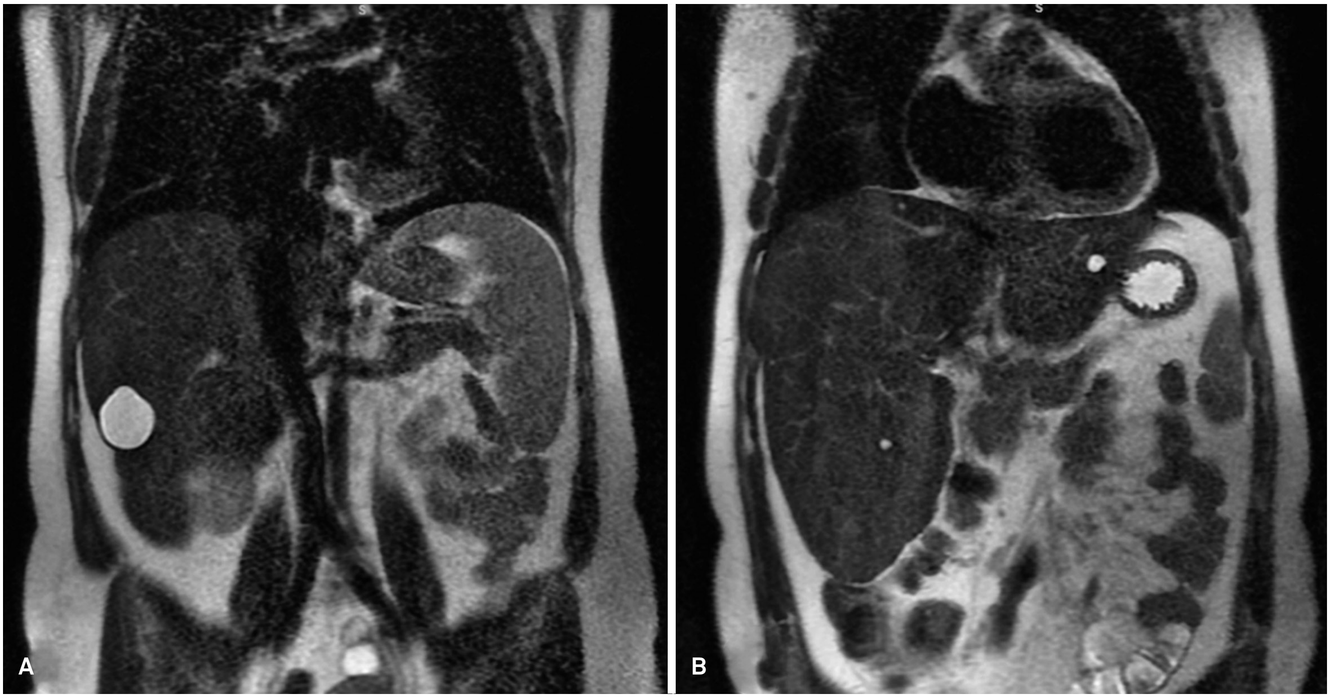

Figure 1. Coronal T2-weighted view of total abdominal MRI, highlighting hepatomegaly with signs of chronic liver disease and associated splenomegaly. Hepatomegaly associated with signs of chronic liver disease. Hypervascular hepatic nodule, nonspecific (LI-RADS 3). Imaging follow-up is suggested at the clinician's discretion. Multiple hepatic cysts are also observed.

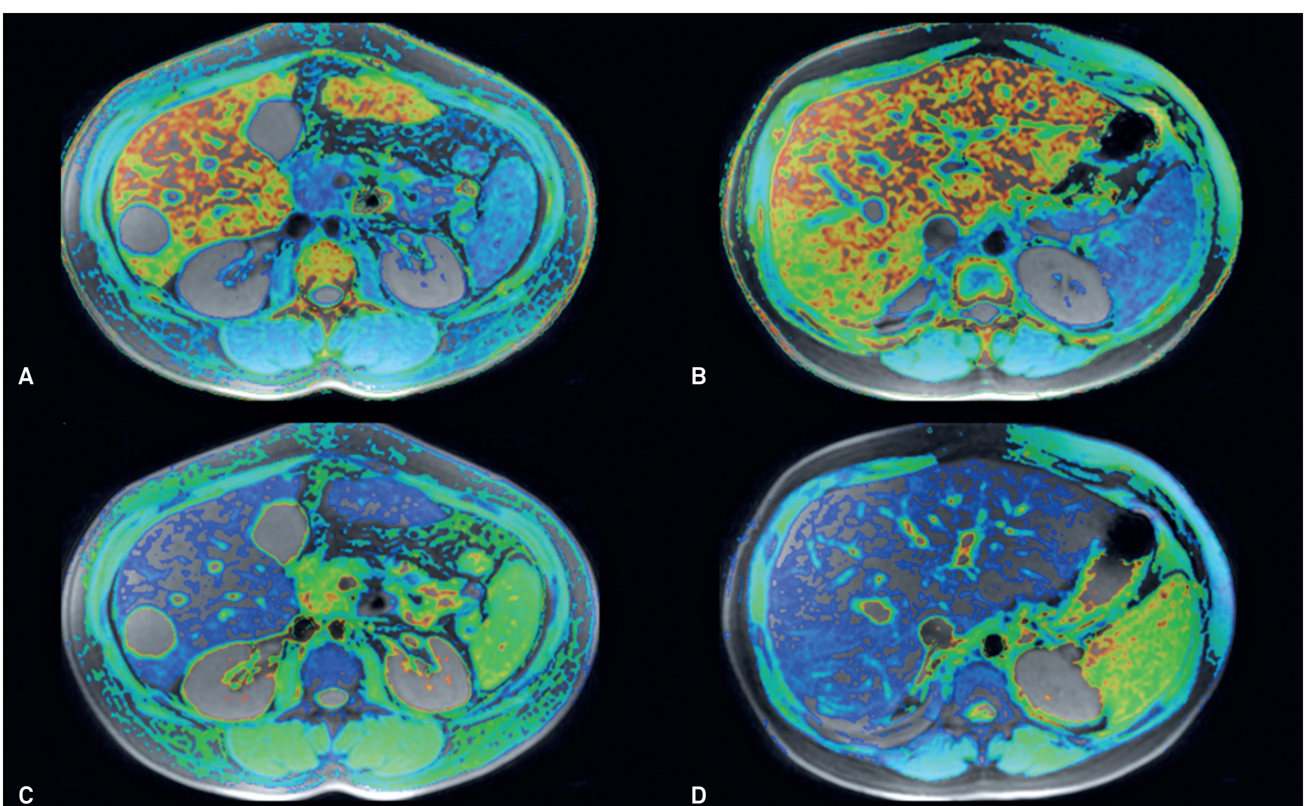

Figure 2. Axial view of total abdominal MRI, showing hepatomegaly with chronic liver disease features and associated splenomegaly. Magnetic resonance imaging findings are compatible with mild fatty liver disease and signs of iron overload.

In this case, genetic testing confirmed the diagnosis early, bypassing differential diagnoses. However, due to the rarity of the disease, therapeutic advancements are limited, and research investments remain sparse.

There is no curative treatment for Tangier Disease. Current management focuses on lifestyle modifications and, in some cases, statin use, though evidence supporting the latter is limited[1,5]. Future therapeutic strategies may involve genetic interventions to enhance cholesterol uptake by hepatocytes or modulate HDL metabolism, potentially through ABC1 overexpression[1,2].

CONCLUSION

This case underscores the rarity and diagnostic challenges of Tangier Disease. The lack of effective therapeutic options highlights the need for increased research and awareness. Early diagnosis can aid in managing cardiovascular and systemic risks. Moreover, developing targeted therapies is essential to expand the therapeutic arsenal and mitigate the disease's severe complications, including high cardiovascular risk, visual disturbances, and hematopoietic system abnormalities.

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