Background: Cerebrotendinous xanthomatosis (CTX) is a rare autosomal recessive disease where deficiency of sterol 27-hydroxylase leads to reduced production of CDCA. In such cases, life expectancy is only 4–6 decades, with progressive neurologic dysfunction such as dementia and spinal cord paresis, unless the condition is diagnosed early and treated appropriately. Herein, we aim to raise awareness regarding the importance of ophthalmic examination in evaluating of xanthoma. Clinical Cases: Case 1: In a 58-year-old man with no neurological symptoms; bilateral cataracts were detected during the initial diagnostic process. This patient had two siblings with xanthoma; one died from cerebral infarction and the other from biliary tract cancer. Another sibling had premature acute cardiovascular disease without xanthomas. Baseline lipid profiles were nearly within the normal range, while lipoprotein A was approximately 2.5 times higher than the normal. CTX was confirmed by the detection of a homozygous mutation in the CYP27A1 gene and high plasma cholestanol level (8.5 mg/L; reference range 0.0–5.0 mg/L). He has been taking oral CDCA (250 mg, three times daily). Case 2: In a 24-year-old man with no neurological symptoms or intellectual disability, premature bilateral cataracts were detected 1 year prior to diagnosis of CTX. None of his family members had xanthoma or premature cardiovascular disease. Lipid profile showed a similar pattern to that of Case 1; CTX was confirmed by the detection of a homozygous mutation in the CYP27A1 gene and high plasma cholestanol level (21.33 mg/L). One year after starting CDCA (250 mg, three times daily), cholestanol levels dropped to 7.34 mg/L. They were measured annually and identified as 5.08 mg/L, 4.2 mg/L, 4.7 mg/L, and 3.8 mg/L at 24, 38, 61, and 72 months, respectively. It took approximately 2 years for the normalization of his cholestanol level. There were no recurrences of xanthoma or progression of complications in target organs after 6 years of treatment. Conclusion: Early diagnosis improves the outcomes of CTX, allowing proper treatment. Bilateral cataracts caused by cholestanol buildup on the crystalline lens due to CTX usually occur within the first three decades of life. This manifestation does not occur in patients with xanthoma, familial hypercholesterolemia, or sitosterolemia. Taken together, this report suggests that premature bilateral cataracts are a specific marker that can accelerate early diagnosis of CTX. References: (1) Duell PB et al. Diagnosis, Treatment and Clinical Outcomes in 43 Cases with CTX. Journal of Clinical Lipidology. 2018;12:1169 (2) Salen G, Steiner RD. Epidemiology, diagnosis, and treatment of CTX. J Inherit Metab Dis 2017: 40:771

Cardiovascular Endocrinology

CARDIOVASCULAR ENDOCRINOLOGY AND LIPIDS DISORDERS CASE REPORT

Trimethylaminuria and Vascular Complications

Antonio Fernandes Oliveira-Filho, MD1, Paula F V Medeiros, MD, PhD2, Renata N. Veloso, Miss3, Erika C S Lima, Miss1, Inna M. Aquino, Dr, Miss4, Adriana Bezerra Nunes, MD, MSc PhD5.

1Endocrinology Clinic Dr Antonio Fernandes, Campina Grande, Brazil, 2Federal University Campina Grande, Campina Grande, Brazil, 3Federal University Rio Grande Norte, Natal RN, Brazil.

Background: Trimethylaminuria (Fish-Odour Syndrome) is a rare metabolic disorder characterized by an unpleasant odour in body secretions similar to rotting fish. The disorder is most commonly caused from mutations affecting the Flavin containing monoxygenase 3 (FMO3) gene, the vital enzyme for the metabolism of trimethylamine. Although uncommon, it is important to be conscious of this condition, which can be devastating psychosocially even with reliable diagnostic tests. We present here an individual with this syndrome who, in addition to the psychosocial difficulties, presented physical complications that we relate to the disease’s physiopathology. Case: R.M.F., 56 years old, lawyer, self-diagnosed at 25 after identifying himself with a disease description in a local newspaper. He describes fish odour symptoms from infancy and his mother used to demand excessive hygiene habits. He has always suffered from social disturbances. At 44, a physician’s investigation detected FMO3 mutation. The patient is not obese, has never smoked and denies any comorbidity, except erectile dysfunction for 10 years. He presented 4 years ago extensive acute venous thrombosis in the right lower limb femoral veins, lateral and medial gastrocnemius, solar and fibular popliteal veins. Laboratory investigation excluded other causes and negative antibodies. Besides, ENMG confirmed last year peripheral motor sensitive polyneuropathy, axonal pattern, distal both lower extremities. The patient failed treatment with modifications in diet and hygiene, but achieved symptomatic improvement after metronidazole. Genetic analysis showed a new homozygous variant in the FMO3 gene, with substitution of adenine for cytosine and exchange of Threonine for proline at position 307 of the FMO3 protein with protein dysfunction computably predicted. Comments: Considering the deep venous thrombosis and symmetrical peripheral neuropathy developed by the patient, we searched for a possible association with TMAU but we did not find previous reports. However, Weifei Zhu et al. (Circulation, 135(17), 1671–73, 2017) have shown TMAO generated by gut microbes contributing to platelet hyper reactivity and causing a prothrombotic phenotype in vivo. Plasma TMAO levels could predict incident thrombosis risk. Also, direct TMAO exposure enhanced platelet activation from multiple agonists stimulus. Although the “chemical sensor” for TMAO within platelets remains unknown, these findings could increase our understanding of the relationship between TMAO and CVD risk. Although the disorder might not appear to be a significant health problem, its social and psychological burden can be devastating, since the few treatments available provide modest benefits. In addition, it may be associated with other complications, including CVD, to which we would like to draw attention with this report.