MILD TRIMETHYLAMINURIA SEEN IN JAPANESE SUBJECTS WITH LIVER DAMAGE

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Trimethylaminuria (TMAU), or fish-like odor syndrome, is thought to be a genetic disease characterized by excretion of excessive unmetabolized trimethylamine (TMA). Individuals suffering from TMAU have a decreased capacity to oxidize free malodorous TMA to non-odorous trimethylamine N-oxide (TMAO) by the polymorphic flavin-containing monoxygenase form 3 (FMO3). Other TMAU-causing factors such as viral infection, hormonal modulation, and intake of competitive FMO3 substrates have been suggested in TMAU patients while there is no clear evidence for the involvement of liver damage. We report herein data supporting the idea that liver damage can be an additional factor causing TMAU. Several TMAU-affected individuals among self-reported males and females suffering from malodor in Japan had no apparent mutations in the coding regions of the FMO3 gene previously observed in severe TMAU cases of Caucasians. In a total of 41 subjects, there were significant inverse correlations between the FMO3 metabolic capacity, defined as the urinary ratio of TMAO to total TMA (% of TMAO/(TMA+TMAO)), and lactate dehydrogenase (LDH, $r = -0.53$, $p < 0.05$) and aspartate aminotransferase (AST, $r = -0.62$, $p < 0.05$). The FMO3 metabolic capacity did not correlate with the levels of alanine aminotransferase (ALT) in all subjects tested, while it highly correlated with ALT in the confirmed TMAU-affected patients by urine analysis ($r = -0.80$, $n = 8$, $p < 0.01$). Since ALT is a more specific marker of liver damage than AST or LDH used for screening, these results suggest that liver damage could be associated with one of the causal factors of low metabolic capacity associated with TMAU. Cure of serious liver damage is expected to improve TMAU status in these patients.