Case 3
Strong fishy body odor

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Patient: A 55-year-old Thai female from Bangkok

Chief complaint: Foul-smelling body odor for 20 years

Present illness:
● She had rotten fish-like body odor, which was detected by herself, her mother and her friends.

● The fishy odor did not relate to any activities or conditions.

● She used fragrance, antiperspirant deodorant, bathed more frequently, avoided eating garlic and spices, took oral metronidazole intermittently (as the internet suggested), but did not see any improvement.

● Her mother also faced with the same problem, but with less severity.

Past history: unremarkable

Skin examination and other physical examination:
● Fishy body odor was detected without other abnormalities

Investigation:
Gene sequencing: heterozygous mutation of FMO3 gene Val257Met(0769G>A) in exon 6

Diagnosis: Primary trimethylaminuria

Treatment:
● Activated charcoal 500 mg three times daily
● Low choline and trimethylamine diet

Discussion:
Trimethylaminuria is a rare metabolic disorder, autosomal recessive inheritance that was first described by Humbert et al. in 1970.1 200 cases have been reported worldwide but only 5 cases have been reported in Thailand, according to Thithapandha et al.2,3

A distinct clinical feature of this condition is self-declaration of fishy body odor or detection by family members, relatives or friends, since childhood or early adulthood. The fishy odor is caused by a defect in hepatic trimethylamine metabolism (N-oxidation of TMA) causing excessive malodorous trimethylamine excretion in sweat, breathe, saliva, urine and vaginal secretions. The fishy odor may be enhanced following exertion, emotional change or an increased in temperature.1,4

Primary trimethylaminuria is due to deficiency of flavin-containing monooxygenase 3 enzyme (FMO3) secondary to a mutation in the FMO3 gene.
Secondary trimethylaminuria is an acquired form without the gene mutation or inactivated FMO3 gene. In this form, FMO3 enzyme is overloaded by excessive dietary precursors (choline, trimethylamine-N-oxide, carnitine and lecithin), intestinal bacterial overgrowth, severe hepatic disease or hormonal inhibition of TMA oxidation prior to and during menstruation.1,5

Eggs, legumes (e.g., beans, soybeans), Brassica vegetables (e.g., cauliflower, broccoli), liver and offal (e.g., kidney, intestine) are known to contain high choline and can exacerbate the fishy odor in patients with TMA. Marine fish, cephalopods (octopus), crustaceans (e.g., shrimp, crabs) food supplements and alternative diets can also contain choline, carnitine and lecithin, which may exacerbate this condition.1,6,7

The associated conditions that have been reported include Prader-Willi syndrome, seizures, epilepsy, psychosocial problems (social anxiety, depression, low self-esteem, career disadvantages).8-12 The diagnostic laboratory tests include free urine TMA excretion and oxidizing ratio of TMAO and TMA. However those are not useful in less severe cases. Choline loading test, which puts patients on choline and trimethylamine diet for 3 days and analyzes urine TMA and TMAO can be useful in carrier detection. Finally, gene sequencing can detect FMO3 gene mutation.13,14 The most common mutation is c.458C>T (p.Pro153Leu), followed by c.913G>T (p.Glu305X) mutation.1

Therapeutic approaches are based on dietary restrictions (low choline and low trimethylamine). Fresh water fish may be eaten freely. Restriction of choline intake, particularly in young developing infants, children, pregnant and breastfeeding women is not recommended. Folate supplement should be added when restricting choline intake.1,13 Antiperspirants, deodorants and frequent bathing using soaps and body lotions with low pH (5.5-6.5) can help reduce the fishy odor.13,15 Intermittent antibiotics (metronidazole, amoxicillin and neomycin sulfate), reducing and modulating intestinal bacteria, may be beneficial in patients with clinical and social problems.4,13 Activated charcoal 1.5 g/day for 10 days and copper-chlorophyllin 180 mg/days for 3 weeks had been reported to improve quality of life of patients, by decreasing TMA and increasing FMO3 enzyme activity.16 Riboflavin, a cofactor of FMO3 enzyme, can enhance FMO3 activity. Manning, et al. reported a successful treatment with riboflavin in a patient with homocysteinuria and trimethylaminuria.1,17

Genetic counseling plays a crucial role, especially in primary trimethylaminuria. The course of disease, exacerbating factors and therapeutic options should be discussed with patients. Confirmatory investigations in suspected family member, establishing early diagnosis and prompt initiation of treatment will improve quality of life and prevent psychological problems.

The diagnosis of primary trimethylaminuria was made. According to the distinct clinical feature of fishy body odor and gene sequencing, which revealed newly identified mutation contributed to trimethylaminuria.

Our patient previously treated herself with metronidazole for a while, but her condition did not improve. Consequently, we started activated charcoal 500 mg three times per day. After treated with activated charcoal, the fishy odor dramatically subsided. We also performed gene sequencing for her mother, who had the same problem, but the result is pending.
References: