EJCRIM
European Journal
of Case Reports
in Internal Medicine

TRIMETHYLAMINURIA IN A 58-YEAR-OLD MALE WITH LIVER CIRRHOSIS AND HEPATITIS C

Martina Knapp

Praxis 54, Primary Care Clinic, Pfaeffikon, Switzerland

Corresponding author's e-mail: martina.knapp@hin.ch

Received: 12/05/2025
Accepted: 19/05/2025
Published: 13/06/2025

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Written informed consent from the patient for this publication has been obtained and is available on request.
This article is licensed under a Commons Attribution Non-Commercial 4.0 License

How to cite this article: Knapp M. Trimethylaminuria in a 58-year-old male with liver cirrhosis and hepatitis C. *EJCRIM* 2025;**12**:doi:10.12890/2025_005520

ABSTRACT

Trimethylaminuria (TMAU), also known as fish odor syndrome, is a rare metabolic disorder resulting from a deficiency in the enzyme flavin-containing monooxygenase 3, which is responsible for the detoxification of trimethylamine produced during the metabolism of certain foods. This case report describes a 58-year-old male who presented with a sudden onset of fish-like body odor, diagnosed with secondary TMAU likely triggered by liver cirrhosis and dietary supplements. The report outlines the clinical presentation, diagnostic approach, and management strategies for this rare condition.

KEYWORDS

Trimethylaminuria, fish odor syndrome, secondary TMAU, TMAO, carnitine supplements

LEARNING POINTS

- Doctors must be aware of the side effects of dietary supplements and actively ask about their use.
- Trimethylaminuria is a rare metabolic disorder, but doctors should be aware of it.

INTRODUCTION/BACKGROUND

Trimethylaminuria (TMAU) is a metabolic disorder characterized by the accumulation of trimethylamine (TMA) in the body, which causes a distinct fish-like body odor. TMA is typically produced during the digestion of choline- and carnitine-rich foods, and it is normally metabolized by the liver enzyme flavin-containing monooxygenase 3 (FMO3) *(Fig.1)*. In patients with TMAU, this enzyme is either deficient or impaired, leading to the accumulation of TMA[1].

TMAU can present in two forms:

- *Primary TMAU:* A rare genetic disorder caused by mutations in the FMO3 gene, resulting in a congenital deficiency of the enzyme[2].
- *Secondary TMAU:* This form occurs due to factors such as liver dysfunction (including cirrhosis), hepatitis, or a diet rich in choline and carnitine, all of which can overwhelm the body`s ability to process TMA[2,3].

CASE DESCRIPTION

A 58-year-old male, originally from the USA and living in Switzerland for the past 10 years, presented to the primary care clinic with a new onset of a strong, fish-like body odor, which had persisted for two days. The odor was first noticed by his colleagues at work, although the patient himself was unaware of it. He reported increased sweating but denied any nocturnal sweating. There were no recent changes in his

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

medications. He also denied any other systemic symptoms, including weight loss, fever, or gastrointestinal disturbances.
Medical history:

- *Chronic hepatitis C (genotype 1A):* Diagnosed in 28 years ago, likely acquired in 1985 after an automobile accident with multiple fractures and transfusion requirements.
- *Liver cirrhosis (Child-Pugh A):* Diagnosed 10 years ago, actual model for end-stage liver disease (MELD) score of 6. The patient is under regular follow-up with FibroScan, with the most recent measurement in November 2022 showing liver stiffness of 10.2 kPa (previous in June 2022: 22.3kPa), controlled attenuation parameter (CAP) median 295 dB/m (previous in June 2022: 336 dB/m).
- *Diabetes mellitus type II:* Diagnosed 11 years ago, with associated polyneuropathy and diabetic retinopathy, currently managed with Insulin degludec.
- *Osteopenia:* Noted in the femoral neck (T-score -1.3), with normal bone density in the lumbar spine.
- *History of alcohol use:* Former alcohol abuser, with two previous inpatient detoxifications.

Social History:

- *Living situation:* Lives alone, divorced, no children.
- *Occupation:* Works in international billing.
- *Lifestyle Habits:*
  - *Alcohol:* Drinks up to 4 beers (500 ml each) per evening on weekends.
  - *Tobacco:* Smokes 20 cigarettes per day (cumulative 30 pack-years).
  - *Drug use:* No use of illicit drugs.

Clinical Examination:

- *General Appearance:* Well-groomed, but with a noticeable fish-like odor.
- *Vital signs:* Slightly elevated blood pressure (138/92 mmHg).
- *Physical examination:*
  - Cardiovascular and pulmonary exams were unremarkable.
  - The patient's body mass index was 26.7 kg/m^2, his weight was 78 kg and his height was 171 cm.

The patient had made recent lifestyle changes, including a low-carbohydrate diet with a significant increase in protein intake. He also resumed bodybuilding activities, training three times a week, and successfully lost 10 kg in the past 5 months. Additionally, he had been taking 1000 mg of L-carnitine before each workout as part of his supplement regimen.
The characteristic fish-like odor suggested the possibility of TMAU, particularly in the context of liver cirrhosis and supplementation with L-carnitine, which is a precursor for trimethylamine production.
Diagnostic workup:

- *Trimethylamine N oxide (TMAO) levels:* Blood testing revealed elevated levels of TMAO, with a value of 28.5 µmol/l, which is well above the upper limit (>15.9 µmol/l).
- *Liver function tests:* Mild hepatic dysfunction consistent with cirrhosis but no acute hepatic failure (aspartate aminotransferase 34 U/l, alanine aminotransferase 39 U/l, gamma-glutamyl transferase 104 U/l, Bilirubin 9 µmol/l, international normalized ratio 1.0)
- *Genetic testing:* The patient did not undergo genetic testing, as the diagnosis was strongly suspected based on clinical and biochemical findings[2]. However, primary TMAU could not be ruled out based on family history or genetic confirmation.

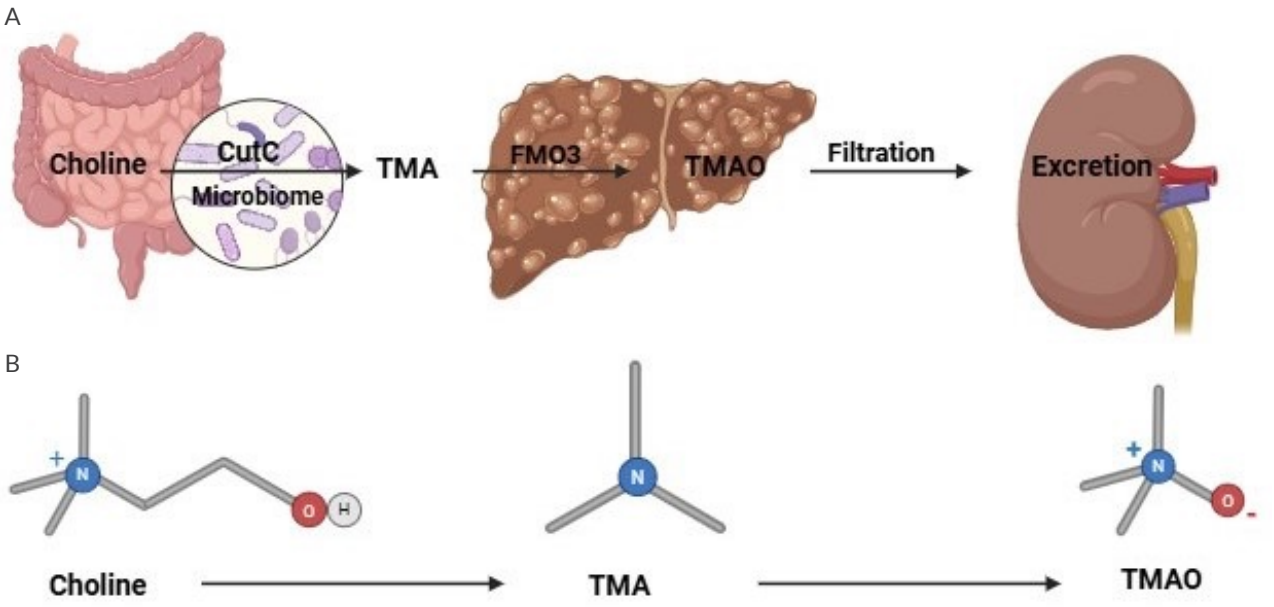


Figure 1. Trimethylamine N-Oxide (TMAO) accumulation in serum. A) The microbiome-liver-kidney axis regulates TMAO production and accumulation. Choline and related compounds from dietary animal proteins and fats are metabolized by gut bacteria expressing choline utilization cluster (Cut) genes including Escherichia coli. The resultant trimethylamine (TMA) is absorbed by enterocytes and metabolized by hepatic flavin-containing monooxygenase (FMO) enzymes. Serum TMAO is excreted via renal glomerular filtration and uptake by proximal tubular cells through organic cation transport proteins. B) Choline, TMA, and TMAO structures[3]. This figure was created with biorender.com.

The elevated TMAO levels, along with the patient's medical history of liver cirrhosis and recent dietary and lifestyle changes, were consistent with secondary TMAU, most likely exacerbated by the use of L-carnitine supplements, which are rich in the precursor for TMA production.

Treatment and management:

- *Immediate cessation of supplements:* The patient was advised to discontinue the L-carnitine supplements, which likely contributed to the elevated TMA production.
- *Dietary recommendations:* The patient was placed on a choline- and carnitine-restricted diet, which involved avoiding foods such as eggs, fish, meat, and cruciferous vegetables (e.g., broccoli)[4].
- *Monitoring*: Follow-up testing for TMAO levels was arranged.
  - *Follow-up TMAO level (2 months after diet change):* The patient's TMAO levels decreased to 5.3 µmol/l, indicating a significant reduction in trimethylamine accumulation after dietary modification and cessation of supplements.
- *Psychosocial support:* Due to the social and psychological impact of the condition, counseling was offered to help the patient cope with the stigma of the odor and manage any associated anxiety. The patient declined this offer.

DISCUSSION

TMAU is a rare metabolic disorder that can manifest in two forms: primary and secondary. In this case, the patient's liver cirrhosis likely contributed to impaired metabolism of TMA, a condition commonly seen in secondary TMAU. The liver's reduced ability to metabolize trimethylamine due to cirrhosis, combined with the intake of L-carnitine, a precursor to TMA, led to the accumulation of TMA in the body.

The management of secondary TMAU is largely dietary, with restrictions on choline and carnitine intake to limit TMA production[4]. The cessation of L-carnitine supplementation was the most effective measure in this patient, resulting in a dramatic improvement in loss of the fishy odor.

REFERENCES

1. Cashman JR, Zhang J, Leushner J, Braun W, Thummel KE, et al. Biochemical and clinical aspects of the human flavin-containing monooxygenase form 3 (FMO3) related to trimethylaminuria. *Curr Drug Metab* 2003;**4**:151-170. doi:10.2174/1389200033489505
2. Fraser-Andrews EA, Manning NJ, Ashton GHS, Eldridge P, McGrath J, Menagé HdP. Fish odour syndrome with features of both primary and secondary trimethylaminuria. *Clin Exp Dermatol* 2003;**28**:203-5. doi:10.1046/j.1365-2230.2003.01230.x
3. Mohan V. K, George M. A Review of The Contribution of Gut-Dependent Microbiota Derived Marker, Trimethylamine N-oxide (TMAO), in Coronary Artery Disease. *Curr Res Nutr Food Sci* 2021;**9**. doi :10.12944/CRNFSJ.9.3.01
4. Rehman HU. Fish odor syndrome. *Postgrad Med J* 1999;**75**:451-452. doi: 10.1136/pgmj.75.886.451