Madam Felicia Tan with her five-year-old daughter Elvia Lim, who was diagnosed with maple syrup urine disease when she was 14 days old. Elvia underwent a liver transplant in 2022 to treat the metabolic disorder and is now an active pre-schooler with a voracious appetite. ST PHOTOS: ONG WEE JIN

MedicalMysteries

Her daughter's sweet scent hid a rare, deadly condition

Genetic metabolic disorder is treated with lifelong diet restricting protein intake

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Sugar and spice, and all things nice – that was what Madam Felicia Tan thought little girls were made of when her daughter Elvia Lim was born in 2019.

"My firstborn, a boy, cried throughout the night. Elvia was different. She smelled as sweet as maple syrup. She hardly cried and always slept," the 36-year-old housewife said, telling The Straits Times that she was blessed to have a baby girl who was naturally this way.

What Madam Tan did not know was that her daughter's sweet fragrance hid a sinister underlying condition.

But she noticed that Elvia, at a week old, was not drinking enough breast milk. Concerned, she contacted Thomson Medical, where she had given birth.

"I thought the issue was mine, so I made an appointment with the lactation consultant and I brought her along," Madam Tan said.

The lactation nurse told the parents to rush the newborn to the emergency department at KK Women's and Children's Hospital.

Elvia was taken to the intensive care unit after she was diagnosed with maple syrup urine disease (MSUD).

She was then 14 days old.

In this rare inherited genetic metabolic disorder, the body cannot process certain amino acids, especially leucine, causing a harmful build-up of substances in the blood and urine. Amino acids are formed when protein in food is digested.

A sudden, severe spike in leucine in the blood can cause brain swelling and damage, seizures, long-term intellectual disability, and even death when left untreated.

Chronic elevations in leucine, even at moderate levels, can predispose individuals to brain damage.

The severity of MSUD ranges from mild or intermittent to severe, the most common form.

A baby with the severe disease may not survive more than a few weeks without treatment.

Leucine is an essential amino acid needed for the healing of skin and bones, and increased muscle growth and lean body mass. It is found in all protein-containing foods, so MSUD is treated with a strict, lifelong diet that restricts protein intake.

When Elvia was first admitted to hospital, her skin was mottled.

"I was told her toxic amino acid levels were more than 3,600 and that she should have been critical, but she was able to breathe on her own and there was no fever. After they brought the levels down, she was allowed home," Madam Tan said.

Several months later, she and her husband Andy Lim learnt that liver transplantation was an effective long-term treatment for the disease, and decided to pursue this option to give their daughter a shot at a better future.

MSUD affects an estimated one in 180,000 babies born.

"In Singapore, we expect one child in every five to six years to have this condition, and, as far as I know, we already had three in the last 18 years," said Associate Professor Denise Goh from the National University Hospital (NUH), who was part of the team that managed Elvia before and after her transplant surgery.

In some cases, the babies are very ill and exhibit symptoms, leading doctors to suspect the disease.

But with advanced newborn screening, many cases are now picked up before the babies become severely sick, explained Prof Goh, who heads the genetics and metabolism division in the department of paediatrics at NUH.

Newborn screening is optional, and Madam Tan did not opt for it.

But at three months old, Elvia was back in hospital as she had stopped drinking and swallowing milk.

She was found to have laryngomalacia, a common disorder in babies where the tissues above the voice box soften and fall over the airway.

"The doctors' attention was on her MSUD so her laryngomalacia was missed," her mother said. "She had to have a gastrostomy tube inserted to feed fluid and nutrients directly to her stomach."

Elvia spent three months in the hospital, and had to continue the tube-feeding at home.

"She had to be fed every two hours and her stomach capacity then was only 100ml," her mother said.

It was a very trying period, and Madam Tan said she was racked with guilt, wondering if it was the right decision to have the gastrostomy tube inserted.

Her daughter's skin was breaking down due to her nutritional deficiency, and she had to be admitted to hospital each time the tube leaked or when the baby was having a fever.

It was during this time that Elvia's parents learnt about the promising results liver transplantation could have for MSUD.

"It was by chance that surgeons in the United States discovered that liver transplant was an effective cure for MSUD," Prof Goh explained. "A girl with MSUD required a liver transplant after she was given too much vitamin A, and it turned out to be an effective cure."

The team who managed Elvia before and after her liver transplant surgery: (from left) Adjunct Associate Professor Vidyadhar Mali, Associate Professor Denise Goh and Assistant Professor S. Venkatesh Karthik.

The Lims moved their baby to NUH, where Madam Tan sought out Adjunct Associate Professor Vidyadhar Mali, surgical director of the paediatric kidney and liver transplantation programmes.

"I knew of Dr Mali through an article about a previous case of MSUD, so we went to the emergency room at NUH and demanded to see him," Madam Tan recalled.

It was an eight-month wait before a suitable living donor was found.

"Usually we would ask one of the parents to donate, but in Elvia's situation, part of the genes that caused her MSUD came from the parents, which meant that we could not take any of their livers," Prof Mali explained.

"In such situations, we either put the child on the national waiting list or we look to the National Organ Transplant Unit for an altruistic anonymous living donor."

Prof Mali said: "Things were happening in parallel. Elvia had come to us with feeding issues, and we were sorting that out. At the same time, tests were being carried out to ensure the donor was suitable and healthy."

Prof Goh said Elvia's MSUD made the transplant more challenging.

To ensure that she would be strong enough for the operation, Elvia was taken off gastrostomy tube-feeding the day before the transplant and fed a special nutritional formula intravenously.

This provided her little body with the nutrients, including special amino acids that did not cause her MSUD to worsen.

The formula was specially prepared by hospital pharmacists with special amino acids sourced from around the world.

The surgery was finally carried out in 2022, when Elvia was three.

Elvia received a third of the donor's liver in an operation that took about 10 hours.

"The liver needed to work immediately, otherwise Elvia would develop a metabolic crisis," said Prof Mali.

Elvia's pre- and post-surgery nutritional health was taken care of by Assistant Professor S. Venkatesh Karthik, a senior consultant with the paediatric liver transplantation programme.

Fondly dubbed Elvia's "foster father" by her parents and her other doctors, he will be managing her until she is 21.

Prof Karthik said children like Elvia would need lifelong immunosuppression medication to prevent the body from rejecting the organ.

They would have to avoid raw foods and probiotics and observe basic hygiene to avoid infections.

The first year after the transplant would be the most challenging, as this is typically when rejection happens, he added.

Two years on, Elvia now attends pre-school, plays with her classmates and – other than avoiding probiotic foods like yoghurt, sourdough bread and Yakult or Vitagen – eats like any other voracious child.

"This means that her liver is doing well and it is playing catch-up, catch-up with all the nutrients the body needs. Being very active, it is not surprising that Elvia is hungrier than before," Prof Mali said.

Elvia is no longer the sweet-smelling angel her mother thought she was.

"Instead, her teachers have given her a new nickname – the little hungry monster," Madam Tan said, laughing.

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• Medical Mysteries is a series that spotlights rare diseases or unusual conditions.