Medical Mysteries

This is a series that spotlights rare diseases or unusual conditions.

Genetic condition gives 9-year-old 'cafe au lait' spots on body

Girl's condition discovered after pain behind left ear led to hospital visit in 2023

Judith Tan
Correspondent

Phoebe Hu with her doctors – (from left) geneticist Nikki Fong, paediatric dermatologist Valerie Ho and Haematology and Oncology Service senior consultant Enrica Tan – at KK Women's and Children's Hospital. ST PHOTOS: HESTER TAN

Where the marks on Rumi from Netflix's animated film KPop Demon Hunters are purple, those on nine-year-old Phoebe Hu's arms and body are light brown.

As a result, she is often bullied in school, with her schoolmates making unpleasant remarks about her skin.

Often called "cafe au lait" spots by doctors, the flat, light to dark brown birthmarks that resemble "coffee with milk" on Phoebe's skin are the underlying signs of a genetic condition known as neurofibromatosis Type 1 (NF1).

NF1 causes changes in skin pigment, including flat, light brown spots and freckles on the armpits and groin.

It also causes the slow growth of benign tumours that develop on or under the skin from nerve cells. These tumours, called NF tumours, can appear as soft lumps throughout the body.

Phoebe's condition was discovered when she began having pain behind her left ear around March 2023, said her mother Pearlyn Goh, 42.

She was taken to KK Women's and Children's Hospital (KKH) and an MRI scan, three doctors and a genetic test later, Phoebe was diagnosed with NF1.

"Apart from the brown spots on her arms and parts of her body, the scan also showed that Phoebe has a tumour behind her left ear and another near her brain stem," Madam Goh said.

She told The Sunday Times that her research revealed that children with NF1 often have special needs related to learning, such as difficulties with attention and memory. However, Phoebe does not exhibit these difficulties, which is a relief, she shared.

Dr Nikki Fong, a geneticist with KKH, explained that there is a 50 per cent likelihood of NF1 being passed on if one parent has it.

"It can also occur spontaneously from a new gene change," she said, referring to what is also known as gene mutation.

Subsequent investigations revealed that Phoebe's father James Hu, 43, a taxi driver, also has the condition, though his was not inherited from either of his parents.

Like Phoebe, Mr Hu has the "cafe au lait" spots only on his arms, legs and body, "except for this large lump at the back of my head, which is a benign NF tumour", he told ST.

"As I did not know what it was, it was not detected until adulthood," he added.

According to Clinical Assistant Professor Chiang Jianbang from the Cancer Genetics Service at the National Cancer Centre Singapore (NCCS), the adult patients seen at NCCS typically fall into one of two categories: those who were not diagnosed during childhood and those who, despite an initial childhood diagnosis, did not pursue follow-up care as they grew older.

Dr Chiang said that as young NF1 patients transition into adulthood, they often feel capable of managing their own health and symptoms, leading them to believe that regular follow-up appointments are no longer necessary.

He said that it is important for NF1 patients to be regularly monitored as they are at a higher risk for hypertension and various cancers.

"By the age of 50, the risk of cancer in NF1 patients can be as high as 40 per cent, compared with the 5 per cent in the general population," he said.

Treatment for NF1 focuses on supporting healthy growth and development in children and early management of complications.

Dr Enrica Tan, a senior consultant with the Haematology and Oncology Service at KKH, said: "Phoebe was also in a lot of pain, and the pain was making her sick."

The painkillers she was previously prescribed were not effective and also affected her appetite.

Phoebe is now prescribed selumetinib, a medication that treats the benign tumours – called plexiform neurofibromas – in children with NF1. It stops the growth of the tumours and shrinks them, improving pain and other symptoms.

"She is good at taking her meds and takes them like clockwork. She wakes up early to ensure she takes her medicine at 6.45am before school on weekdays, and at 7pm," Madam Goh said.

"On weekends, she wakes up a bit later and takes them at around 9am without prompting."

Paediatric dermatologist Valerie Ho, a senior consultant at KKH's department of dermatology, manages Phoebe's skin condition as there is a need to monitor closely for potential side effects from the medication, such as dry skin, eczema and acne.

As Phoebe grows, she would have to be monitored for other manifestations of the condition such as scoliosis or the curvature of the spine, one of the more common deformities linked to NF1.

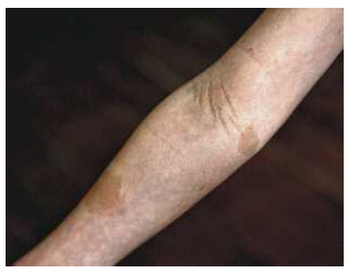
"This is why children with NF1 need to be managed by a multidisciplinary team, which also includes a psychologist to manage the psycho-social impact of the condition," she added.

To help Phoebe understand that there are others who also live with NF1, the family attends events organised by the Neurofibromatosis Society (NFS) Singapore and by KKH.

NFS is a new patient-led group formed to support individuals with neurofibromatosis.

Madam Goh said: "There, she has made friends with other children who have similar spots to hers. At least she knows she is not alone in this fight against her own 'demons'."

judith@sph.com.sg



The "cafe au lait" spots – birthmarks that resemble coffee with milk – on Phoebe's arms made her a target of bullying in school.

GREATER RISK

By the age of 50, the risk of cancer in NF1 patients can be as high as 40 per cent, compared with the 5 per cent in the general population.

CLINICAL ASSISTANT PROFESSOR CHIANG JIANBANG, on how NF1 patients are at a higher risk for various cancers.

Patient-led group gives social, community support for sufferers of neurofibromatosis

Patients with a rare genetic condition called neurofibromatosis have come together to provide emotional, psycho-social and financial support for one another as well as others with the disorder.

They have formed a group, called the Neurofibromatosis Society (NFS) Singapore, which was registered with the Registry of Societies in August.

Neurofibromatosis, or NF, is a rare genetic condition that causes the development of non-cancerous tumours affecting nerves on the skin, brain, spinal cord and other parts of the body.

In Singapore, the number of individuals with NF is estimated to be in the hundreds, with NF Type 1 (NF1) being the most common diagnosis. This condition manifests through symptoms such as multiple flat, light brown spots on the skin, known as "cafe au lait" spots, and neurofibromas – soft bumps under or on the skin.

These patients are primarily treated at the National Cancer Centre Singapore and KK Women's and Children's Hospital (KKH), where they receive comprehensive care from multidisciplinary teams.

A much rarer form of NF is the Type 2 variant (NF2), which causes non-cancerous tumours to develop around nerves in the brain and spinal cord. Its symptoms include hearing loss and balance problems, and it often begins in the late teens or early 20s.

As NF is often underdiagnosed, many patients live with feelings of isolation and a lack of information, made worse by the social stigma and misunderstanding that come with the visible changes in appearance caused by the condition.

NFS co-founder Lai Chee Chong, 45, said: "As a child, living with NF affected my self-confidence. I found it difficult to make friends because people thought my condition was contagious. Now, I want to help create more awareness about NF."

Ms Yessika Sutawijaya, 44, who is also a co-founder, said: "There is power in connection. Knowing you are not alone on this journey can truly be life-changing, whether you are a child or adult. We hope that with NFS Singapore, we can help others on a similar journey find strength and live life fully, even in the face of challenges."

Dr Nikki Fong, a consultant with the Genetics Service at KKH, said: "Beyond medical treatment, young patients and their families need continual emotional and mental support. This group will play a pivotal role in addressing those unseen needs, complementing the clinical journey with peer and psychological support."

Judith Tan

Her world is dark and silent because of a rare disorder

Life for Ms Tan Siew Ling, 38, an assistant manager in the innovation division at SG Enable, is not only dark, but also silent.

Ms Tan lost her sight when she was 10 and, after fully depending on her hearing thereafter to navigate life, she also lost her auditory sense when she was 32.

"She was around the age of eight or nine when she complained she could not see very well. Thinking it was short-sightedness, our mother took her to the optician to get a pair of glasses made. It did not help her at all," her brother and primary caregiver Tan Yan Cai, 41, told The Sunday Times.

She was then taken to the Singapore National Eye Centre, where she was diagnosed with vision loss due to weak optical nerves. To prepare her for a life of blindness, she went to the Singapore Association Of The Visually Handicapped to learn braille, he said.

Determined not to let her visual impairment hinder her education, Ms Tan completed her secondary education, passed her A levels and pursued a degree in economics and finance at the London School of Economics and Political Science.

"I did so relying on my hearing and with close friends motivating me and cheering me on. I do not want to be a burden to anyone – not friends, not family. With my education and a well-paying job, I would say I am now financially independent," she said.

However, Ms Tan faced further challenges as her hearing began to deteriorate. In 2016, she lost hearing in her left ear, just a year after her mother's death. And in 2019, hearing in her right ear was gone too.

Dr Amanda Cheang, who is currently a consultant at the department of otorhinolaryngology at Woodlands Health, said when Ms Tan lost her hearing in her left ear, an MRI scan showed that it was because of a growth on the nerve responsible for hearing.

With her vision loss as a child and hearing loss in adulthood, doctors suspected she had neurofibromatosis Type 2 (NF2), a rare genetic disorder that causes benign tumours to grow on nerves, including those affecting the brain and spinal cord.

The estimated prevalence of NF2 is one in 50,000 people worldwide.

"NF2 is caused by mutations in the NF2 gene located on chromosome 22, which encodes a protein called merlin, which functions as a tumour suppressor. When it is inactive or defective, nerve cells can grow uncontrollably and form tumours," said Dr Cheang, who is also a visiting consultant at Tan Tock Seng Hospital (TTSH).

Adjunct Associate Professor Yeo Seng Beng, emeritus consultant at TTSH's department of otorhinolaryngology, said that while the tumours are benign, where they are located and their size can result in debilitating consequences.

For example, tumours compressing the hearing nerves can result in hearing loss, those on the optic nerves may lead to blindness, and those along the spinal cord can result in pain, weakness, or numbness in the arms and legs.

Dr Cheang said in most patients, these tumours grow slowly, so management typically involves periodic scans to monitor for any changes in their size.

"In patients with progressive or rapid growth in tumours, particularly tumours affecting the hearing and balance nerves, bevacizumab can be prescribed as a treatment option. It is given intravenously every few weeks over the course of several months, sometimes extending to long-term use," said Dr Cheang.

Bevacizumab is a laboratory-made protein that mimics the immune system's natural antibodies, enabling it to find and bind to a specific target, such as an antigen on a cancer cell or a virus.

Dr Cheang cautioned that careful evaluation is essential before starting this treatment, as it may lead to side effects such as kidney issues and elevated blood pressure.

In Ms Tan's case, she completely lost her vision due to the benign tumours affecting both optic nerves.

"She then developed bilateral vestibular schwannomas – tumours affecting the nerves responsible for hearing and balance – which led to the profound hearing loss. She also has multiple meningiomas – tumours arising from the lining of the brain – but fortunately, these have not caused any symptoms," Dr Cheang said.

Said Ms Tan: "I was angry and frustrated. I spent so much time and put in so much effort to maintain my independence, and then (the hearing loss) happened."

Nevertheless, she expressed gratitude to her close friends and her brother for "rallying in my corner".

In 2021, Ms Tan underwent right cochlear implant surgery to provide hearing stimulation in her right ear.

Her hearing rehabilitation journey is supported by TTSH staff Jocelynn Khoo, a senior audiologist who programmes her cochlear implant, and Francoise Lim, a principal speech therapist who oversees her post-surgical hearing rehabilitation.

Dr Cheang said: "While we were hopeful that she might regain the ability to understand speech through the implant, we were also mindful that the tumour affecting her right hearing and balance nerve could limit her outcomes compared with most patients.

Ms Tan Siew Ling says she takes life "a day at a time, hoping for the best". With her is her brother and caregiver Tan Yan Cai. ST PHOTO: BRIAN TEO

"After the surgery, she was able to perceive environmental sounds, such as the beeping of MRT doors and approaching footsteps. But, despite intensive rehabilitation, she was unable to achieve clear speech recognition."

To facilitate communication, her brother, an information technology engineer, discovered a Bluetooth-enabled keyboard that allows words to be translated into braille on a tactile display. Using this device, Ms Tan can "read" what he types and communicate more effectively.

Her groups of friends also take her jogging in the park, creating their own taps and hand signals to keep her safe during their jogs.

"Moving forward, she is being considered for an auditory brainstem implant, a device that sends hearing signals directly to the brainstem, bypassing the tumour affecting her hearing and balance nerve. This will be a more major surgery than the cochlear implant surgery and is still a work in progress," Dr Cheang said, adding that Ms Tan is now undergoing assessments to evaluate her eligibility for the procedure.

Ms Tan remains uncertain about what lies ahead for her. She admitted, her eyes welling up with tears, that she does not know how to hope or plan, whether for the immediate or distant future.

"I just take life a day at a time, hoping for the best," she said.

Judith Tan