Summary Medical Record

The patient is a 28-year-old Dutch woman whose chief complaint is tingling pains in her legs (feet, lower and upper legs) which started at the beginning of 2017.

In July 2018 her GP referred her to Internal Medicine with a 1.5-year history of tingling pains in the legs along with low vitamin B12 (87). The patient was also experiencing muscular pains, cramps and involuntary muscle spasms. She particularly complained of a burning sensation on the bottom of her feet and in her calves. Recently, she had started to feel tremors in her upper arm muscles as well. Physical examination and blood tests revealed no abnormalities.

In August 2018 the patient was seen again by the Internal Medicine specialist. Oral vitamin B12 supplementation had had no effect on her symptoms. The specialist indicated that he could do nothing for her and referred her to Neurology.

From August 2018 onwards, the patient was followed up by a neurologist. She had constant numbness, tingling and a burning sensation from the soles of her feet throughout her lower legs up to her knees. Additionally, she had stabbing pains in the lower legs (left>right), worse at night than during the day. As a result she slept poorly. She had cramps in her legs, arms, feet, wrists and fingers a couple of times per week, particularly in the evening. The GP had observed fasciculations, and the patient herself reported subcutaneous twitching in her arms and legs at least 10 times per day. She also experienced tingling sensations in the fingers of her left hand and stiffness which caused her difficulty in moving her hand. Her left leg sometimes felt stiffer than her right leg while walking. There were no fasciculations upon physical examination; sensitivity and mobility were intact. MRI of the spine showed no indication of myelopathy. The neurologist concluded that the patient was suffering from paraesthesia and burning pain in her feet and lower legs (left>right); most likely differential diagnosis: sequelae from a vitamin B12 deficiency. There were no indications of polyneuropathy or myelopathy. Amitriptyline 10 mg was prescribed (until February 2019), and initially this seemed to be effective for the pain. In December 2018, the skin on the patient's legs was painful when touched. In February 2019, an EMG was performed, which showed no indications of (small fibre) peripheral neuropathy.

In March 2019, the GP took a blood sample to test for Lyme disease (Borrelia IgM negative and Borrelia IgG positive). She had had a tick bite in 2011, and a subsequent erythema migrans behind the knee. She took a course of doxycycline, one 100 mg tablet twice daily for 4 weeks.

In May 2019 the patient was seen again by the neurologist. Her symptoms were non-specific for Lyme disease and MS, and an MRI was requested. MRI of the brain and lumbar spine in July 2019 showed no abnormalities. The neurologist offered a lumbar puncture but the patient was reluctant to consent so the procedure did not take place.

The patient's burning pain was increasing so the GP prescribed pregabalin, which was effective in the first few weeks (the pain almost went away), but later the symptoms returned.

In July 2019 the patient returned to the neurologist for a check-up. His diagnosis: idiopathic sensory disorder. She was then referred to the university hospital.

In July 2019 the patient attended the infectious diseases clinic in the university hospital for suspected Lyme disease. Her symptoms at that time were tingling pains and numbness in her legs and feet. Over the previous year and a half, the patient had developed shooting pains in the legs and numbness from the navel. She felt as if her legs and feet were on fire and her skin was sensitive to her clothing. She had 'pins and needles' in her feet. She was also still experiencing spasms in the corner of her mouth from time to time. Physical examination and blood tests (including total IgA, anti-tTG (IgA), anti-endomysial antibodies (IgA), HIV, anti-Treponema pallidum antibodies) showed no abnormalities. The infectious disease specialist concluded that the fatigue and pain in the legs was probably caused by an inadequately treated vitamin B12 deficiency and advised long-lasting parenteral supplementation; therefore vitamin B12 injections were started. Lyme disease was considered unlikely.

Starting in July 2019, the patient attended the original hospital's pain clinic. At that time, she was taking pregabalin 75 mg twice daily. MRI of the cervical and thoracic spine (September 2018) and MRI of the brain and lumbar spine (July 2019) showed no abnormalities. The anaesthetist concluded that the patient had idiopathic pain and sensitivity disorder in both lower legs and feet, probably as a result of Lyme disease. He prescribed a TENS machine, which had no effect. The last appointment was in August 2019.

As of now, she still has pain in both legs (left = right). This is a burning pain, as if boiling water has been poured over the legs. On average, the pain scores 8 and at its worst, it is a 10. When a severe pain episode happens, the pain starts off as a burning pain then turns into a feeling of numbness. It can also be burning and numb at the same time. These episodes last at least a couple of hours. She feels 'pins and needles' when walking. Tight jeans trigger unbearable pain in the legs so have to be removed. Leggings and tights are better. Cold weather, massage and crossing her feet all cause pain. The only situation in which she is pain-free is when she floats at the edge of a swimming pool and is truly weightless. The pain comes back straight away when she gets out of the water. When she lies in bed her symptoms are bearable, and propping up her legs also reduces the pain. She feels the least pain when she lies on her back with her legs up (as she was when she was born). She does not feel limited as to mobility, but the pain reduces her ability to concentrate and to enjoy things. Since summer 2019 she has had tingling and throbbing sensations in her fingertips and also burning pain (score of 6).

Getting to sleep is still a problem a couple of times a week, but not as bad as before. She often feels throbbing in the area between her lower back and buttocks, particularly in the morning. Her boyfriend notes that it feels very firm (left>right). Applying pressure via a hand flat on her lower back is extremely painful, using only the fingertips this is lessened. She also mentions that her right shoulder is higher and sits further forward. Her left hip sits further backward compared to the right, as if it had grown askew.

Previous medical history

Born breech, and with a fractured clavicle. Her legs stayed in an upward position after birth, but no X-ray of the pelvis was possible at that time. The problem resolved itself.

Jan 2018: Road accident on the motorway (hit the barrier at 130km/h (80mph) due to slippery conditions). Her symptoms worsened after this incident.

Travel abroad: She visited Bali and Australia in 2016.

In 2016 she had a droop in the corner of her mouth, which resolved by itself.

Specialists and other professionals consulted: Local hospital Internal Medicine physician (Jul 2018): Advice: Referral to neurologist

Neurologist (Aug 2018 – Jul 2019): no indications of polyneuropathy or myelopathy. Symptoms non-specific for Lyme disease or MS.

Pain clinic (Jul 2019 – Aug 2019): TENS tried, no effect.

University hospital: Internal Medicine / Infectious Diseases specialist (Jul – Sep 2019): fatigue and leg pain probably caused by inadequate treatment of B12 deficiency, long-lasting injections recommended. Lyme disease is unlikely.

Physiotherapy (2019): Possible piriformis syndrome. Treatment had no effect.

Rehabilitation (Apr – Sep 2019): psychological support, physiotherapy, manual therapy and dry needling. The pain symptoms are still present and unchanged.

Acupuncture (Jan – Mar 2020): no effect

Osteopath (Jul – Oct 2020): no effect

Medication history:

2018 Amitriptyline 10 mg once daily. Initially effective
2018 Cyanocobalamin 1000 ug tablet once daily. Taken for approx. 6 months

2019 Pregabalin 75 mg twice daily
2019 Vitamin B12 injections starting dose 2 per week 10 injections in July and August. In the period from October 2019 to March 2020: 4 injections of vitamin B12. Afterwards cyanocobalamin 1000 ug lozenges.

2020 Medicinal cannabis oil (CBD-THC combination) discontinued after a few weeks due to side effects

2021 Nortriptyline 10 mg once daily

Current medications:

Nortryptiline 10 mg once daily

Hydroxycobalamine 1000 ug inj. Once per 2 months

Lab results (abnormal values are in bold): March 2018 Vit B12 **87**pg/ml**=64** pmol/l, creat **95** umol/l

July 2018: CRP 3 mg/l Hb 8.9 mmol/l Ht 0.43 l/l MCV 86fl platelets 342x10^3/l leucocytes 5.2x10^9/l Na^+ 142 mmol/l K^+ 3.8 mmol/l creat 78 umol/l Cl^- 103 ppm bicarb 22.7 mmol/l Ca^{2+} 2.24 mmol/l Phos 1.12 mmol/l Mg^{2+} 0.82 mmol/l uric acid 0.26 mmol/l LDH 157 u/l CK 61u/l Chol 4.8 mmol/l albumin 43 g/l Alpha 1 glob 3.1% Alpha 2 glob 5.9% Beta glob 8.2% Gamma glob 10.9% TSH 1.65 mu/l fT4 17.2 pmol/l PTH 3.5 pmol/l Vit B12 400 pg/ml folic acid 13.5 nmol/l Vit D 95.2 nmol/l anti-parietal cell antibodies (APCA) neg; anti-intrinsic factor (IF) antibody neg; ANA neg anti-double stranded DNA (anti-dsDNA) neg.

July 2019 Vit B1 153 Vit B6 89 Vit B12 208 pg/ml methylmalonic acid (MMA) 136 umol/l folic acid **5.8 nmol/l** ferritin 26 g/l gluc 4.7 mmol/l Zn^{2+} 11umol/l Borrelia IgM neg**; IgG pos** anti-parietal cell antibodies (APCA) neg; anti- intrinsic factor antibody (IF) neg. Calprotectin <30 anti-tTG neg HIV 1/2 Ag neg + p24 ag neg Treponema Pallidum neg.

Nov 2018 Vit B12 301 pg/ml

Mar 2019 Vit B12 257 pg/ml

Oct 2019 Vit B12 605 pg/ml

Jan 2020 Vit B12 314 pg/ml

Jan 2020 CMV IgA neg **IgG pos;** Borrelia IgM neg **IgG pos**