2nd of April 2022

Concerning

Bendt Nielsen CPR: 030358 (mail aged 64)
Dr. Med. Sci, Specialist in hematology, and internal medicine

Reason for referral: Any use of muscles, including sitting up or starvation causes the following: Loss of muscle power, muscle pain, sleepiness and later confusion, nausea, cough or hoarseness and tingling in hand and feet. The level of muscle work or starvation needed to elicit symptoms has varied. But symptoms have become worse with time, and presently I am bedridden, but able to sit in a wheelchair while eating. Any overexertion causes the same symptoms for days or even weeks. I have normal strength in any muscle for the first few contractions, and no muscle atrophy.

Medical History:
Vasectomy
Paraumbilical hernia (surgery x 3 – since then no problems)
Nose surgery (deviation of nasal septum)
I have always had tendency to clinical hypoglycemia. For instance, I am sure to have hypoglycemia if I sleep to little, then go to work, then eat candy and drink coffee and start playing tennis. Sugar works within minutes. If I continue playing without sugar the symptoms eventually subsides, but I will have very sore muscles for a day. I have never measured my blood sugar.
2010: Angina treated with stent in the LAD. Since then, treatment with low-dose acetylsalicylic acid. Pronounced tendency to muscle spasms due to atorvastin and ended up on a dose of 10 mg with an acceptable cholesterol level. No cardiac problems since (see later)
2019: 3 mild bouts of diverticulitis. The symptoms have largely disappeared after a change in diet

Family history:
Father was unable to tolerate statins due to muscle spasms. Active sportsman all his life. Two brothers are both active sportsmen.
No known hereditary diseases in the family, no premature deaths.

Present story:
Usually very active, playing single tennis, running and doing work-out. From late summer 2020 unable to run as fast as normal. There were no difficulties with breathing and no muscular cramps, but if I exerted myself, I had very sore leg muscles the following day. There was no tenderness of muscles on palpation. When I did push up's, it was the same story. On the 12th of October I paused atorvastatin. Before that, I had a wide range of blood samples taken. The only abnormality was a slightly elevated CK. I was without medication for a month and thought the symptoms got better. CK was normalized. I switched to ezetimibe. Nonetheless, the symptoms progressed. From the beginning of January, I could only walk about 100 m at a slow pace before I had a pronounced tendency to cramps/weakness that started in the calves but spread to the rest of the body with pain radiating to both sides of the neck and out into the left lower jaw. Even at rest I had constant muscle pain in every part of my body. On the 22nd of January I was hospitalized. I was examined with blood samples for myocardial infarction, with echocardiography, coronary angiography, and later CAT scan of thorax but no explanation was found. CK was normal. Ammonium was not tested. I was discharged after a few days with ezetimibe, metoprolol and amlodipine. My symptoms got worse, so that I could only walk a few meters. The walking provoked a dry cough, and I became more and more "light-headed"/dizzy/confused. I had constant pain in every muscle and was sleeping all the time. I discontinued ezetimibe, metoprolol and amlodipine, and acetylsalicylic acid.
On the 5th of February I suspected a metabolic myopathy. As every shop with dietary supplement was closed due to COVID 19, I ate tartare in the evening and already felt better the next morning (apart from a clinically mild diverticulitis attack), so I have been eating raw minced beef ever since.

My condition improved very rapidly. Within days cough, hoarseness and the constant muscle pain that I had disappeared. I could think clear again, and I could walk much, much further (> 2 km at a slow pace) before I got symptoms. On the 15th of February, I was examined by a specialist in rheumatology. He ruled out inflammatory muscle disease. All examinations where normal except a CAT scan of the thorax, abdomen and pelvis with signs of diverticulitis.

I trained intensively and on the 18th of February I walked altogether 6 km, but as I had nausea/epigastric burn, I started 40 mg of pantoprazole (never tried this before). Within 12 hours I experienced pronounced muscle weakness, so I stopped pantoprazole, but the symptoms progressed, and at the 2nd of Marts I could walk less than 10 very small steps. Then I became more and more stiff, the muscles burn, and I am no longer able to move. It does not matter which of the major muscle groups I use it spreads to all other muscles. At the same time, I first became very tired, then unable to think clear, got difficulties from the airways with hoarse voice cough and stridor, and became nauseated. Afterwards it took hours to days to recover. The only possible neurologic abnormality was tingling on the upper site of hands and feet. Since then, I have had the same symptoms whenever overexerting myself or fasting, but the limit for use of muscles have varied as described later. I sleep all the time. A hot shower improves my muscle power.

I was only capable to cope in my own home with the use of wheelchair and assistance from my wife.

I was examined at Neurologic Department, Aarhus University Hospital on the 2nd of Marts. Only possible neurological abnormality was an increased patellar reflex, but normal reflexogenic zone.

On the 15th of marts. After blood sampling, I started a diet including raw beef meat, corn starch, Q10, creatine, B-combine, D-ribose, carnitine, Calcium-Magnesium-Citrate, MCT, and alpha lipoic acid 500 mg x 1. At the same time, I found out that I cannot tolerate starvation. If I did not eat for 2 or 3 hours, I developed symptoms either in the form of the clinical hypoglycemia that I have known from childhood, or symptoms as if I had overexerted myself, or a mixture of the two. Intake of sugar helped within 3- 10 minutes. I had to eat two times every night two avoid attacks. Measurements of blood sugar are normal.

I have had side-effects in the form of nausea and stomach pain from the food supplements– and have in periods paused or reduced them. I have in periods taken rifaximin (with good effect) to treat supposed bacterial overgrowth due to carnitine.

At the 17th of Marts, the first abnormal blood analysis showed up. Pyruvate is abnormal 195 (34-80). It has been repeated altogether 10 times. It has always been clearly elevated, reaching values that could not be measured. The two times I have felt worst is at the times with the highest levels. (Se “pyruvate levels”

From Marts I was very careful not to overexert myself and around the 13th of May I felt better and started training as hard as I could (as adviced from the department of Neurology). From the 13th of May, I increased the number of steps I could take before developing symptoms, as described above, from about 10 slow steps to about 100 slow steps at the end of May.

From approximately the 30th of May, I have a complete breakdown with rapid deterioration, and on the 22nd of June, I have symptoms of overexertion even if I lie completely still, including constant symptoms as if I have hypoglycemia. Sugar every hour helps a bit, but not enough to let me sleep. Any use of muscles worsens my symptoms.

I am admitted to hospital where I follow a regimen of complete rest, only eat white bread, or other carbohydrates, and are treated with intravenous glucose at night, where the nausea prevents me from eating. The neurologists made it clear that they found my symptoms hysterical (in modern terms “functional”), and made it clear that they would offer no form for treatment without a diagnosis. As I am a physician myself I tested selfmedication as described below.

During the next 7 weeks I slowly get better. I become able to eat other things than easily digested carbohydrates, and I can sit in a chair 3 to 4 times a day for 20 to 30 minutes. I am still not able to do without glucose infusion during the nights. A huge number of physical and paraclinical examinations have been normal. I have been examined by a number of specialists including specialists in infectious diseases, rheumatology, endocrinology, hematology, clinical immunology, and neurology. I was discharged from dept. of Neurology, Aarhus 12th of August and had a second opinion on the dept. Neurology, Rigshospitalet, Copenhagen in October. Conclusion: no sign of neurological or muscular disease, and no suggestions for further examination.

Late autum I suspected that I suffer from ME/CFS (myalgic encephalopathy/Chronic fatigue syndrome) as I think I full fill any of the several clinical definitions I can find (see (ME/CFS criterias 1-3)). And that two of

my main symptoms, that is severe aggravation of symptoms with overexertion, and my deterioration when sitting up, are welldescribed and has names (PEM (post exertional malaise), and OI (orthostatic intolerance). Furthermore, I find that 2 groups of researchers independently have reported that pyruvate is often elevated in this disease (se Pyruvate in ME/CFS 1-2). As there are no causal treatment and as I myself, taught by experience, have followed the symptomatic treatment recommended, I did not elaborate on the matter. Instead I went to DIAKO, a public hospital in Flensburg, Germany for proper treatment with plasma exchange (larger volume, and higher number of treatments than in Aarhus).
As I tell the nephrologist in charge that I suspect ME/CFS, he advice me to test for G-protein related autoantibodies, as 2 groups of researchers (se G-protein aoto ab 1-2) have reported that many patients with ME/CFS have autoantibodies against 2 of these, and that there is a German experimental treatment for such patients. It turns out that I am positive for these two autoantibodies. (See paraclinical analysis). I receive their experimental treatment in the form of plasma exchange x 5 again with a minor response, and in accordance with the German experience stoped treatment.
My further study of ME/CFS shows that PEM can give both acute and chronic severe sequelas, as can delay in diagnosis (search NICE guidelines ME/CFS 2021). As I suspect the severe deterioration I experienced in May where I briefly was able to do without wheelchair, and to sit and work, was caused by missing diagnosis, and wrong instruction I decided to seek a danish specialist in ME/CFS (coauthor of several guidelines and publications from the danish health authorities). He confirmed the diagnosis (ME/CFS), and were well aquatinted with the abnormalities in pyruvate and G-protein related auto antibodies being frequent in this disease.
As the character of my symptoms has been exactly the same from the first time I was seen on the Dept. of Neurologt, and as it is a disease that should be well known to any physiotherapist or physician working on a Neurological department, I have filled complaints and raised claim for damage to the danish health authorities.

Allergy: Proton pump inhibitors? Ondansetron: obstipation.

The treatments that have been tested are:
Low dose immunoglobulin
Testosterone
High dose glucocorticosteroids 15/7-18/7, 29/7-1/8, 12-15/8
Removal of a lipoma
High dose ribose
Intravenous treatment with thiamin 200 mg x 1 and B-combin (dexpantheol 10 mg, pyridoxine chlorid 5 mg, riboflavin 4 mg, nicotinamide 50 mg).
Vaccination against COVID19 (Moderna) x 3. The last time with clinical deterioration and eosinophilia.
Plasma exchange (with plasma) 3 times (only 0,5 of total plasma volume) 8.10 to 13.10. Some clinical effect. S-pyruvate measured before and after. Pyruvate fell (significant?). During 4 times of plasmaexchange with albumin, my clinical condition deteriorated, and there was no change in pyruvate before and after exchange.
A 5 days course of piperacillin/taxobacin as enteral decontamination.
A 5 days course of antihelmintic enteral decontamination (praziquantel and albendazole).
A 4 days course of metformine (deteriorated my clinical condition).
Interferon alfa for 7 weeks the last 2 weeks combined with valaciclovir 2 g x 4.
Dietary supplements. At present q10, e-vit, B-vit, raw beef. Acetacylic acid, and diazepam p.n.
The only one with certain effects was raw minced beef. The effect was astonishing but only lasted for 1 month.
As earlier mentioned i.v. glucose at night keeps my symptoms away.
Finally 5 time plasma exchange with plasma (3000 ml) finishing 28.2. A small improvement since.

Paraclinical examinations:
Blood analysis: see “paraclinical analysis”
Pyruvate has repeatedly between elevated, once exceeding max area for exact measurement. Positive for autoantibodies beta2 and M2 (measured in Germany in January 2022)

There is an abnormal CK before I stopped atorvastatin, and there is an increase in lactate during a physical test. At last, there is a single subnormal IgM, and a brief elevation of CRP during a mild bout of diverticulosis.
Free carnitine was high supposedly because I was eating raw minced beef
There is a finding of multiple deletion of muscle mitochondrial DNA (this is a test only meant to detect deletions (double electrophoresis)), but this could be age related.
Electron microscopy of muscles showed some abnormal mitochondria, but not enough to be deemed abnormal.

Normal examinations include:
ECG, echocardiography, coronary arteriography, CAT scan for thoracal aneurysm, CAT scan of thorax and abdomen, MR scan of CNS and spinal cord, EMG x 2 (one for an overview, one with regard to stiff man syndrome), blood analysis for autoimmune diseases including myositis. Blood analysis for neurological disease, and neoplastic diseases, MR scan of lower extremity muscles, Genomic analysis for > 400 myopathy related genes, Muscle biopsy microscopy. PET-CAT (enlarged lymph nodes in axilla after COVID vaccination), Respiratory chain enzymes, Dexamethasone suppression test, alfa-glucosidase. Amino acid analysis for metabolic myopathy, and acylcarnitine analysis for metabolic myopathies. A whole genome sequencing on blood and muscle is normal. Forearm test (non-ischemic), Urine metabolic screening.