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Orofacial pain in a female patient with MELAS syndrome. A case report

Postępowanie u pacjentki z zespołem MELAS. Opis przypadku

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ABSTRACT

Introduction: A great number of hereditary diseases have been correctly diagnosed and treated recently as a result of the rapid progress and constant development of genetic research.

Case report: This study presents the case of 24-year-old female patient suffering from MELAS syndrome, which is inherited in the maternal line – as are other mitochondrial diseases. This disorder was first described in 1984 by Steven G. Pavlakis et al. Our paper describes prosthetic procedures that were undertaken as treatment for the patient mentioned above, who had been referred from a hospital neurological clinic for consultation and possible treatment due to her refractory migraines. Regardless of the previously noted symptoms, the patient was examined for bruxism, and considering the positive outcome of the test, typical treatment, including a stabilization appliance was implemented. It gives significant improvement and lesser occurrence of neurological symptoms.

Conclusions: The patient stays under the constant, periodic control of our department.

Keywords: MELAS syndrome; occlusal splint; bruxism; doxepin; venlafaxine; surface electromyography.

ABSTRAKT

Wstęp: Ogromny postęp i dynamiczny rozwój badań genetycznych, mający miejsce w ostatnich latach, sprawił, że rozpoznawanych i właściwie prowadzonych jest coraz więcej zespołów uwarunkowanych dziedzicznie.

Opis przypadku: W pracy przedstawiono przypadek 24-letniej pacjentki obciążonej zespołem MELAS, który dziedziczony jest, jak inne choroby mitochondrialne, w linii matczynej. Chorobę jako pierwsi opisali Pavlakis i wsp. w 1984 r. Przedstawiono opis postępowania protetycznego u pacjentki skierowanej z poradni neurologicznej celem konsultacji i ewentualnego dalszego leczenia wieloletnich, migrenowych bólów głowy opornych na dotychczasową terapię. Zastosowano szynę o charakterze odciążająco-relaksacyjnym oraz modyfikację dotychczasowego leczenia.

Wnioski: Pacjentka odczuła znaczną poprawę i pozostaje pod stałą, okresową kontrolą poradni.

Słowa kluczowe: MELAS; szyna okluzyjna; bruksizm; doksepina; wenlafaksyna; elektromiografia powierzchniowa.

INTRODUCTION

A vast number of hereditary diseases have been correctly diagnosed and treated recently as a result of the swift progress and continual development of genetic research. What is remarkable is that these steps forward would not be possible without geneticists' constantly growing contribution to the foundation of these morbidities. The study presents the case of a 24-year-old female patient suffering from MELAS syndrome, which is inherited in the maternal line – as are other mitochondrial diseases. This disorder was firstly described in 1984 by Steven G. Pavlakis et al. Our paper describes the procedures that have been undertaken as a modality of the multidisciplinary treatment of the patient mentioned above. She had been referred from a hospital neurological clinic for consultation and possible treatment due to her chronic headache and migraines, which soon turned out to be refractory for conventional therapy.

MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis, stroke-like episodes) is a disease conditioned by mutations in mitochondrial DNA [1]. The primary reason for the difficulty in identifying MELAS syndrome is the fact that clinical symptoms vary over time for each patient, and yet are neither distinctive nor highly specific. Symptoms may also occur with fluctuating intensity at different ages. Psychomotor development in the early years of life is usually good. However, the majority of patients (31%) will develop the first subtle, non-specific symptoms around 6–10 years of age: seizures (28%), migraine headaches (28%), gastrointestinal problems (recurrent vomiting, food aversion; 25%), weakness of the upper and lower extremities (18%) eventually resulting in low height in comparison with peers (18%), stroke (17%), mild mental and cognitive problems (12%), impaired hearing (10%), and intolerance of physical exercise (10%). Most patients with MELAS syndrome develop the distinctive, specific and more severe symptoms before 20 years of age, which may include:

— myopathy with ragged red fibres,
— encephalopathies,
— lactic acidosis, which can lead to vomiting, abdominal pain, extreme tiredness and fatigue, muscle weakness, loss of bowel control, and difficulty breathing,
— hyperlactatemia in serum and cerebrospinal fluid,
— stroke-like episodes before 40 years of age, at the beginning primarily in the parietal lobes and the occipital ones, later on in other parts of the brain – can be often misdiagnosed as epilepsy by a physician not aware of the MELAS condition,
— recurrent headaches, migraine,
— seizures, loss of intellectual function (dementia),
— retinitis pigmentosa, cortical deafness,
— sensory neuropathy,
— type II diabetes,
— hypoparathyroidism, low height,
— cardiomyopathy and nephropathy (less).

There is no known treatment for the underlying disease, which is progressive and can be fatal. Patients are managed according to what areas of the body are affected at a particular time. Enzymes, amino acids, antioxidants and vitamins have been used, but there have been no consistent successes reported. Symptomatic therapy and moderate rehabilitation, coenzyme Q at doses up to 300 mg per day, and dietary supplements from the group of antioxidants in high dosages might be taken under consideration [2].

Proper identification of the MELAS syndrome is even more problematic as it lacks specific symptoms – the fluctuating development of concomitant disorders and the specificity of their co-occurrence might lead to mismanagement in many cases. Confirmation of the diagnosis is achieved only after finding pathogenic mutations in the mtDNA, which is possible only in specialized centres.

CASE STUDY

The patient – K.B., aged 24, was referred from a neurological clinic for consultation and possible further treatment, and was diagnosed with recurrent migraine headache pain refractory to former treatment. It escalated quickly since the patient has been confirmed with MELAS syndrome 2 years before on the basis of clinical symptoms (hearing loss, diabetes, hormonal disorders, severe headaches, memory impairment, blurred vision, abnormal EEG, heart rhythm disturbances), family history, but also on the basis of molecular testing for non-malignant diseases in the Genetic and Prenatal Diagnostics Clinic in Pomeranian Medical University in Szczecin (Poland), where the recommendations for further actions were issued as follows: Three stepsisters, W.K., born 2001, K.B., born 1990, and J.K., born 1997, with a metabolic disease, with a family history confirmed by molecular analysis. All three patients need a common, uniform neurological, ophthalmological and internal-metabolic protocol of care and rehabilitation at a high level of referral. Particularly indicated for constant supervision function and the state of the heart, liver, pancreas and kidneys. It is recommended to treat all the sick family members in one centre, regardless of their age. The syndrome found in patient K.B. is an inherited disease, genetically determined, and incurable. Due to the unfavourable prognosis and the progressive nature of neurological symptoms the patient cannot take a job in order to make a living. Excessive exercise can accelerate the progression of the disease. Only appropriate, comprehensive and cautious physiotherapy may keep the 24-year-old female patient at a sufficient level of functionality. As the disease is transmitted from the cytoplasm of the ovum, carriers are always women, with offspring suffering regardless of gender, but symptoms can occur in all ages and with varying severity. Getting pregnant is not recommended, although prenatal screening is available'.

Almost simultaneously, she was diagnosed with major depressive disorder and received doxepin treatment at a dose of 75 mg/day, which she took regularly. After some time the patient was referred to our orofacial pain unit with a major complaint about headaches and recurrent migraines. We collected a medical history (quite remarkable for a young person), pre-existing seizures, alleged seizures, 3 times the ablation of the heart muscle due to Wolff–Parkinson–White syndrome, several brief hospitalizations in neurological and psychiatric wards, and a clinical examination was carried out (Fig. 1).

Regardless of the previously noted symptoms, the patient was examined for bruxism, and the test by means of surface electromyography and RDC/TMD protocol was positive (Fig. 2).

As we believed at this stage, it occurred due to stress accompanying the diagnosis of the underlying disease. However, she later admitted taking tricyclic antidepressants (TCA) prescribed by a neurologist, which sparked the idea of a probable paradoxical side effect of TCA usage. Pain in the area of the head and face in the Visual Analogue Scale (VAS) scale periodically fluctuated throughout the day from 4–8, with a tendency to have higher values in the morning. Nevertheless, due to the patient's vast previous medical experience she turned out to be reluctant to undergo additional testing, and did not agree to a further polysomnographic examination. Firstly, we decided to use the stabilization appliance by Okeson [3] and arginine supplementation in a dose of 3000–6000 mg a day [4, 5, 6]. She was also referred to a specialist for conservative dentistry consultation (Fig. 3).

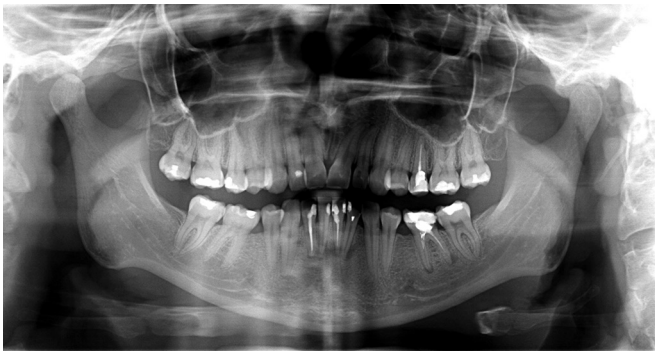

FIGURE 1. Orthopantomograph

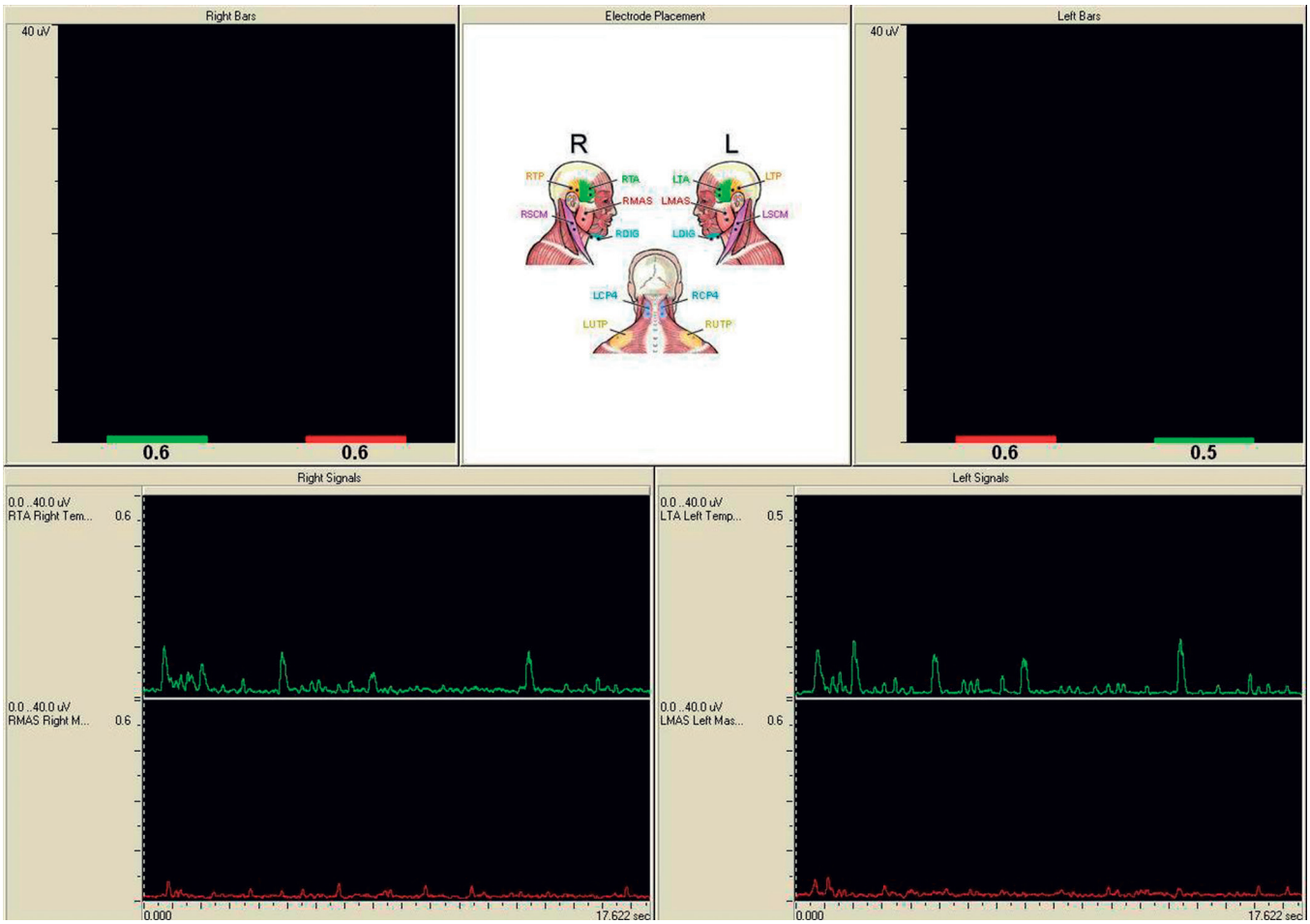

FIGURE 2. Relaxation test, temporalis anterior and masseter muscles, before treatment, Zebris Bluetooth SEMG, 4 channels

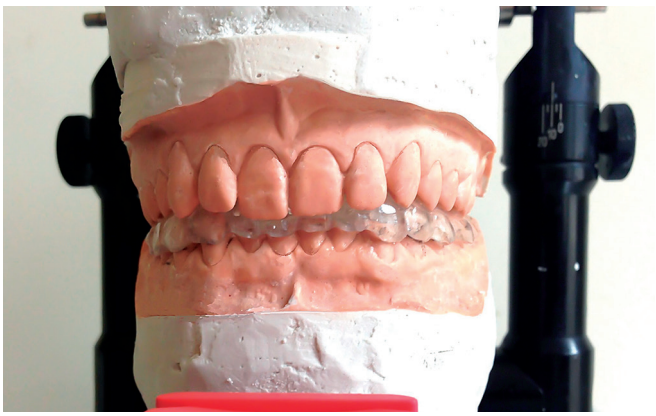

FIGURE 3. Stabilization appliance for the lower jaw, Artex articulating system (Amann Girrbach, Austria), visible left lock set for Bennet angle 10°, canine guidance restored bilaterally

However, because the pain persisted longer than three months, components of neuropathic pain had to be considered as well. Therefore, after a brief talk with the consultant neurologist who was her leading physician throughout that time we attempted to try changing the currently taken doxepin before bedtime to serotonin and norepinephrine reuptake inhibitors. We picked venlafaxine in sustained-release at an initial dose of 150 mg in two 75 mg doses a day. After 6 months the patient reported a major improvement, so we decided to reduce the dosage in 3-month cycles (SR 112.5 mg, 75 mg SR, now SR 37.5 mg/day), which also gives good results in neuropathic pain. Venlafaxine has also been confirmed to have a positive effect on antioxidant status in these particular cases, where mood disorders are accompanied by stress and frequent steroid therapy [7, 8]. In conjunction with the common chronic pain and comorbid states with increased muscle tension within the masticatory and neck muscles, the patient was referred for physical therapy. After acute symptoms partially decreased, moderate physiotherapy was applied due to numerous contraindications associated with MELAS syndrome. Mainly isometric exercises or exercise of the masticatory muscle, relaxation techniques of the neck and shoulder girdle muscles were implemented, intermittent with dry massage (Fig. 4).

CONCLUSIONS

All the treatment modalities turned out to be a major breakthrough for the patient's headaches and migraines. The pain almost diminished to 0–1 according to the VAS scale. She uses the stabilization appliance overnight and has reduced the

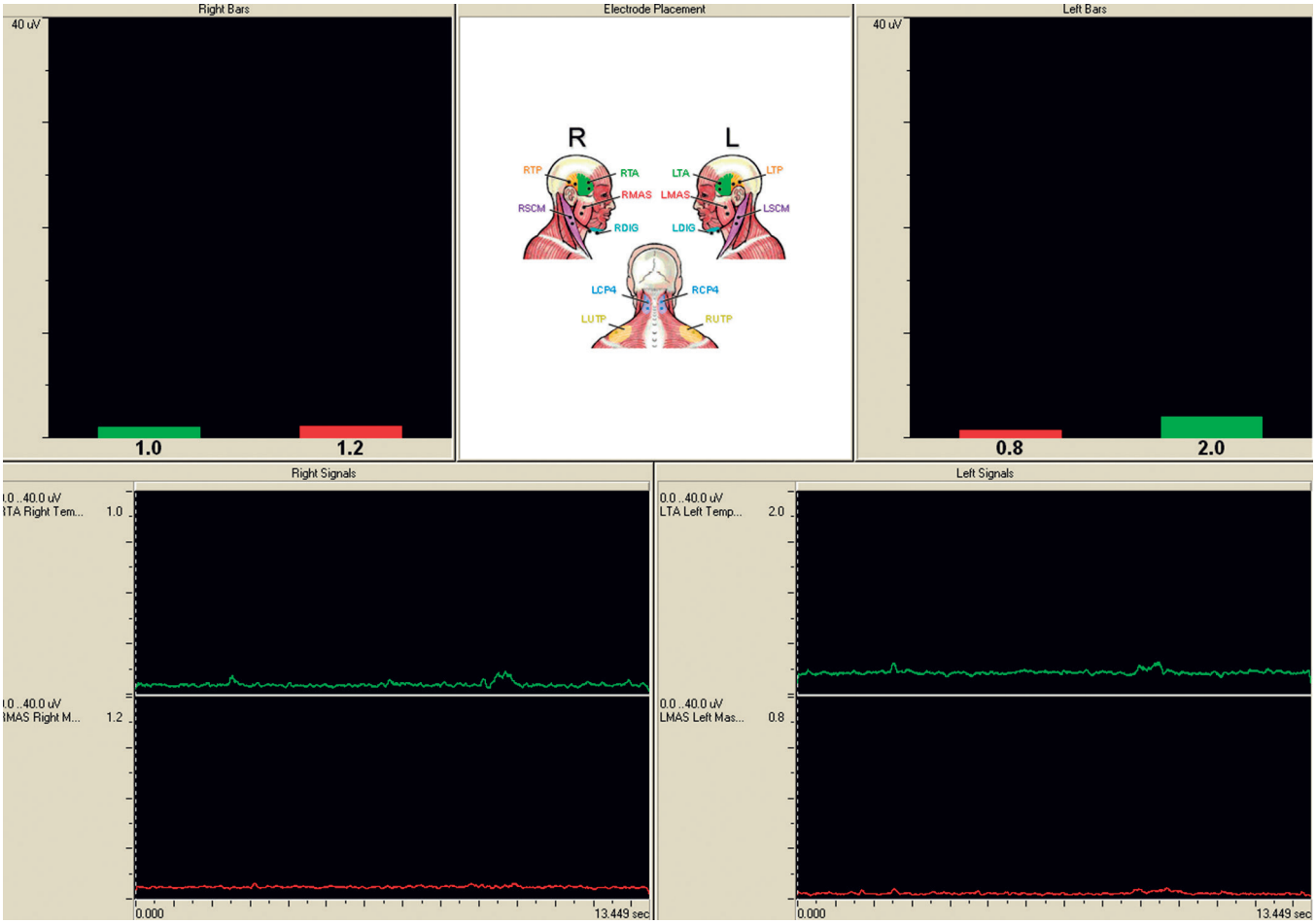

FIGURE 4. Relaxation test, temporalis anterior and masseter muscles, after 3 months of treatment, Zebris Bluetooth SEMG, 4 channels

venlafaxine dosage. She also claims that it gave her a significant improvement and less frequent occurrence of neurological symptoms. The patient remains under the constant, periodic control of our department.

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