MEMORIES BY A MYOLOGIST

How we developed, at the Centre/Institute for Neuromuscular Diseases, differential diagnostics of Spinal Muscle Atrophies / Amyotrophic Lateral Sclerosis (SMA/ALS) and tried to influence the development of the disease

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In our research, we placed the emphasis on delimiting fatal diseases against those that have some similar symptoms, but can be improved, even completely cured. More often we succeeded in differentiating the local compressive factor. In our search for early symptoms, we also found physiological, although quite unusual EMG phenomena. High amplitude neural potentials confirmed the malignant disease diagnosis. The spinal angiography discovered arterial pathology, while CT demonstrated localised hydromyelia. Amyotrophic syndromes caused by chronic led intoxications represented a separate group. Patients would recover significantly on d-penicillamine. We applied it successfully in amyotrophic syndromes with laboratory confirmed copper metabolism disorders. A very significant therapeutic effect was obtained in a patient with SMA without similar laboratory, even in recidivism. Exceptionally, we were able to achieve significant remission with corticosteroids, too. The remaining patients, differentiated as certainly fatal, represented a separate group. We tried to elaborate the special psychosocial and ethical problems connected with its outcome in "round table discussions". The first one was in 1989, at the workshop with King Engel, and the second in 1990, on the Fourth Yugoslav Symposium on Neuromuscular Diseases. In 1990, I visited Cicely Saunders and the St. Christopher's hospice in London, and in 1994 I started to organised hospice movement in Croatia.

Key words: amyotrophic syndromes, d-penicillamine, Hospice Movement in Croatia

Introduction

"The Motor Neurons Disease" (MND) - with its more frequent form Spinal Amyotrophy (SMA) and its rarer form Amyotrophic Lateral Sclerosis (ALS) - was, along with Myasthenia Gravis, the disease I was mostly occupied with. It is still an incurable, fatal disease. However, there are similar clinical forms, which have an entirely different prognosis regarding the speed of spontaneous development, in which the differential diagnostic analysis and therapeutic attempts result with some results. Moreover we have in medicine the diagnosis "ex iuvantibus". When we are dealing with a deadly disease, even the least likely alternative must be taken into account, and we have to help, even slightly and temporarily. In this report I put the emphasis on differential diagnostics, as precise as possible, primarily obtained by electroneurography and electromyography, the methods I menaged in the best way.

Differential diagnosis

While still in the early phases of our development of sensory neurography, we had a paper published in Lon-

don (1). Atrophy of hand muscles with high neural potential proximally, point to MND. In our plurisegmental electrophysiological analises, besides the basic disease, we also succeeded to differentiate the local compressive syndrome, in which the neurolysis represents stopping the deterioration of at least one muscle group (2). The positivity of ischemic test of chronic tetany (3) in typical spinal amyotrophy was unusual. A colleague who had to follow up its appearence as part of his master's thesis, did not finish his work.

During the primary EMG analysis, we were looking, first of all, for differential diagnostic phenomena, in size and frequency of outburst of motor units potentials., In m. Quadriceps (4) we used to find positive "gigantic" potentials. The finding surprised us, so we followed up patients who complained of becoming tired easily. In some, getting tired stopped, but the finding remained. In the end, we found it even in entirely healthy but musculous persons.

The lack of neural potentials (5) in patients with spinal amyotrophy with a lot of fasciculations and cramps, pointed to a very bad prognosis. As a part of a master's thesis (6), the value of neurophysiological techniques in assessment of seriousness of the disease and prognosis of the outcome were worked out. During these detailed analyses, I discovered the phenomenon of variations in innervation zones (6), which I interpreted first as a pathological phenomenon. Very quickly, however, it became clear that, besides variations in motor innervation, there exist also variations in sensory innervation, and we reported on that, in a number of publications.

We dealt with hereditary forms of spinal amyotrophy and the so called pseudomyopathic histology test results (8, 9), as well as cardiological pathology in ECG (10). Unfortunately, at that time we did not have access to genetic research.

By spinal angiography, we used to single out the origins of certain form of spinal amyotrophy as a consequence spinal circulation pathology (11, 12) or, by a CT scan in a young person, hydromyelia with the monomelic amyotrophy syndrome (13).

Our joint research with the Institute for Medical Research and Work Medicine JAZU (the Yugoslav Academy of Sciences and Arts) was very importante. We analysed the patients intoxicated by led, with amyotrophic syndrome (14). With d-penicillamine (Metalcaptase) therapy and eliminating the exposition, we managed to stop the progression, even achieved recovery. The research brought me to direct exchange of experiences with Pamella Fullerton, Middlesex Hospital, London, who was at that time considered to be the leading expert in this area.

In the seventies, we repeatedly had patients with Wilson disease, which we also treated with d-penicillamine (Metalcaptase) We applied the group of differential diagnostic laboratory tests for this disease on some SMA/ ALS patients as well. The positive results were published (15-17).

In 1977, in one patient with SMA (18) without copper metabolism disorder, or led intoxication, we applied d-penicillamine, because the disease progressed relatively fast. The result was satisfactory, even in recidivism. Applied on other patients with the same diagnosis, the results varied. In 1979 we (19) published correlation with concentration of D-DALK, according to which, the worst results were achieved with its highest concentrations.

We worked out some "rules of the game" in application of corticosteroides on Myasthenia Gravis, and we achieved a relatively low percentage of complications, so we attempted this therapy on SMA/ALS, too. We described the effects on three cases with more or less pronounced signs of immunological processes also in biopsy of skin or muscles. The results were of various intensity and duration (20). The best result was achieved in two young women with asymmetric atrophy of arm muscles and significant humoral signs of autoimmune process (21). We started also with specific liquor analysis (22).

Malignant forms of ALS in terminal stage

Every now and then, the patients were differentiated as suffering of malignant disease for sure. It was especially painful to follow up and listen to younger, lonely patients with bulbar symptomatology. I could not help them, and I could not keep them on the ward, either. There was a shortage of beds and pressure from those coming for comprehensive differential diagnostics.

I started looking for a solution. The first step was the scientific workshop on ALS. I organised it as a full-day event, in english, in the great hall at the Rebro hospital, with guests from Los Angeles, V. Askanas and K.W. Engel, the co-directors of the Centre for Neuromuscular Diseases of the Neurological Clinic at the Good Samaritan hospital. The round table discussion, entitled "Procedures in Terminal Stadium of Amyotrophic Lateral Sclerosis" was central. The solutions that K.W. Engel offered were for rich patients and a rich public health system.

The discussion on the same subject was repeated at the Fourth Yugoslav Symposium on Neuromuscular Diseases, 1990 in Zagreb. Title was "Medicolegal aspects of terminal stages in neuromuscular diseases". The rich discussion about the principles and attitudes — legal, as well as ethical issues was recorded, and published 1999 (22).

In 1990, in search of a better solution, I went to "The First International Symposium on MND / ALS", Solihull,

England. It was only there I was referred to Cicely Saunders and St. Christopher's Hospice. I visited London, and that visit defined my main activities during next twenty years, as a retired neurologyst.

I started the hospice movement in the Republic of Croatia by establishing the Croatian Society for Hospice/ Palliative Care of the Croatian Physicians' Society, two other citizien's associations and the Regional Hospice Centre, Zagreb, supported by the Health Ministry. I published more than a hundred articles, edited several books and brochures, founded and edited the Bulletin for Palliative Medicine/Care and so on. As the President of the Committee for Palliative Care of the Ministry of Health of Republic of Croatia, I mediated the first inclusion of the basic terms of palliative care into the Croatian health legislation. Nevertheless, we did not come closer to the English, not even Polish models. As usal , the new ideas to be accepted, must be based on the change of major mentality . And that takes time... which is so precious!

Conclusion

A physician must always try to suppress particular symptoms. It is nice when he or she manages to restore patients health at least partially. The triumph is to save the life. In every patient, we try to have, as precise differential diagnostics, as possible. That is the first step and basic for eventually successfull treatment. In some cases, we were positively surprised when we found a therapeutic way out from a tragic situation. We sometimes managed to save a life as well.

In other cases we stumbled upon an unsolvable problem. What the modern hospice movement offers, as defined by Cicely Saunders, was in such cases all that was left. It should never be said: "there is nothing else we can do for you". There is a lot that can be done. One thing we can and should always give - is the psychological support.

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