lesions (infarcts), in the absence of supratentorial involvement or antecedent illness indicated posterior circulation stroke as the aetiology. The distribution of these ischaemic lesions was multifocal, in the areas supplied by left superior cerebellar, left anterior inferior cerebellar and the penetrating left pontine branches of basilar arteries, thus involving the middle and distal posterior circulation territories (apart from the non-territorial right paravermal infarct). Miyakita et al. reported the first case of transient cerebellar mutism after brainstem infarction following traumatic injury of right vertebral artery. However, our patient had involvement of both brainstem and cerebellar structures in the non-traumatic context. It is noteworthy that there was transient disturbance in the level of consciousness at the onset along with transient right hemiplegia and gait ataxia in both cases. This finding was in agreement with the reported association of cerebellar mutism with the reported association of cerebellar mutism with cerebellar structures in the non-traumatic context. It is noteworthy that there was transient disturbance in the level of consciousness at the onset along with transient right hemiplegia and gait ataxia in both cases. This finding was in agreement with the reported association of cerebellar mutism with a spectrum of neurological deficits including pyramidal, cerebellar and eye movement signs.1

We believe that a complex interaction of cerebellar and brainstem involvement might be the cause of mutism in our patient. One of the suggested mechanisms for postoperative cerebellar mutism includes brainstem ischemia and subsequent edema, to account for the transient nature of the syndrome. The vascular basis of this syndrome in the nonsurgical setting is better exemplified by our report. The good outcome of the speech disorder (including the improvement of dysarthria with the return of near normal speech during the subsequent period of observation), despite the presence of established infarcts, could be attributed to unilateral brainstem infarction, resolution of edema or neuronal plasticity. The behavioral disturbance also normalized with the resolution of mutism. Hence recognizing this syndrome is important in informing the parents about the prognosis and rehabilitation of speech and behavioral disorder, as most of these cases were encountered in the pediatric age group.

R. Nandagopal, S. G. Krishnamoorthy
Department of Neurology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India. E-mail: mandagopal@yahoo.com

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Diagnostic approach for adult mitochondrialopathy with limited resources

Sir,

We appreciated reading the paper by Challa et al.1 on the findings in 60 adult patients with respiratory-chain-disorder (RCD), diagnosed during 12y according to Bernier's criteria.2 The study raises the following concerns:

What was the indication for muscle-biopsy in those patients without evidence for myopathy? Only 18/60 patients presented with proximal weakness, only 5/35 had elevated CK, and only 12/31 myopathic EMG.

Why was the left vastus lateralis muscle chosen in all cases? It appears unlikely that this muscle was affected in all 60 patients, given the facts that 26 had only chronic external ophthalmoplegia (CPEO), that only 3 of those with CPEO and other signs had myopathy, and that only 30% had proximal weakness. Thus, RRFs >2% in 25/60 investigated muscles suggests subclinical involvement of certain limb muscles in MCP.

Why did only 8% of the patients present with additional non-neurological manifestations? Multisystem involvement is a dominant feature in the majority of MCP patients.3 Could the low number of patients with cardiac involvement result from the small number of patients undergoing comprehensive cardiologic examination? Only 35 had an ECG and only 13 underwent echocardiography. Which specific abnormalities were found in the 13 who underwent echocardiography? Did the investigators also look for left-ventricular hypertrabeulation?

Also noteworthy are the low prevalence of diabetes, hyper CK-aeemia, and polyneuropathy. In a retrospective study on 130 MCP patients, the prevalence of diabetes was 12%,4 that of hyper-CK-aeemia 42%, and that of polyneuropathy 35%.5 Latency between onset and diagnosis was relatively short. The number of 6.7y remains questionable given the fact that mean age at onset was 19.7y and mean age at diagnosis 29.3y.

We don't agree with the statement that MCP is mostly associated with various central-nervous-system (CNS) symptoms. Although subclinical abnormalities, like cortical or cerebellar atrophy, homogenous parieto-temporal hyperintensities, non-specific white matter lesions, or uni- or bilateral basal ganglia calcifications are often found in adult MCP patients, overt CNS-affection, including dementia, migraine, stroke, Parkinson syndrome, spasticity, ataxia, or dystonia, is rather rare among adults. The authors themselves report only 5/60 patients presenting with encephalomyopathy.

Overall, there is subclinical muscle-affection in MCP long before any clinical manifestation; MCP can be diagnosed even without sophisticated and cost-expensive methods; there is

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multi-organ involvement in MCP; onset of MCP is quite variable, and patients with suspected MCP should be thoroughly investigated for clinical and subclinical affection of the CNS, PNS, endocrinologic system, heart, eyes, ears, guts, dermis, and bone-marrow.

Josef Finsterer  
Department of Neurology, Krankenanstalt Rudolfstiftung, Univ.Doz. DDR. J. Finsterer, Postfach 20, 1180 Wien, Austria, Europe, E-mail: duarte@aonmail.at

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In mitochondrial myopathies the serum CK is almost always normal or only mildly elevated (less than 3 times the upper limit of normal). Rather normal serum CK in patients with significant weakness raises the possibility of mitochondrial dysfunction. Electromyography (EMG) may be normal.

The discrepancy between the mean age at onset, mean age at diagnosis and mean disease duration is probably related to wide range age of the 60 patients, 10 were in the pediatric age groups (one month to 15 years).

Nizam’s Institute of Medical Sciences, Hyderabad, *The Institute of Neurological Sciences, Care Hospital, Hyderabad, **L V. Prasad Eye Institute, Hyderabad, India. E-mail: tennetirkm@yahoo.com

References


Diagnosis of mitochondrial diseases: Clinical and histological study of sixty patients with ragged red fibers: Authors’ Reply

Sir,

We thank Dr. Finsterer for his interest in our study. The aim of our study was to find the usefulness of the diagnostic criteria proposed by Bernie et al1 to diagnose mitochondrial diseases when the patients present to the clinician. The clinical characteristics present at the initial visit were considered while categorizing the patients into various clinical syndromes. We have taken the presence of ragged-red fibers (RRFs), > 2% in the skeletal muscle as one of the important criteria for the diagnosis as we have no facilities for studying defects in respiratory chain (RC) complex expression and molecular studies to identify nuclear or mtDNA mutation of probable pathogenicity. The following is the clarifications to the concerns raised by Dr Finsterer.

Presenting phenotypic syndromes was the indication for muscle biopsy in 26 (43%) patients. In the remaining 34 patients we considered the possibility of mitochondrial disease clinically as they had two of the three clinical criteria proposed by Bernie et al.1

We categorized the patients into various clinical syndromes based on the presenting clinical characteristics at the initial visit. In mitochondrial diseases RRFs can be demonstrated in the clinically uninvolved muscles. Like in many center we do EMG in the right vastus lateralis and use left vastus lateralis biopsy.

We agree that multisystem involvement is a feature in a significant proportion of patients. As mentioned above we considered the presenting clinical characteristics at the first visit for the analysis. This may probably be one limitation for the low frequency of some of the systemic manifestations. It is quite possible that the patients would have developed some of these features in the course of the illness.

Particular abnormality in mitochondrial DNA may cause characteristic cardiac change in mitochondrial diseases and clinical features of cardiac involvement vary according to the different subgroups of mitochondrial disease: Kearns-Sayre syndrome - AV conduction disturbances in Kearns-Sayre syndrome, asymmetrical septal hypertrophy progressing to dilated cardiomyopathy in MERRF, and symmetrical ventricular hypertrophy with or without abnormal wall motion in MELAS. Cardiac involvement is atypical in oculare myopathy.2 This may explain the low frequency of cardiac involvement in our series. In our series of the 60 patients studied progressive external ophthalmoplegia was the presenting clinical syndrome in 26 (43%) patients. Lack of comprehensive cardiac workup might have also been a factor. ECG showed evidence of complete block in 3 patients and one of them had dilated cardiomypathy. All the three patients had permanent pace maker implantation.

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Nizam’s Institute of Medical Sciences, Hyderabad, *The Institute of Neurological Sciences, Care Hospital, Hyderabad, **L V. Prasad Eye Institute, Hyderabad, India. E-mail: tennetirkm@yahoo.com

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