Journal of Pediatric Neurology 3 (2005) 197–198
IOS Press


Editorial

# Clinicopathological findings in mitochondrial disorders

Harvey B. Sarnat*
*University of Calgary Faculty of Medicine, Calgary, Alberta, Canada*

Received June 03, 2005
Accepted June 04, 2005

Mitochondrial encephalomyopathies have shifted from being regarded just a few years ago as a category of rare metabolic diseases to a current recognition that they are much more common than previously thought, are a large and heterogeneous group of distinct diseases, and that they may occur not only as primary biochemical and genetic defects, but also as secondary defects in a wide spectrum of both genetic and acquired diseases of the nervous system ranging from Pompe disease (glycogenosis II, acid maltase deficiency), spinal muscular atrophy, septo-optic-pituitary dysplasia, some inflammatory myopathies, and secondary to a broad range of drugs that include immunosuppressive and chemotherapeutic agents, statins and valproic acid. Most of the research on mitochondrial diseases has been generated, not surprisingly, in the countries with the greatest funding and biochemical laboratory resources for investigating them, including detailed biochemical and genetic studies, neuroimaging and neuropathological studies, mainly from western Europe and North America. It is therefore encouraging to see studies of mitochondrial diseases eminating also from countries with fewer resources, such as the paper by Selim et al. [1] from Egypt, in this current issue of the *JPN*.

*Correspondence: Harvey B. Sarnat, M.D., F.R.C.P.C., Alberta Children's Hospital, Division of Pediatric Neurology, 1820 Richmond Road S.W., Calgary, Alberta T2T 5C7, Canada. Tel.: +403 943 7131; Fax: +403 943 7649; E-mail: harvey.sarnat@calgaryhealthregion.ca.

New histochemical and immunocytochemical methods used in the neuropathology of both muscle biopsies and brain tissue, both surgical and at autopsy, represent major recent advances in understanding the manifestations of mitochondrial encephalomyopathies [2, 3]. Many of these techniques are feasible to perform in the laboratories of large academic teaching hospitals of developing countries, and efforts should be made to incorporate them. An example, in relation to this paper by Selim et al. [1] is the use of succinate dehydrogenase (SDH) to compare activity in myofibres that have lost cytochrome-c-oxidase (COX) activity. The authors have reported scattered fibres with loss of COX, but the demonstration of strong or even hyperintense SDH in those same fibres would distinguish fibres affected by mitochondrial disease from nonspecific degenerating myofibres from any cause, such as a necrotizing myopathy or a muscular dystrophy. Other specific changes in brain at postmortem examination, particularly in infants dying with Leigh encephalopathy, include abnormal distribution of synaptic activity in the inferior olivary nuclei of the medulla oblongata, as demonstrated by synaptophysin immunoreactivity, and calcified individual neurons in the thalamus and hypothalamus [3]. Whereas the scope of this study by Selim et al. [1] did not include postmortem neuropathology, this example is offered as another precise finding that could be achieved in the pathology laboratories of developing countries. The demonstration of specific activities of each of the Respiratory Chain Complexes

is yet another precision that helps define the type of mitochondrial disease, which often is quite different in adults and children. In adults, Complexes I and IV are more likely to be involved, whereas in infants and children, reduced activities in Complexes III and V are more frequent [4]. These pathological and biochemical features allow for more exact correlations with clinical expression and with imaging findings, in sorting out the multiple old and new mtDNA point mutations and deletions that continue to be reported in numerous medical journals each month.

Selim et al. [1] have done an outstanding job of documenting, in a planned, prospective manner rather than as a retrospective review, the clinical and neuroimaging findings in 31 Egyptian children with mitochondrial diseases, followed in Pediatric Neurology and Metabolic Clinics at Cairo University Children's Hospital. They have made correlations with laboratory studies of blood (e.g. serum lactate, creatine kinase, other metabolic markers and enzyme assays), electrophysiological studies (electromyography, nerve conduction time) and histochemical and ultrastructural alterations in the muscle biopsy. Though the resources available to the authors permitted partial biochemical studies of specific enzymatic activities of the respiratory chain complexes, Coenzyme-Q10 measurement in blood or muscle tissue and analysis of mtDNA for point mutations and deletions in only six of their cases, these data and the clinical and other laboratory data they provide are valuable for showing that a similar spectrum of findings and distribution of specific mitochondrial diseases are demonstrated in Egyptian children as in those countries from which most mitochondrial disorders to date have been reported. Their novel data are a useful contribution to the world literature and unique in a population for whom similar studies have not previously been conducted. The detail with which they have meticulously recorded and analyzed their data is in the highest tradition of scientific medicine and will serve well for these and other future investigators, both in Egypt and elsewhere in the world. I therefore congratulate them for their contribution and encourage them to continue their studies. Not only should this paper serve as an inspiration to investigators in other developing countries, but it is a work that I and other investigators in more scientifically developed countries can proudly cite in our publications, on an equal standing.

## References

[1] L.A. Selim, H.A. Ghaffar, M.M. Hamdi, A.M. Hagras, G.A. Nakhla, A.M. Kamel, A clinicopathological and brain MRI study in Egyptian children with mitochondrial disorders, *J Pediatr Neurol* **3** (2005), 207–215.

[2] A. Oldfors, Tulinius M. Mitochondrial encephalomyopathies, *J Neuropathol Exp Neurol* **62** (2003), 217–227.

[3] H.B. Sarnat and J. Marín-García, Pathology of mitochondrial encephalomyopathies, *Can J Neurol Sci* **32** (2005), 152–166.

[4] J. Marin-Garcia, M.J. Goldenthal and H.B. Sarnat, Probing striated muscle mitochondrial phenotype in neuromuscular disorders, *Pediatr Neurol* **29** (2003), 26–33.