MITOCHONDRIAL MYOPATHY WITH RESPIRATORY MUSCLE INVOLVEMENT

A CASE REPORT

J. A. LEVY *
ANA M. TSANACLIS **
P. A. P. SARAIVA ***
CARMEN C. MION ****
PAULO N. B. SALUM ****

As from 1956, a series of congenital myopathies benign in character have been described, the diagnosis of which can only be effected by means of histochemistry and electronic microscopy. Within this group of affections, some are characterized by alterations in number, form or aspect of striated muscle mitochondria [2,4,7,8]. In 1971 Engel & col. described a familiar congenital myopathy involving especially axial and respiratory muscles that presented ultrastructural alterations of the mitochondria and Z-line [1].

The present article concerns a patient with benign congenital myopathy, except for presenting severe alterations in respiratory muscles.

OBSERVATION

R.L., female, 10 years old, examined on January 29, 1979 complaining of difficulty in walking ever since she began to walk at the age of 16 months, and a crooked spine. Her parents said that the clinical picture was stationary. *Familiar antecedents*: parents first cousin, normal sister age 12. *Clinical examination* — raised palate, thoracic scoliosis, and increase of lumbar lordosis. *Neurological examination* — global hypotonia to a moderate degree, slight proximal motor deficit in the four limbs and trunk. Slight involvement of facial muscles. *Complementary examinations* — Spinal X-ray: rectification cervical spine, concave dextral dorso-lumbar scoliosis and augmented lumbar lordosis. Electromyography: characteristic trace of primary muscular lesion. Normal serous enzymes (CPK, GOT, GPT, LDH). Muscular biopsy (optical microscopy): alterations compatible with primary myopathic process.

With the diagnosis of benign congenital myopathy, the patient was sent on to physiotherapy. Her condition remained unaltered up until the end of 1980 when she began to present episodes of cyanosis and drowsiness sometimes accompanied by headaches, having been on two occasions interned in an intensive care unit, where

---

This work was carried out at the Center for Investigations in Neurology of the Neurological Clinic of São Paulo University Medical School: * Adjunct Professor; ** Assistant Professor, Department for Pathological Anatomy; *** Director, Service of Anaesthesiology; **** Associated Researcher.

she improved only after a tracheostomy and assisted respiration. The neurological examination remained unaltered, with the exception of an increase in the deficiency of respiratory muscles that were, by then, considerably involved. Radioscopy revealed almost complete absence of diaphragm movement.

With electronic microscopy an accumulation of mitochondria was observed, especially in sub-sarcolemmous position. These mitochondria had crests thickened by material that was moderately electron-dense, sometimes abnormal on form. A discrest dilation of sarcomera was observed in system T (Figis. 1 and 2).

Forced expirometry on the patient showed a severely restricted pulmonary picture reflected in all parameters (Table 1). Compared to the standard, vital capacity is much diminished in the patient (34%). Analysis of forced respiratory volume in the fast segment suggested there is no component to obstruct the upper respiratory pathways, for it was diminished in the same proportion to vital capacity. Comparing results in different positions, it could be seen that the values observed in the different decubitus positions are much smaller than those obtained with the patient in a sitting position. In this position, the force of gravity aids the movement of the diaphragm downward, whereas in a decubitus position, it does not. In right dorsal decubitus, the diaphragm seems less efficient. Based on this data, the patient was assisted with mechanical pulmonary ventilation at night. A further expirometry was carried out after a period of 26 days.

Comparing results obtained in the morning with those obtained in the afternoon (Table 2), it was observed a reduction in the parameters studied in the latter, suggesting the possible effect of fatigue, for at night, the patient received assisted ventilation.

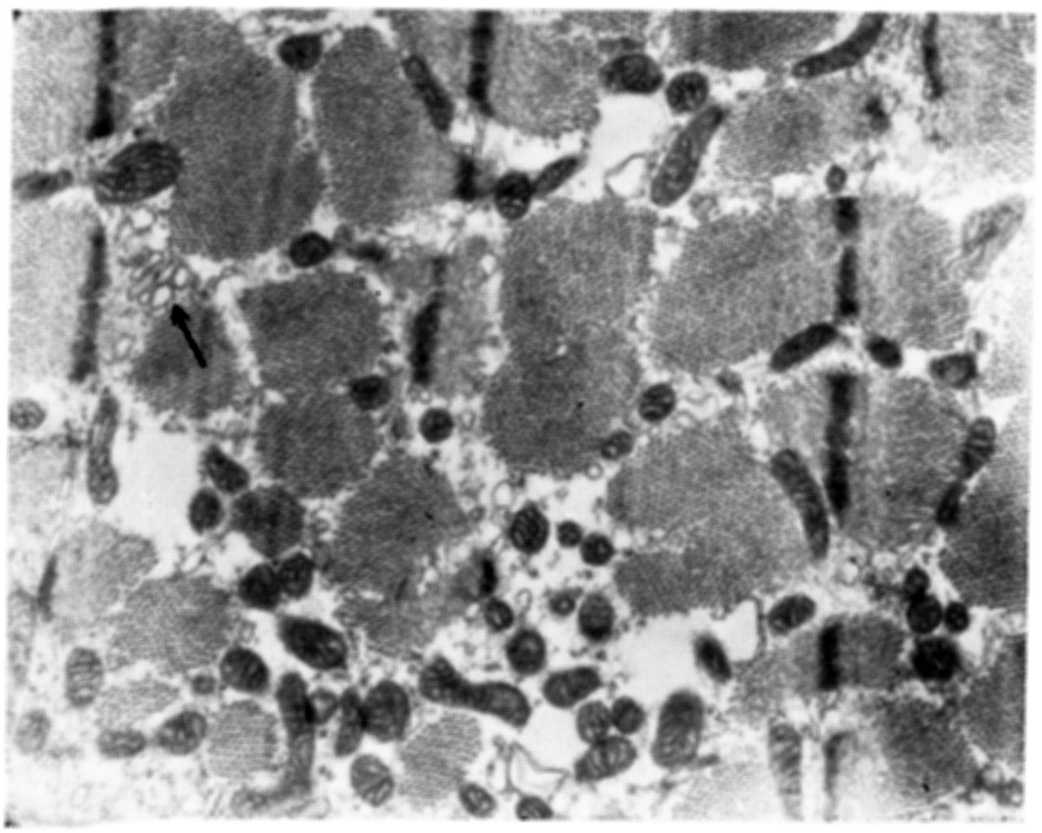

Fig. 1 — Case R.L. Ultrastructural aspect of muscle showing number of mitochondria, enlargement of T-system (arrow) and normal aspect of fibrils (Electronic microscopy: 24.070 x).

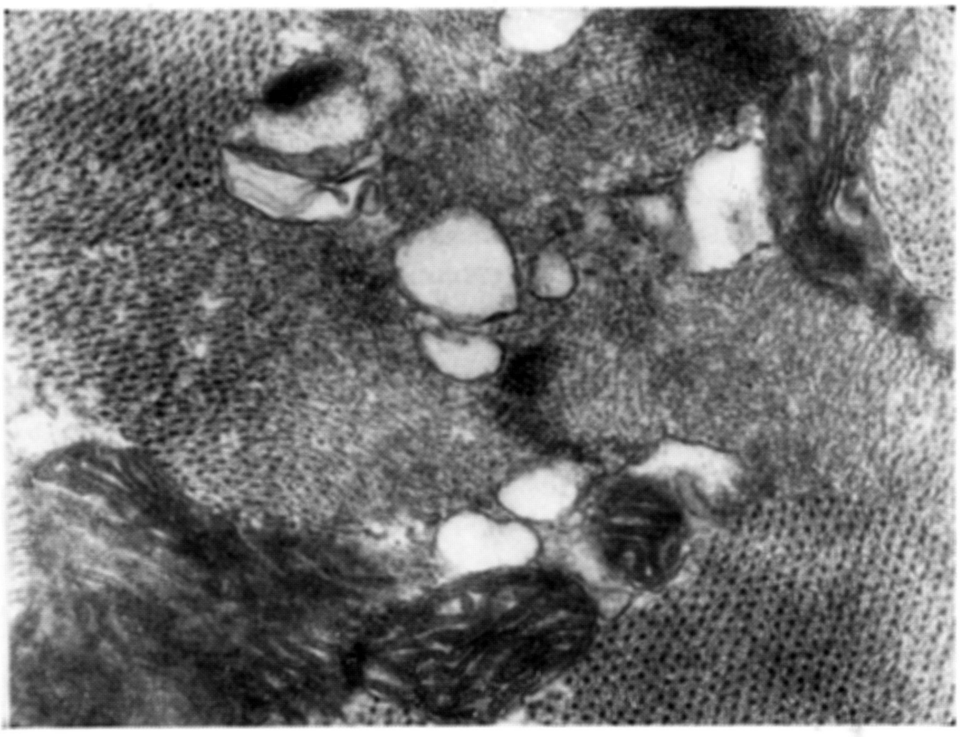

Fig. 2 — Case R.L. Detail of mitochondria. Christae are enlarged by a homogenous electron dense material (Electronic microscopy: 70.000 x).

Parameter	Standard	SIT	%	HDD	LLD	RLD
FVC	1.97	0.68	34	0.39	0.48	0.39
$FEV_{1.0}$	1.85	0.64	34	0.36	0.42	0.36
$FEV_{1.0}$%	94	94	—	92	89	92

Table 1 — Case R.L. Forced expirometry (March 25, 1981). FVC, forced vital capacity; $FEV_{1.0}$, forced expiratory volume in the first second; $FEV_{1.0}$%, (FEV 10/FVC x 100); HDD, horizontal dorsal decubitus; LLD, left lateral decubitus; RLD, right lateral decubitus.

Parameter	Standard	Morning	%	Afternoon	%
FVC	1.97	0.82	42	0.71	36
$FEV_{1.0}$	1.85	0.78	42	0.65	35
$FEV_{1.0}$%	94	94	—	92	—

Table 2 — Case R.L. Forced expirometry (April 20, 1981).

Probably the values shown in this second table (FVC and $FEV_{1.0}$), that indicate a lower involvement of the respiratory function than those referred to in Table 1, were the result of rest during artificial ventilation (carried out at night).

COMMENTS

The patient described by us presented a congenital myopathy relatively benign by nature and that seemed to keep to stationary symptomatology, suggesting favourable evolution that would allow the patient to lead a practically normal life. However after the age of 10, severe complications arose that were characterized by respiratory deficiency, above all because of mal-function of the diaphragm, which as was natural, worsened in a horizontal position. This picture was naturally due to an accumulation of CO_2 accompanied by cyanosis, drowsiness and headache (chronic alveolar hypoventilation).

Only then did the biopsy examination, carried out with electronic microscopy, permit us to form a diagnosis of mitochondrial myopathy.

With the use of assisted pulmonary ventilation at night and for one or two hours after lunch, the patient returned to a practically normal life, returning to school, and carrying on with practically all activities of a child her age. We call attention to this extremely important fact that, in cases of diaphragmatic deficit, even in patients with progressive muscular distrophy (limb girdle form), in which this deficit is much accentuated, assisted pulmonary ventilation at night can, as referred by several authors [3,5,6], allow these patients regarded as total invalids to resume a useful life.

SUMMARY

A case of a 10-year-old patient with a benign congenital myopathy, suddenly aggravated because of an accentuated deficit in respiratory muscles is reported. The institution of assisted respiration at night allowed the patient to return to her daily activities. Examination of muscular biopsy with ultra-microscope permitted the diagnosis of mitochondrial myopathy.

RESUMO

Miopatia mitocondrial com acometimento severo da musculatura respiratória.

É relatado o caso de uma paciente de 10 anos de idade com miopatia congênita benigna que agravou-se subitamente em virtude do déficit acentuado da musculatura respiratória. A instituição de respiração assistida durante a noite permitiu a volta da paciente a suas atividades diárias. O exame de biópsia muscular ao ultra microscópio permitiu o diagnóstico de miopatia mitocondrial.

REFERENCES

1. ENGEL, A. G.; GOMEZ, M. R. & GROOVES, R. V. — A recently recognized congenital myopathy associated with multi-focal degeneration of muscle fibres. Proc. Mayo Clin. 646:666, 1971.
2. JULIEN, J.; VALLAT, J. M.; VALLAT, M. & Le BRANC, M. — Oculopharyngeal muscular dystrophy. J. neurol. Sci. 21:165, 1974.
3. LOH, L. H. & NEWSON-DAVIS, J. — Bull. eur. physiopathol. Resp. 15 (suppl.): 137, 1979.
4. LUFT, R.; TKVOS, D.; PALMIERI, G.; ERNSTER, L. & AFZELMO, B. — A case of severe hipermetabolism of non-thyroid origin with a defect in maintenance of mitochondrial respiratory control. J. clin. Invest. 81:1776, 1982.
5. NEUSTADT, D. E.; LEVY, R. C. & SPIEGEL, I. J. — Carbon dioxide narcosis in association with muscular dystrophy. J. am. Med. Assoc. 187:616, 1964.
6. NEWSON-DAVIS, J. — The respiratory system in muscular dystrophy. Brit. med. Bull. 36:135, 1980.
7. SENGER, R. C.; TERHAAR, B. G.; TRIJBELS, J. M.; WILLENS, J. L.; DANIELS, G. & STHADDUDERS, A. M. — Congenital cataract and mitochondrial myopathy of skeletal and heart muscle associated with lactic acidosis after exercise. J. Pediat. 86:873, 1975.
8. SHY, G. M.; GONATAS, N. K. & PEREZ, M. — Two children myopathies with abnormal mitochondria. Brain 89:135, 1966.

Centro de Investigações em Neurologia — Caixa Postal 5199 — 01000 São Paulo, SP — Brasil.