CASE REPORT

On a case of respiratory failure due to diaphragmatic paralysis and dilated cardiomyopathy in a patient with nemaline myopathy

ANTONELLA TAGLIA, PAOLA D’AMBROSIO, ALBERTO PALLADINO AND LUISA POLITANO

Cardiomyology and Medical Genetics, Department of Experimental Medicine, Second University of Naples, Italy

Nemaline myopathy is a rare congenital disease that generally occurs in childhood. We report a case of a 50-year-old man who presented with severe heart failure as the initial manifestation of nemaline myopathy. Soon after he developed acute restrictive respiratory failure due to the diaphragmatic paralysis. The diagnosis of “nemaline myopathy” was obtained on muscle biopsy performed one year later. After starting appropriate cardiologic treatment and non-invasive ventilation, his cardiac and pulmonary functions improved substantially, remaining stable for over the 10 years since diagnosis. In the last two years the patient had a progressive deterioration of respiratory function, enabling him to attend daily activities.

Few cases of respiratory failure in patients with adult-onset nemaline myopathy are reported, but the insidious onset in this case is even more unusual. This case highlights the wide spectrum of presenting features of adult-onset nemaline myopathy and the temporary efficacy of non invasive ventilation on respiratory function.

Key words: Nemaline myopathy, heart failure, respiratory failure

Introduction

Nemaline myopathy, included in the group of congenital myopathies, is characterised by the presence of rod-like nemaline bodies in the muscle fibers. It is associated to the presence of particular phenotypic features such as elongated face, high palate, thoracic deformities, scoliosis, and diffuse muscle weakness (1, 2). It has a usually childhood onset and – except for severe congenital forms – it is a benign disease with a slight progression.

From a genetic point of view, nemaline myopathy can be due to mutations in nebulin (NEB), α- skeletal actin (ACTA1), α-tropomyosin (TPM3), β-tropomyosin (TPM2), troponin T (TNNT1), or coflin (CFL2) genes.

Respiratory failure – constant in more severe types – can occur also in patients with mild presentation (3, 4). Cases with cardiac involvement have been rarely described (5-8). The association between cardiomyopathy and respiratory insufficiency is very rare (9). Here we describe a case of nemaline myopathy presenting as dilated cardiomyopathy and heart failure, complicated by respiratory failure.

Case report

The patient is a 50-year-old man. His medical history was not contributory. At the age of 37 years, he complained of persistent fatigue and dyspnoea even for modest efforts and oedema of lower limbs. The patient was examined at the department of internal medicine of the local hospital, and hospitalised with a diagnosis of dilated cardiomyopathy probably consequence of a myocarditis process. Soon after he was transferred to the cardiology department of the regional hospital, and pharmacologically treated for heart failure and pulmonary hypertension. Two weeks later the patient presented several episodes of oxygen desaturation, despite a clinical improvement in the heart failure. Blood gas analysis showed an arterial partial pressure of carbon dioxide (PaCO2) of 125.5 mmHg, suggesting marked hypercapnia, while chest X-ray revealed a diaphragmatic paralysis. Assisted respiration by non-invasive continuous positive-pressure ventilation was introduced, after consultation with the patient and his family.

Once the respiratory parameters stabilized, the patient was referred to a neurology department to investigate the presence of an underlying neuromuscular disease. Elec-
Tromyography revealed a nontypical myogenic pattern. Muscle biopsy, by EE staining, showed marked variation in fibre size, with the co-existence of hypotrophic and hypertrophic fibres, together in small groups, containing nemaline bodies. The same pattern was confirmed by the Gomory’s trichrome staining (Fig. 1). ATPase staining revealed preferential atrophy of type 1 fibres. The ultrastructural analysis confirmed the presence of nemaline “rods”. These findings confirmed the clinical diagnosis of “nemaline myopathy”.

For about 11 years the patient performed periodical cardiac and respiratory investigations, showing stability of the clinical conditions.

In the last year a deterioration of respiratory parameters was observed. At the last control at our Service, the muscle examination showed a slight decrease in muscle strength at both the upper and lower limbs (MRC Scale score 4), a marked decrease in the neck muscles strength (MRC Scale score 3) and diffuse muscle atrophy. The patient was able to walk unassisted and to stand up from the squat-down position. The deep tendon reflexes were diffusely and symmetrically reduced. Tibio-tarsal contractures were observed. Scoliosis was not present.

Electrocardiography revealed a sinus rhythm, with a heart rate of 60/minute, incomplete right bundle branch block, anterior left hemi-block and pulmonary hypertension.

Echocardiography revealed left ventricular dilation with reduced systolic function (EF = 50%), dilation of right ventricle, moderate mitral regurgitation and mild tricuspid regurgitation (Fig. 2). PAPs were 58mmHg. Patent foramen ovale was observed.

Spirometric tests showed a reduction in percentage of FVC (20% of the expected values), PEF (40%) and FEV1 (25%).

Laboratory tests showed a slight increase in CK values (289 U/L vs 190U/L), in total LDH (483 U/L vs 480 U/L) and in LDH5 isoenzyme (24,2% vs 17%), in bilirubin (2,87 vs 1,2). On the other hand creatinine values were reduced (0,65 vs 0,67 mg/dL).

The patient is currently on ivabradine (5 mg/die), ace-inhibitors (ramipril 1,25 mg/die), diuretics (furosemide 25 mg/die and canrenone 50 mg on alternate days), coenzyme Q10 (100 mg/die) and magnesium pidolatum (1,5 g/die). The patient is ventilatory assisted 24h/24h and unable to attend daily activities.

Discussion

Nemaline myopathy is the most frequent form of congenital myopathies. It is characterised from a clinical point of view by a continuous spectrum of phenotypes ranging from severe congenital forms to mild childhood—juvenile forms and adult-onset forms. Recently a sixth group has been added that includes cardiomyopathy and ophthalmoplegia (3).

In our patient the type of nemaline myopathy was classified as an adult form. From a genetic point of view, nemaline myopathy can be caused by mutations in six different genes. The analysis of gene mutations in our patient is still in progress.

Cardiac involvement is a frequent autopsy finding in patients with nemaline myopathy (5-8), presenting as hypertrophic cardiomyopathy, dilated cardiomyopathy, pulmonary hypertension or congenital defects (ventricular septal defect).

In our patient the presenting symptoms were those of heart failure; however echocardiography also revealed patent foramen ovale and severe pulmonary hypertension.
On a case of respiratory failure due to diaphragmatic paralysis and dilated cardiomyopathy in a patient with nemaline myopathy

According to the individual case reports, nemaline dilated cardiomyopathy ultimately led to fatal outcome in most patients.

The combination therapy with beta-blockers and ace-inhibitors, the standard therapy in patients with symptomatic dilated cardiomyopathy (10), contributed to the relief of heart failure in the last 12 years; the recent substitution of beta-blockers by ivabradine further ameliorated the general conditions of our patient. Despite the improvement in cardiologic parameters, a severe respiratory failure occurred few months after the cardiac symptoms, with several episodes of oxygen desaturation, due to the paralysis of the diaphragm. The restrictive respiratory syndrome evolved over time so that the patient is currently on continuous ventilatory support.

In our case, it is not clear whether symptoms of respiratory failure preceded in a subtle way the onset of heart failure or they were masked by the symptoms of heart failure. However it should be stressed that respiratory monitoring is necessary in all cases of diagnosed or suspected nemaline myopathy.

Acknowledgements

The work was in part supported by a Telethon grant (GTB07001H) to LP.

References

1. Shy GM, Engel WK, Somers JE, et al. Nemaline myopathy. A new congenital myopathy. Brain 1963;86:793-810.
2. Sharma MC, Jain D, Sarkar C, et al. Congenital myopathies. A comprehensive update of recent advancements. Acta Neurol Scand 2009;119:281-92.
3. Wallgren-Pettersson C, Laing NG. Report of the 70th ENMC International Workshop: nemaline myopathy. 11-13 June 1999, Naarden, The Netherlands. Neuromuscular Disord 2000;10:299-306.
4. Raveau T, Lassalle V, Dubourg O, et al. Nemaline rod myopathy revealed by acute respiratory failure after an outpatient cataract surgery. Ann Fr Anesth Reanim. 2012;31:638-40.
5. Stoessl AH, Hahn AF, Malott D, et al. Nemaline myopathy with associated cardiomyopathy. Report of clinical and detailed autopsy findings. Arch Neurol 1985;42:1084-6.
6. Muller-Hocher J, Schafer S, Mendel B, et al. Nemaline cardiomyopathy in a young adult: an ultraimmunohistochemical study and review of the literature. Ultrastruct Pathol 2000;24:407-16.
7. Meyer C, Voellmy W, Gertsch M, et al. Nemaline myopathy appearing in adults as cardiomyopathy. A clinicopathologic study. Arch Neurol 1984;41:443-5.
8. Sun-Young K, Young-Eun P, Hyang-Sook K, et al. Nemaline myopathy and non fatal hypertrophic cardiomyopathy caused by a novel ACTA1 E239K mutation. J Neurol Sci 2011;307:171-3.
9. Nagata R, Kamimura D, Suzuki Y, et al. A case of nemaline myopathy with associated dilated cardiomyopathy and respiratory failure. Int Heart J 2011;52:401-5.
10. Politano L, Nigro G. Treatment of dystrophinopathic cardiomyopathy: review of the literature and personal results. Acta Myol 2012;31:24-30.