SHORT REPORT

Cardiomyopathy in motor neuron diseases

H-J Gdynia, A Kurt, S Endruhn, A C Ludolph, A-D Sperfeld

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Objective: Myocardial involvement in motor neuron diseases (MND) is an uncommon feature. In amyotrophic lateral sclerosis (ALS) abnormalities of the autonomic nervous system affecting cardiac function have been described, for the hereditary spastic paraplegias (HSP) comparable manifestations are unknown. This study observed ALS and HSP patients with coexisting cardiomyopathy without major cardial risk factors.

Methods: Four patients with definite ALS and two pHSP patients. In all patients detailed clinical, cardiological, electrophysiological and laboratory data were analysed. In two ALS patients skeletal muscle biopsy was performed.

Results: In all investigated MND patients cardiomyopathy was present. Beside hyperlipoproteinaemia and mild hypertension in one case, none of the patients showed major cardiovascular risk factors. There was no evidence for a secondary cause of cardiomyopathy like coronary heart disease, myocarditis, or mitochondrial damage mimicking MND.

Conclusion: This report could not conclude that the occurrence of cardiomyopathy is rare logically. Although an underlying pathophysiological cause was not obvious, it is proposed that in all MND patients a routine cardiological evaluation should be performed.

Motor neuron diseases (MND) are a heterogeneous group of neurodegenerative disorders mainly characterised by selective damage of the central or peripheral motor system, or both. MND may be classified into three groups. The hereditary spastic paraplegias (HSP) are characterised by degeneration of the corticospinal tracts,[1] the spinal muscular atrophies (SMA) marked by degeneration of the lower motor neurons,[2] and the amyotrophic lateral sclerosis (ALS) caused by degeneration of the corticospinal tracts as well as the motor neurons within the anterior spinal horns and the brain stem.[3] Cardiac involvement has been occasionally described as part of the MND phenotype: cardiac denervation attributable to involvement of the sympathetic nervous system has been described in patients in the early stages of ALS.[4] Congenital heart defects have been seen in a few cases of SMA.[5–7] We now report on four patients with definite ALS and two patients with pure HSP in whom cardiomyopathy occurred in the absence of major cardiovascular risk factors or coronary heart disease.

METHODS

Patients

Patients with cardiac symptoms and echocardiographic abnormalities were retrospectively ascertained from our motor neuron outpatient clinic over a two year period. About 150 patients with MND are screened at this clinic each year. There are six patients with MND having cardiac involvement (four ALS, two HSP). The ALS patients were 59 to 80 years old (mean 67.5 (SD 10.7) years) and had an age of disease onset between 55 and 78 years (mean 63.5 (SD 10.4) years). All fulfilled the criteria of definite ALS (http://www.wfnals.org.articles/elescorial1998.schema.htm). Two women (aged 60 and 74 years) were diagnosed with autosomal dominant pure HSP. Both fulfilled the criteria to HSP and underwent the exclusion diagnostics as advised by Fink.[1] All patients are still alive and were consecutively studied from the disease onset on. In all patients family history for heart diseases was unremarkable.

Clinical and laboratory examinations

Beside clinical examination all six patients underwent routine laboratory investigations, cerebrospinal fluid analysis to rule out inflammatory disorders, neurophysiological testing, and radiological studies. Electrocardiography, treadmill electrocardiography, and echocardiography were performed in all cases and two patients underwent coronary angiography. Cardiomyopathy was diagnosed non-invasively by abnormal ventricular contractility, ventricular hypokinesis, and reduction of ejection fraction below 45%.

Skeletal muscle biopsy of the vastus lateralis was performed in patients 1 and 2. Specimens underwent standard histological studies, including haematoxylin-eosin, Gomori trichrome, oil-red-o, period acid schiff, nicotinamide adenine dehydrogenase, adenosine triphosphatase, cytocrome-c-oxidase, and acid phosphatase. Electron microscopy and biochemical analysis of mitochondrial content were performed on both specimens.

RESULTS

Table 1 outlines the clinical characteristics and demographics of the patients. All patients were negative for superoxide dismutase 1 mutation. All patients fulfilled the El Escorial criteria for definite ALS. The HSP patients were spastin mutation negative. All patients were alive as of the date of publication and so therefore cardiac tissue was not available.

In the ALS patients three cases had spinal onset and one patient had bulbar onset disease. All ALS patients were treated with riluzole. None of the ALS patients had a history of cardiac events like myocardial infarction before onset of ALS symptoms. Laboratory analysis showed increased activities of serum creatine kinase (CK) in all ALS patients, but cardiac creatine kinase (CK-MB) was normal in all cases. Both vastus lateralis muscle biopsies (patient 1 and 2) showed a chronic neurogenic pattern. In patient 2, secondary myopathic changes were found in addition to a prominent neurogenic damage. ATPase stainings showed fibre typing in both cases. No abnormalities were found in oxidative stainings and in the biochemical analysis. Electron microscopic investigation showed no structural or storage abnormalities.

Abbreviations: ALS, amyotrophic lateral sclerosis; CM, cardiomyopathy; HSP, hereditary spastic paraparesis; pHSP, pure hereditary spastic paraparesis; MND, motor neuron disease; SMA, spinal muscular atrophy

Table 1 Summary of clinical and laboratory findings in cases studied

	1 (ALS)	2 (ALS)	3 (ALS)	4 (ALS)	5 (HSP)	6 (HSP)
Sex	F	M	F	M	F	F
Age (y)						
Recent	65	59	80	66	74	60
At onset of MND	57	55	78	64	15	20
At onset of CM	53	54	76	63	60	55
Site of disease	unilateral	bilateral	unilateral	bulbar	bilateral	bilateral
Onset	UL	LL	LL		LL	LL
Reflexes	↑/↑ in all limbs	norm	↑/↑ in all limbs	norm	↑/↑ in LL	↑/↑ in LL
Babinski	−/−	−/+	+/+	+/+	+/+	+/+
Fasciculations	ubiquitous	ubiquitous	ubiquitous	UL	none	none
Sensory deficits	–	–	–	–	–	–
CK (U/l, normal < 100)	330	380	290	320	norm	norm
LDL-cholesterol (mmol/l, normal < 4.91)	6.13	7.63	5.56	7.11	5.66	6.78
Echocardiographic findings	EF 25%, LVD, GH	EF 30%, LVD, GH, reduced free wall thickness	EF 23%, GH, increased septal wall thickness, aortal valve stenosis	EF 40%, LVD, GH	EF 39%, LVD , GH	EF 43%, LVD, GH, reduced free wall thickness

ND, neurological disease; CM, cardiomyopathy; LVD, left ventricular dilation; GH, global hypokinesis; UL, upper limb; LL, lower limbs; ↑/↑ raised; norm, normal; +/+, bilateral positive; −/+ unilateral positive; EF, ejection fraction.

The two autosomal dominant HSP patients had spastic paraplegia of the lower limbs, pyramidal tract signs, and bladder and bowel dysfunction.

Cardiomyopathy was seen in the four ALS and two HSP patients. All patients had dyspnea on minimal exertion and patients 2 and 3 showed jugular venous distension. Paroxysmal heart palpitations were present in all patients. Patient 1 (a 65 year old woman with ALS) complained of acute onset of dyspnea caused by pulmonary oedema. Patient 3 (an 80 year old woman with ALS) presented with pectanginous pain caused by acute myocardial infarction and reduced ejection fraction. All six patients showed increased LDL-cholesterol and one patient had mild hypertension (<140/90 mm Hg) that did not require treatment. Electrocardiography showed previous myocardial infarction in patient 3 and non-specific repolarisation abnormalities were observed in all patients without evidence for previous silent myocardial infarctions. Echocardiography showed dilated cardiomyopathy in five cases and hypertrophic-obstructive form in patient 3. In all cases left ventricular failure with reduced ejection fraction and global ventricular hyopkinesis were seen. Treadmill electrocardiography showed no evidence for ischaemic heart disease in any of the patients; coronary angiography did not show structural abnormalities in patients 1 and 2.

DISCUSSION

In this study we report a case series of six MND patients with idiopathic cardiomyopathy that could not be explained by coronary heart disease, myocarditis, or other aetiology.[8] There are few reports of cardiac involvement occurring in patients with either ALS or SMA. One 75 year old woman with ALS developed postoperative ''Takotsubo'' cardiomyopathy,[9] defined as a reversible left ventricular dysfunction with wall motion abnormalities with apical akinesis and basal hyperkinesis.[10] Dysfunction of the sympathetic nervous system influencing the cardiac function has been described in ALS.[4] Congenital heart defects are known to occur in SMA.[5–7] Furthermore, hypertrophic cardiomyopathy was described in a patient with a SMA-like syndrome attributable to cytocrome-c-oxidase deficiency in skeletal muscle.[11 12] In contrast, cardiac involvement has not been previously described in HSP.

The pathogenetic mechanism leading to a higher incidence of cardiomyopathy in ALS and HSP patients is not clear. One possibility is that hyperlipidaemia contributed to the development of the cardiomyopathy in these patients. However, in our patients cardiomyopathy was a concomitant feature. The ALS patients noticed cardiac symptoms before onset of neurological symptoms, in one case pectanginous pain caused by acute myocardial infarction was the first noticed cardial symptom. In this case echocardiography showed aortal valve stenosis. One patient showed two cardiovascular risk factors, in the other cases isolated hyperlipoproteinaemia was found. Treadmill electrocardiography found no evidence for ischaemic disease in all cases. Family and personal history showed no cardiovascular and heart diseases in all patients. Muscle biopsy showed a regular pattern in the oxidative stainings, no signs of cytocrome-c-oxidase deficiency or mitochondrial disorder.

We found six patients with cardiomyopathy in a population of about 300 patients with MND, the reported annual incidence of dilated cardiomyopathy varies between five and eight cases per 100 000 population, depending on the diagnostic criteria used.[13] Based on our data, we hypothesise that cardiomyopathy is underdiagnosed in the ALS population, possibly because symptoms are masked by the patient's inability to exert themselves. We believe that in all MND patients a routine cardiological evaluation should be performed, including yearly echocardiography.

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Authors' affiliations

H-J Gdynia, A Kurt, S Endruhn, A C Ludolph, A-D Sperfeld, University of Ulm, Department of Neurology, Oberer Eselsberg, Ulm, Germany

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Correspondence to: Dr H-J Gdynia, University of Ulm, Department of Neurology, Oberer Eselsberg 45, 89081 Ulm, Germany; hans-juergen.gdynia@uni-ulm.de

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REFERENCES

1 **Fink JK**, Heiman-Patterson T, Bird T, *et al*. Hereditary spastic paraplegia: advances in genetic research. Hereditary Spastic Paraplegia Working group. *Neurology* 1996;**46**:1507–14.
2 **Hausmanowa-Petrusewicz I**, Vrbova G. Spinal muscular atrophy: a delayed development hypothesis. *Neuroreport* 2005;**16**:657–61.
3 **Ince PG**, Lowe J, Shaw PJ. Amyotrophic lateral sclerosis: current issues in classification, pathogenesis and molecular pathology. *Neuropathol Appl Neurobiol* 1998;**24**:104–17.
4 **Oey PL**, Vos PE, Wieneke GH, *et al*. Subtle involvement of the sympathetic nervous system in amyotrophic lateral sclerosis. *Muscle Nerve* 2002;**25**:402–8.
5 **Mulleners WM**, Van Ravenswaay CMA, Gabreels FJM, *et al*. Spinal muscular atrophy combimed with congenital heart disease: a report of two cases. *Neuropediatrics* 1996;**27**:333–4.
6 **Lagarde P**, Bakouche P, Lamotte-Barrillon S. The Wohlfart-Kugelberg-Welander disease. A clinical case with nonobstructive myocardiopathy. *La Semaine des hôpitaux* 1976;**52**:1017–21.
7 **Yasuma F**, Kuru S, Konagaya M. Dilated cardiomyopathy in Kugelberg-Welander disease: coexisting sleep disordered breathing and its treatment with continuous positive airway pressure. *Intern Med* 2004;**43**:951–4.
8 **Olson TM**, Keating MT. Mapping a cardiomyopathy locus to chromosome 3p22-p25. *J Clin Invest* 1996;**97**:528–32.
9 **Takayama N**, Iwase Y, Ohtsu S, *et al*. ''Takotsubo'' cardiomyopathy developed in the postoperative period in a patient with amyotrophic lateral sclerosis. *Masui* 2004;**53**:403–6.
10 **Akashi YJ**, Sakakibara M, Miyake F. Reversible left ventricular dysfunction ''takotsubo'' cardiomyopathy associated with pneumothorax. *Heart* 2002;**87**:e1.
11 **Rubio-Gozalbo ME**, Smeitink JA, Ruitenbeek W, *et al*. Spinal muscular atrophy-like picture, cardiomyopathy and cytochrome c oxidase deficiency. *Neurology* 1999;**52**:383–6.
12 **Pons R**, Andreetta F, Wang CH, *et al*. Mitochondrial myopathy simulating spinal muscular atrophy. *Pediatr Neurol* 1996;**15**:153–8, .
13 **Dec GW**, Fuster V. Idiopathic dilated cardiomyopathy. *N Engl J Med* 1994;**331**:1564–75.

NEUROLOGICAL PICTURE

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Temporal arteritis or phlebitis?

A 75 year old woman came to us with a 2 day history of pain in the right temple on combing her hair. On examination, a thin walled, dilated tortuous vessel was seen on the right temple with a tender 20 mm cord along the course of the vessel, under the hairline. She also had enophthalmos and ptosis in the right eye. On questioning, she acknowledged that the tortous vessel had been visible for the last few years. Her ESR was 15 mm/hour. Contrast enhanced computed tomography (CT) of the orbit showed a right orbital venous angioma extending onto the scalp. The acute scalp pain was probably due to thrombosis of the extracranial draining vein.

Neurologists immediately suspect temporal arteritis when elderly patients complain of scalp pain on touch. However, this case demonstrates the unusual occurrence of a temporal phlebitis simulating temporal arteritis.

B V Maramattom
Department of Neurology, Lourdes Hospital, Kochi, Kerala, India

Correspondence to: Dr B V Maramattom, Department of Neurology, Lourdes HospitalKochi, Kerala, India; bobvarkey@gmail.com

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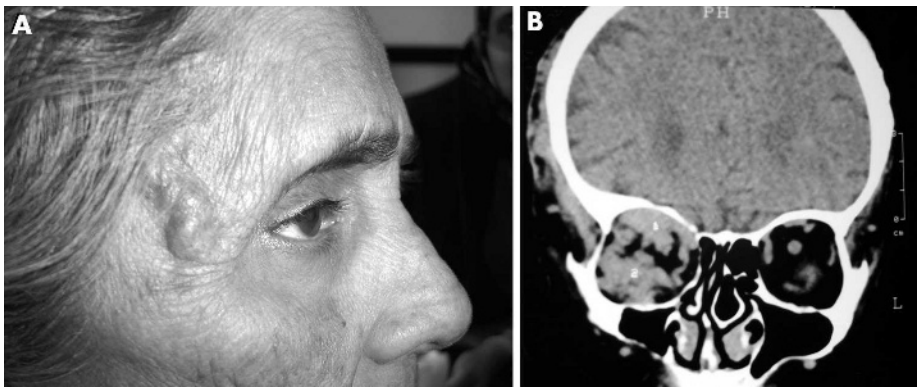

Figure 1 (A) Clinical picture showing distended and tortuous temporal vein; (B) CT orbit showing venous angioma situated in the right orbit. Informed consent was obtained for publication of this figure.