Journal of Neuromuscular Diseases 1 (2015) S55–S56
DOI 10.3233/JND-159049
IOS Press

Poster Abstract: Diagnostic

Frequency of Cerebrovascular Abnormalities in Patients with Late-Onset Pompe Disease: Our Experience

C. Sancricca*, G. Primiano, D. Bernardo, D. Sauchelli, C. Cuccagna and S. Servidei
Department of Neurology, Catholic University, Rome, Italy

BACKGROUND

Although muscle skeletal dysfunction is generally the prominent manifestation of late-onset Pompe disease (LOPD), the disease can present with a broad spectrum of clinical manifestations reflecting multisystem involvement with glycogen accumulation in several tissues, including smooth muscle and blood vessels. In recent years, cerebrovascular abnormalities have also been described. To date, Laforêt and colleagues reviewed eight previously published reports of cerebral vessel involvement in Pompe disease, and also described three cases of vascular abnormalities in their LOPD population.[1] Sacconi and colleagues reported the presence of cerebrovascular anomalies in four out of six LOPD patients.[2]

METHODS AND RESULTS

We report data from our population of 11 LOPD patients who underwent magnetic resonance or TC angiography. Three patients were revealed to have significant brain vascular abnormalities (Table 1). One patient (P11) presented three different aneurysms both on intra- and extra-cranial cerebral vessels (Fig. 1), and has been proposed for surgical intervention. None of patients reported clinical symptoms related to the arteriopathy.

CONCLUSIONS

Our data confirm that LOPD patients have a predisposition to dilative arteriopathy of cerebral vessels, even if the real incidence of these abnormalities has yet to be exactly assessed. We also confirm that ectasic/dolichomega basilar artery is the most common abnormality in LOPD patients with cerebral vessel involvement.

Clinical presentation can be very heterogeneous,[1–3] and rupture of a cerebral aneurysm has recently been described as a presenting symptom in an LOPD patient.[4] In regard to this, none of our patients have had "vascular" symptoms, highlighting the need for a careful cerebrovascular investigation for the early recognition of such abnormalities in order to properly address the clinical management and prevent potentially fatal events. Brain and neck angio CT scans and cerebral angiography are, in our experience, the most sensitive procedures to detect vascular abnormalities, while magnetic resonance can, in some cases, not be conclusive.

The pathogenesis of cerebrovascular abnormalities is probably related to the presence of vacuolar degeneration and glycogen accumulation in the smooth muscle cells of cerebral arteries.[1] Thus, important open questions remain as to the possible relationship with other systemic vascular anomalies, and, more importantly, the possible effect of ERT on arteriopathy, as seems to be in vitro in the smooth muscle of LOPD patients.[5]

REFERENCES

[1] Laforêt P, Petiot P, Nicolino M, Orlikowski D, Caillaud C, Pellegrini N, Froissart R, Petitjean T, Maire I, Chabriat H, Hadrane L, Annane D, Eymard B. Dilative arteriopathy and basilar artery dolichoectasia complicating late-onset Pompe disease. Neurology. 2008;70(22):2063-6.
[2] Sacconi S, Bocquet JD, Chanalet S, Tanant V, Salviati L, Desnuelle C. Abnormalities of cerebral arteries are frequent

*Correspondence to: C. Sancricca, Department of Neurology, Catholic University, Rome, Italy. E-mail: cristinasancricca@me.com.

ISSN 2214-3599/15/$27.50

Table 1
Characteristics of LOPD patients

	Age (yr)/ sex	Age at onset (yr)	GAA genotype		Enzyme assay	ERT	Brain vascular abnormalities
P1	62/F	45	IVS 13 T->G	c.670 C>T	lymphocytes: 9.000 pmol mU liberato/ min/mg	Yes	Dolichomega basilar artery, ectasic L vertebral artery, fetal origin of R posterior cerebral artery
P2	61/F	42	IVS 13 T->G	c.962+2_3del	muscle: 0.730 nmol/ hr/mg	Yes	No
P3	42/F	35	IVS 13 T->G	_	muscle: 0.400 nmol/ hr/mg	Yes	No
P4	29/F	11	IVS 13 T->G	_	muscle: 0.390 nmol/ hr/mg	Yes	No
P5	38/F	20	IVS 13 T->G	_	lymphocytes: 7.540 pmol/min/mg	Yes	No
P6	50/F	48	_	_	muscle: 0.440 nmol/ min/g	Yes	No
P7	53/M	44	IVS 13 T->G	p.LYS849FS	muscle: 0.58 nmol mU liberato/min/g	Yes	Dolichomega basilar artery
P8	62/F	40	_		muscle: 11.7 pmol/ min/mg	Yes	No
P9	32/F	30	IVS 13 T->G	c.2530_2541del12	muscle: 1.26 nmol/ MU liberato/min mg	Yes	No
P10	51/F	44	_	_	muscle: 0.28 nmol MU/min/g	Yes	No
P11	60/M	48	_	_	muscle: 0.91 nanomol mU liberato/min/g	No	2 different aneurysms of R internal carotid, saccular aneurysm of R carotid bulb (9 mm diameter)

GAA, acid a-glucosidase enzyme; ERT, enzyme replacement therapy; L, left; R, right.

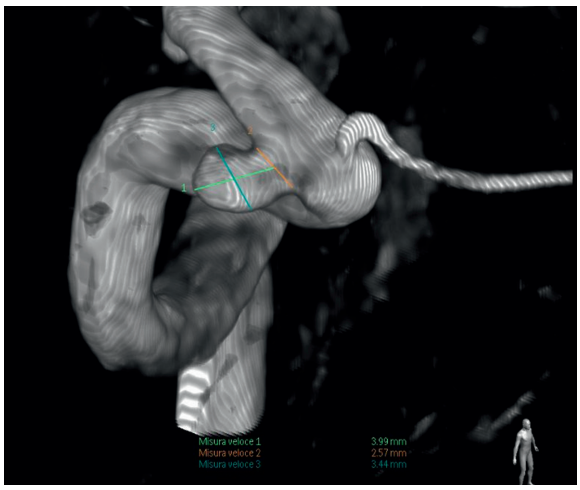

Fig. 1. 3D reconstruction from arteriography of Patient 11.

in patients with late-onset Pompe disease. J Neurol. 2010;257(10):1730-3.
[3] Winkel LP, Hagemans ML, van Doorn PA, Loonen MC, Hop WJ, Reuser AJ, van der Ploeg AT. The natural course of non-classic Pompe's disease; a review of 225 published cases. J Neurol. 2005;252(8):875-84.
[4] Peric S, Fumic K, Bilic K, Reuser A, Rakocevic Stojanovic V. Rupture of the middle cerebral artery aneurysm as a presenting symptom of late-onset Pompe disease in an adult with a novel GAA gene mutation. Acta Neurol Belg. 2014;114(2):165-6.
[5] Winkel LP, Kamphoven JH, van den Hout HJ, Severijnen LA, van Doorn PA, Reuser AJ, van der Ploeg AT. Morphological changes in muscle tissue of patients with infantile Pompe's disease receiving enzyme replacement therapy. Muscle Nerve. 2003;27(6):743-51.