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Letter to the Editor

Enzyme replacement therapy and antibodies in late-onset Pompe disease

Keywords:
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Patients with late-onset Pompe disease receiving enzyme replacement therapy (ERT) usually develop IgG antibodies against algucosidase alpha (anti-rhGAA) within the first 3 months. The role of these antibodies in adults is not fully understood. Patel et al. recently published an article entitled: 'The impact of antibodies in late-onset Pompe disease: a case series and literature review', Mol. Genet. Metab. 106 (2012) 301-9 [1]. They describe three adult Pompe patients with high, sustained antibody titers (HSAT = anti-rhGAA IgG titer > 1: 51,200 on two or more occasions at or beyond 6 months on ERT) associated with deterioration under ERT.

We analyzed long-term testing for these antibodies performed by Genzyme Corporation using the same methods as described by Patel et al. in 10 genetically confirmed patients with late-onset Pompe disease: None of our patients met the criteria for HSAT.

It is noteworthy that 3/10 patients (P1,8,9) had anti-rhGAA IgG titers that were undetectable or borderline (Table 1). These three patients maintained a stable disease course under ERT. One of those patients with antibodies (P6) developed a sudden increase of the antibody titer to 1:25,600 after 40 months of ERT, which was associated with the need for noninvasive ventilation and walking aids. Nevertheless, in another patient (P2) an antibody titer of 1:25,600 had no impact on the functional status.

In conclusion our data as the data from Patel et al. suggest that peaks of anti-rhGAA IgG antibody titers can occur even after several years of ERT. In our small cohort no clear correlation between anti-rhGAA IgG titer and clinical outcome under ERT can be figured out although those patients without antibodies remained stable under ERT after 4 years compared to deterioration in some patients with antibodies.

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Reference

[1] T.T. Patel, S.G. Banugaria, L.E. Case, S. Wenninger, B. Schoser, P.S. Kishnani, The impact of antibodies in late-onset Pompe disease: a case series and literature review, Mol. Genet. Metab. 106 (2012) 301–309.

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Table 1
Demographic and clinical data and anti-rhGAA antibody titers in 10 adult patients with late-onset Pompe disease.

Pat. nr.	Sex	*GAA* genotype	Age at start start of observation (years)	Duration of ERT at start of observation (months)	Start of observation		Comment	Anti-rhGAA antibody titers 4 year observation period				End of observation		Comment
					6MWT (m)	VC (%)		1st year	2nd year	3rd year	4th year	Δ6MWT (m)	Δ VC (%)	
1	M	c.-32-13T>G p.C103G	52	53	375	46	NIV since 2/2005	0	0	0	0	−15	−2	–
2	M	c.-32-13T>G p.W499R	44	43	235	67	2 crutches	6400	12,800	25,600	12,800	−95	−13	–
3	F	c.-32-13T>G c.2481 + 102_2646 + 31del	69	35	60	88	Walking frame	3200	800	3200	3200	−55	−16	Wheelchair since 2nd observation year
4	M	c.-32-13T>G c.2136_2137del	43	29	387	32	NIV since 2007	6400	3200	3200	3200	−37	+3	–
5	F	p.P493L p.L552P	36	21	340	120	–	800	3200	1600	n.a.	−60	−9	–
6	F	c.-32-13T>G p.L552P	47	27	375	65	–	n.a.	1600	25,600	12,800	−195	−7	NIV and 1 cane since 3rd observation year
7	M	c.-32-13T>G p.G309R	63	3	200	50	1 cane	400	n.a.	200	200	−120	−2	NIV since 3rd observation year
8	F	c.-32-13T>G c.1438-1G>C	19	0	510	62	–	Pre 0	200	0	0	−30	−1	–
9[a]	F	p.C103G p.P493L	56	0	420	73	–	–	Pre <100	<100	<100	+/−0	+5	–
10[a]	M	p.C103G p.P493L	47	0	420	103	–	Pre 0	1600	1600	1600	+30	+/−0	–

GAA α − glucosidase; ERT enzyme replacement therapy; 6MWT(m) 6 min walking test in meters; VC vital capacity as % of normal; NIV noninvasive ventilation; n.a. not available.
[a] Patients 9 and 10 are siblings.

I. Schneider*
M. Deschauer
F. Hanisch
Department of Neurology, Martin-Luther-University Halle-Wittenberg, Ernst-Grube-Str. 40, D-06120 Halle (Saale), Germany
*Corresponding author. Fax: +49 345 557 3335.
E-mail address: ilka.schneider@medizin.uni-halle.de (I. Schneider).

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