ACTUALITES BIBLIOGRAPHIQUES 2010 MALADIE DE GAUCHER

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The risk of Parkinson's disease in type 1 Gaucher disease.

- We estimated the risk of PD in a cohort of 444 consecutively evaluated patients with GD1 compared to that in the general population.
- Eleven patients developed parkinsonian syndrome during a 12-year follow-up period. The adjusted life-time risk ratio of PD in GD1 compared to that in the general population was 21.4 [95% confidence interval (95% CI) 10.7-38.3], with a higher risk in men compared to women.
- In our cohort, GD1/Parkinson's disease phenotype (GD1/PD) was characterized by higher GD1 severity score, due to higher incidence of avascular osteonecrosis.

Bultron G , J Inherit Metab Dis. 2010 Apr;33(2):167-73. 2010.

The incidence of Parkinsonism in patients with type 1 Gaucher disease: Data from the ICGG Gaucher Registry

- The matched study cohort comprised of 68 patients with reports of Parkinsonism and 649 patients without Parkinsonism.
- The probability that a patient with GD1
- will develop Parkinsonism before age 70 years is 5 to 7% and 9 to 12% before age 80 years.

B Rosenbloom Blood Cells, Molecules, and Diseases (2010)

Spontaneous regression of disease manifestations can occur in type 1 Gaucher disease; results of a retrospective cohort study.

Table 2
Criteria of disease course, applied for each individual patient.

Patient number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Progression criteria; at least one criterion																		
Increase of liver ratio >10%																		+
Increase of chitotriosidase ≥30%								+								+		
Decrease of QCSI to ≤23%																		
Progression criteria; at least two criteria																		
Increase of spleen volume >10%		+																
Decrease of hemoglobin male<12.8/female<12.0																		
Platelet count decrease <150, decrease >30×10^9															+			
Relative decrease QSCI of ≥20%																		
Regression criteria; at least one criterion																		
Decrease of liver ratio ≥10%		+		+	+		+											
Decrease of chitotriosidase ≥30%			+				+		+			+						
Increase of QCSI to >23%				+					+									
Regression criteria; at least two criteria																		
Decrease of spleen volume >10%			+				+		+									
Increase of hemoglobin male >12.8/ female >12.0			+															+
Platelet count increase >150, rise of >30×10^9/l																		
Relative increase QSCI of ≥20%	+	+	+	+					+									+
Finale conclusion																		
Progression of GD disease								+								+		+
Regression of GD disease		+	+	+	+		+		+			+						+
Stability of GD disease	+					+				+	+		+	+	+		+	
Started with treatment		+								+			+	+	+	+	+	+

Boomsma JM, Blood Cells Mol Dis. 2010 Mar 15;44(3):181-7. 2010.

Abnormal nonstoring capillary endothelium: a novel feature of Gaucher disease. Ultrastructural study of dermal capillaries

- Ultrastructural study of skin biopsies in two cases of Gaucher disease (GD) patients
- Alteration of the blood capillary endothelial cells (ECs)
- …
- The spectrum of changes suggests that a significant positive growth effect on EC occurs in GD.

H Hůlková, J Inherit Metab Dis (2010) 33:69–78

Disease severity in sibling pairs with type 1 Gaucher disease.

- 90 pairs of siblings: two sets of identical twins; 24 pairs of brothers, 24 pairs of sisters, and 42 pairs of mixed gender.
- in general, the phenotypic expression in the younger sibling will be similar enough to that of an older affected sibling that genetic counseling may use those findings in a prognostic way.

Elstein D, J Inherit Metab Dis. 2010 Feb;33(1):79-83. 2010.

A validated disease severity scoring system for adults with type 1 Gaucher disease

Weinreb NJ, Genet Med. 2010 Jan;12(1):44-51.

Potential biomarkers of osteonecrosis in GD.

- 100 adult patients. 92 Gaucher patients received imiglucerase. 43 had experienced osteonecrosis (ON), and eight had ON despite enzyme therapy.
- VEGF and CCL5/RANTES did not differ between Gaucher and control samples.
- Concentrations of CCL3/MIP-1α, CCL4/MIP-1β, CCL2/MCP-1, CXCL8/IL-8, IL-1ra and CCL18/PARC were elevated in Gaucher patients ($p = 0.05$ for each).
- the 8 patients with ON despite imiglucerase had median concentrations of CCL3/MIP-1α, CCL4/MIP-1β, CXCL8/IL-8, CCL5/RANTES and CCL18/PARC, which significantly exceeded the values in 84 patients now free of ON.

Pavlova EV, Blood Cells Mol Dis. 2010.

Bone events and evolution of biologic markers in Gaucher disease before and during treatment

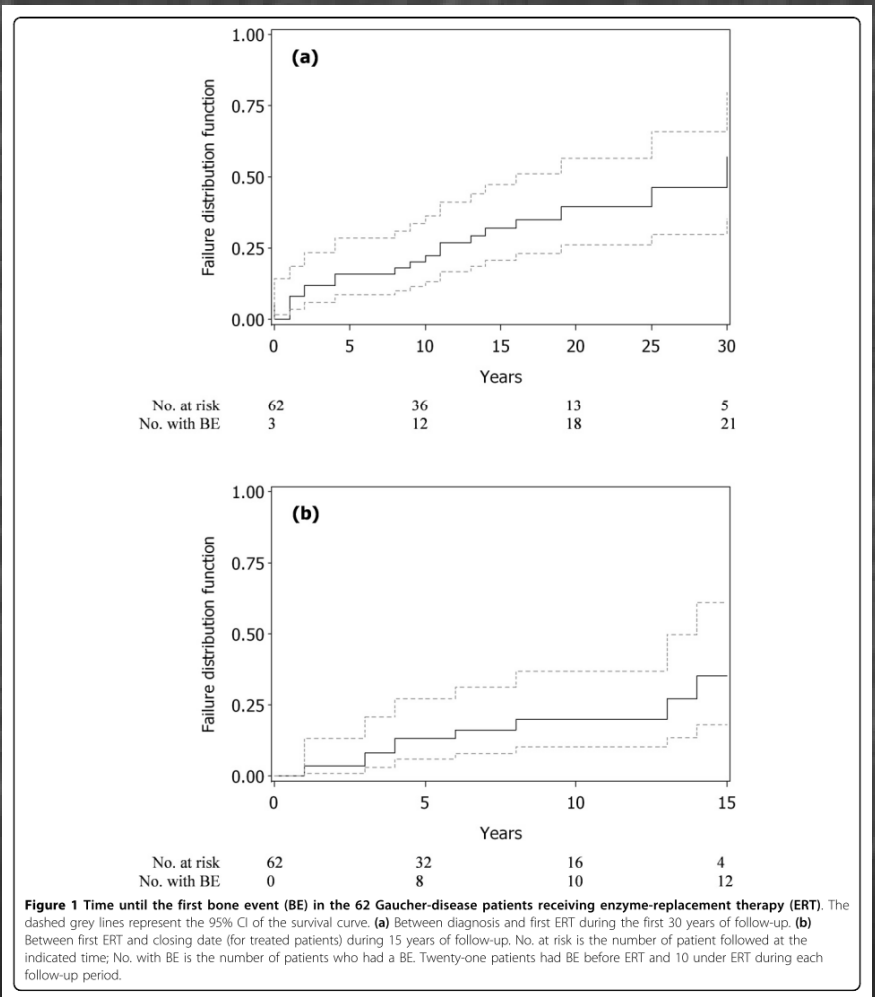
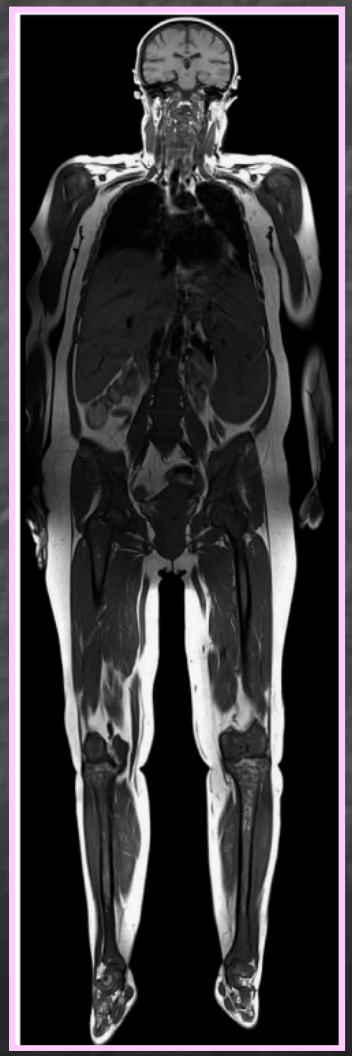


Figure 1 Time until the first bone event (BE) in the 62 Gaucher-disease patients receiving enzyme-replacement therapy (ERT). The dashed grey lines represent the 95% CI of the survival curve. **(a)** Between diagnosis and first ERT during the first 30 years of follow-up. **(b)** Between first ERT and closing date (for treated patients) during 15 years of follow-up. No. at risk is the number of patient followed at the indicated time; No. with BE is the number of patients who had a BE. Twenty-one patients had BE before ERT and 10 under ERT during each follow-up period.

- High ferritin levels and low platelet counts (Non splenectomized) at ERT onset were significantly associated with BE during ERT (P=0.019 and 0.039, respectively).

Stirnemann J, Arthritis Research & Therapy 2010, 12:R156

Whole body MRI in type I Gaucher patients: Evaluation of skeletal involvement



Humeral involvement and humeral head AVN as determined by MRI in 39 patients and relationship with splenectomy.

	Splenectomy	No splenectomy
Humeral involvement	4 (40%)	11 (38%)
No humeral involvement	6 (60%)	18 (62%)
Total number of patients	10	29
p-value[a]	0.28	
AVN of the humeral head	2 (20%)	4 (14%)
No AVN of the humeral head	8 (80%)	25 (86%)
Total number of patients	10	29
p-value[a]	0.32	

Determining and monitoring the extent of bone involvement in type 1 Gaucher patients.
The humerus may be a site of significant disease involvement warranting greater attention in bone evaluation and monitoring protocols.

L.W. Poll, Blood Cells Mol Diseases (2010)

Preimplantation genetic diagnosis (PGD) for a treatable disorder: Gaucher disease type 1 as a model

- Presentation of two couples who performed Pre-implantation genetic diagnosis for type 1 Gaucher disease.
- The mother in couple #1 is N370S/N370S; the father is a carrier of the 84GG stop codon. They have one child who is N370S/84GG and receives ERT since the age of 2 years.
- The mother in couple #2 is a carrier of the N370S mutation; the father is a carrier of the rare mutation, R359Q. They had one child with the N370S/R359Q genotype who developed massive hepatosplenomegaly and Gaucher-related lung disease necessitated lung transplantation ; she died at age 5 years.

G Altarescu, Blood Cells, Molecules, and Diseases (2010)

Type 1 Gaucher disease: significant disease manifestations in "asymptomatic" homozygotes.

- 37 Ashkenazi Jewish (AJ) were identified, previously unrecognized GD homozygotes (1:897).
- 65% reported no GD medical complaints.
- However, 49% had anemia and/or thrombocytopenia.
- Among the 29 who had imaging studies, 97% had mild to moderate splenomegaly and 55% had hepatomegaly;
- Skeletal imaging revealed marrow infiltration (100%), Erlenmeyer flask deformities (43%), and bone infarcts (14%).
- Dual energy X-ray absorptiometry studies of 25 homozygotes found 60% with osteopenia or osteoporosis.

Balwani M, Arch Intern Med. 2010 Sep 13;170(16):1463-9

Sixteen years of prenatal consultations for the N370S/N370S Gaucher disease genotype: what have we learned?

- Of 34 children born, 1 died in utero, 5 fetuses (N370S/N370S) aborted. Of 21 genotyped N370S/N370S, 7 children had Gaucher-like symptoms/signs but for only one child (two symptoms) were these ascribable to Gaucher disease; four children had non-Gaucher symptoms/signs.
- none has presented with severe disease with follow-up of 15 years

Eitan Y, Prenat Diagn. 2010 Oct;30(10):924-7.