EFFECTS OF A SHORTAGE OF IMIGLUCERASE ON THREE PATIENTS WITH TYPE I GAUCHER DISEASE

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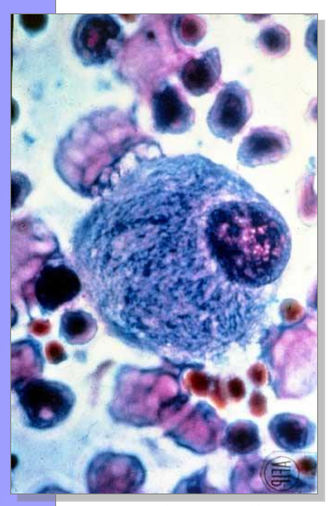
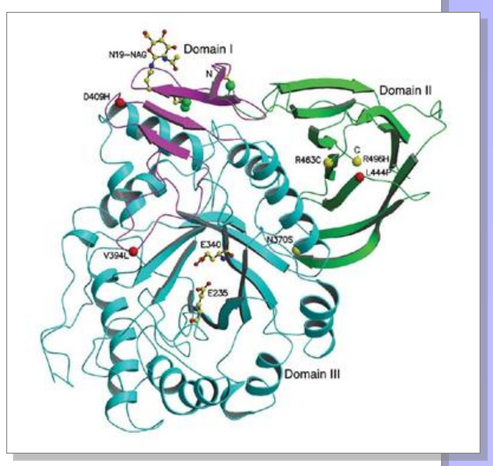


Gaucher Cell

INTRODUCTION

- Gaucher disease (GD) is the most prevalent lysosomal storage disorder (1:50.000)
- It is caused by an autosomal recessive inherited deficiency of the lysosomal enzyme glucocerebrosidase.
- Children and adolescents with GD are usually treated with enzyme replacement therapy (ERT) at an initial dose of 30-60U/kg body weight every 2 weeks.
- In August 2009, due to an acute shortage in the supply of imiglucerase, a reduced dose or a reduced infusion frequency was recommended.



Glucocerebrosidase gene

AIM

- To evaluate the effects of a reduced infusion frequency of imiglucerase over 18 months of follow-up

POPULATION AND METHODS

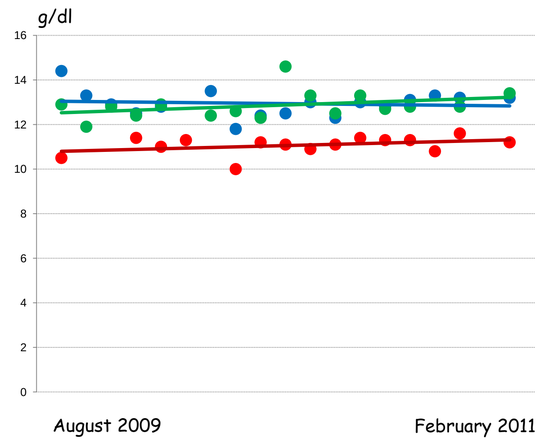
- Patients with type 1 GD treated with ERT: 3 (1M:2F)
- Median actual age: 11 Y (range 7 - 21)
- Median age at symptoms onset: 6 Y (range 3 - 8)
- Median age at the beginning of treatment: 7y (range 5 - 12).
- Median duration of treatment before dose reduction: 3y (range 1 - 8).
  - total regression of symptoms and hepatosplenomegaly
  - normalization of hematological parameters
  - improvement of quitotriosidase
- In August 2009: 40-45U/Kg every 2 W→ 40-45U/Kg every 4 W
  - Clinical and laboratory data were analyzed
  - Hemoglobin, platelet count and chitotriosidase levels were analyzed by linear regression

	Patient 1	Patient 2	Patient 3
Gender	F	F	M
Date of birth	30/10/88	28/4/99	01/04/2003
Manifestations	Anemia Thrombocytopenia Hepatomegaly Splenomegaly Bone crisis	Anemia Thrombocytopenia Hepatomegaly Splenomegaly	Anemia Thrombocytopenia Hepatomegaly Splenomegaly
Chitotriosidase (nmol/h/ml)	26.848	7.230	12.806
Tartrate resistant acid phosphatase (nmol/h/ml)	2.656	2.489	2.363
Glucocerebrosidase activity (nmol/h/mg protein)	Leucocytes: 0,53 Fibroblasts: 6,4	Leucocytes: 1,9 Fibroblasts: 15,0	Leucocytes: 1,0 Fibroblasts: 7,0
Genetic study	N370S/ g.3389-3390delCT	N370S/L444P	N370S/p.D24N
Beginning ERT	February 2001	April 2006	May 2008

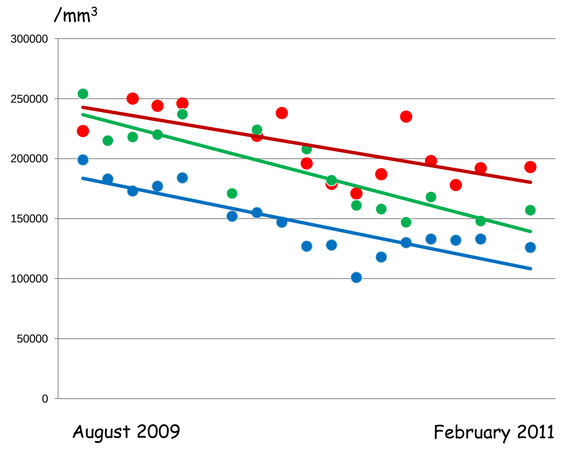
RESULTS

- All patients remained asymptomatic
- All patients remained with no major change on hematological parameters except for the patient with bone crisis who presented subnormal platelet count.
- All patients showed an upward trend in chitotriosidase values

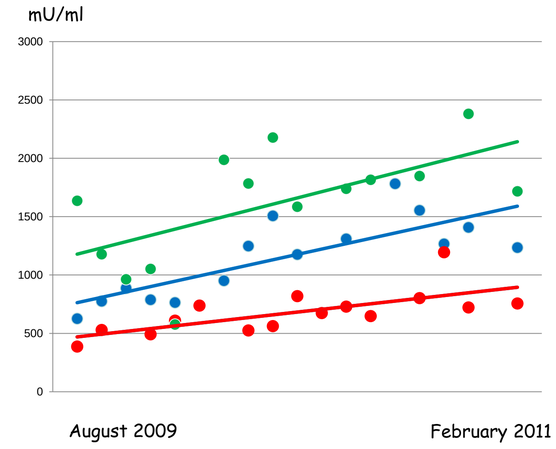
Hemoglobin levels after frequency reduction



Platelet count after frequency reduction



Chitotriosidase levels after frequency reduction



Patient 1 Patient 2 Patient 3

COMMENTS

- Although a longer follow-up is needed, is probable that even children completely stabilized can probably not be kept on lower doses even though the reduction of frequency of the infusions represent a lower social burden.