GAUCHER DISEASE;
A CASE REPORT

CASE REPORT
PROF-1888

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ABSTRACT… Objective: Gaucher disease is a lipid storage disease characterized by the deposition of glucocerbroside in cells of the Reticulo Endothelial cells (RET) system ,which encoded by a gene located on chromosome 1q21-q31.Gaucher disease occurs 1/50000 to1/100000 people in the general population. There are three clinical subtypes delineated by the absence or presence and progression of neurologic manifestation. All 3 types of Gaucher disease are inherited as autosomal recessive traits. **Case report:** A 13-month -old- female infant was born from relative parents referred to the 17-shahrivar hospital with tachypnea, Respiratory distress, and abdominal distension. In the physical examination, the patient was pale, ronchi on both lungs were heard. Respiratory distress and substernal retraction, abdominal distension due to hepatosplenomegaly, fine parallel lines in different sizes on the abdomen due to phlebotomy observed. Laboratory findings, pancytopenia reported and Bone Marrow Aspiration (BMA) Gaucher cells have been observed and abdominal sonography has been reported huge hepatosplenomegaly. For definitive diagnosis, β glucosidase activity was measured and Hydrolase acid β glucosidase activity deficiency was improved. The patient was treated by intravenous acid β glucosidase every other week. Conclusions: Genetic counseling is recommended for prospective parents with a family history of Gaucher disease.

Keywords: Gaucher Disease- Huge Hepatosplenomegaly-Gene

INTRODUCTION

Gaucher disease, first described by a French physician named Dr. Philippe Charles Ernest Gaucher in1882[2,3]. Gaucher disease is an autosomal recessive and the most common lysosomal Storage Disorder (LSD) and the most prevalent genetic defect among Ashkenazi Jews. Gaucher disease affects an estimated 1/50000 to1/100000 people in the general population[5]. Gaucher disease results from the deficient of the lysosomal Hydrolase , acid Bglucosidase, which is encoded by a gene located on chromosome 1q21-q31[1,6]. The enzymatic defect results in the accumulation of undegraded glycolipid substrates, particularly glycosylceramide, in cells of the RET system.(1)there are three clinical subtypes delineated by the absence or presence and progression of the neurologic manifestation. Type 1, the most common form is in the Ashkenazi Jewish population, with an incidence1/450 live births. non neuronopathic form with involves hepatosplenomegaly-pancytopenia –bone pain and broken bone. It can occur at any age.

Type 2, acute neuronopathic form, is characterized by brainstem abnormalities and is usually fatal during the first three years of life .and occurs rarely, with an incidence1/100000 live births.

Type3, the chronic neuronopathic form is uncommon with incidence of 1/50000 live births. The neurologic symptoms type3 are slowly progressive and appear later in childhood than the symptoms (in coordination-mental deterioration-myoclonic seizures)[1,3,4,5,6,and 7].

The pathologic hallmark of Gaucher disease is the Gaucher cell in the RET system, particularly in the bone marrow. All suspected diagnoses should be confirmed by determination of the acid B glycosidase activity in isolated leukocytes or cultured fibroblasts.
Treatment of Gaucher disease type 1 includes enzyme

replacement therapy, with recombinant acid B glucosidase by intravenous infusion every other week. The enzyme replacement does not alter the neurologic progression in patients with types2 and 3 Gaucher diseases.

CASE REPORT

A 13-month old female infant was born from relative parents referred from Fuman hospital to the 17 Shahrivar hospital with tachypnea, respiratory distress, abdominal distension multiple sores and fever. She was the first child of family, born by cesarean section, birth weight was 3350 gram. There was no history of abortion or pregnancy –related problems in mother. There was a history of intermittent productive coughing during the last 5-6 months and abdominal distention (due to hepatosplenomegaly) was appeared from two months ago. There was no medication history. She was hospitalized in Fuman hospital about one month ago because dyspnea and splenomegaly. In the physical examination, the patient was pale without icter.

No erythem or lymphadenopathy was found. The heart was tachycardia without murmur. Ronchi on both lungs were heard. Respiratory distress and substernal retraction were existed. There was abdominal distension due to hepatosplenomegaly .There were fine parallel lines in different sizes on the abdomen which were probably due to phlebotomy. No active bleeding, petechia or purpura was found on the body. Laboratory finding were:

WBC	2500	Na	135
PMN	37.3	K	3.8
Lymph	59.7	BUN	11.6
Eos	3	Cr	0.5
Platelet	87500	Triglyceride	132
Hb	7.6	Cholesterol	100
Hct	22.8	ALT	45
ESR	80	AST	73
PT	13.5	Alk po4	145
PT activity	85%	CRP	2+
INR	1.1	ABG	
PTT	45	PH	7.41
Retic count	0.9	Pco2	26.1
Albumin	3.1	BE	-6.3
Total Protein	6.5		

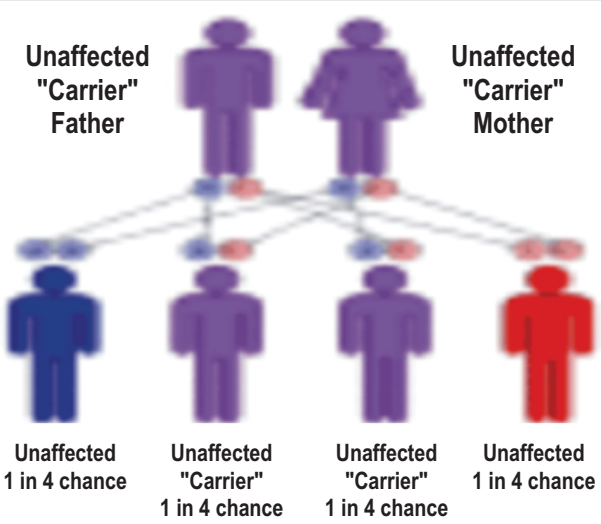
BE	-6.3	Widal	Negative
Beecf	-8.1	Coombs Wright	Negative
BB	41.7	B/C	Negative
Hco3	16.4	2ME	Negative
Po2	181.9	C3-C4-CH50-	ANA-LE cell Negative
O2sat	99.1	TORCH	N
S/E	N	PPD test	N
U/A	N	CXR	N
U/C	N		
Ammoniac	0.8		
Wright	Negative		

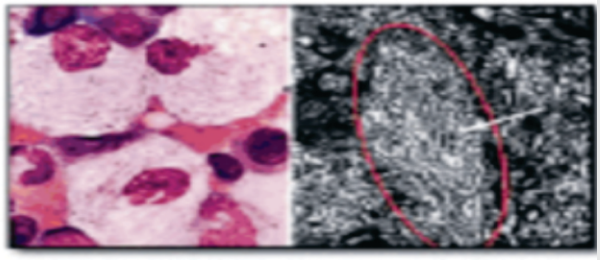
Abdominal Sonography	Huge Hepatosplenomegaly
IGM VCA (Antibody) EBV	Negative
BMA (bone marrow aspiration)	Gaucher cells has been observed.

For definitive diagnosis, β glucosidase activity was measured and Hydrolase acid β glucosidase activity deficiency was improved. The patient was treated by intravenous acid β glucosidase every other week. Hepatosplenomegaly and pancytopenia came back to near normal ranges but unfortunately the child passed away one year later as a result of foreign body aspiration.

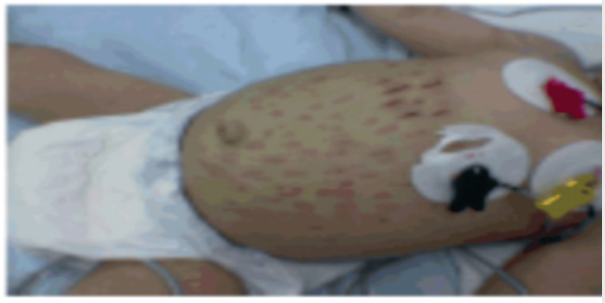
DISCUSSION

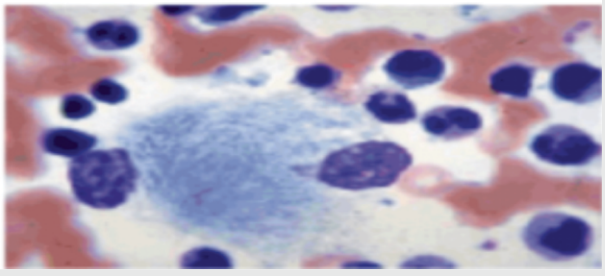
Gaucher disease is a rare autosomal recessive disease resulting from glucocerebroside accumulate in spleen, liver, lungs bone marrow, and sometimes in the brain which it is caused by deficiency of acid β glucosylceramidase enzyme activity in peripheral blood leukocytes or other nucleated cells which encoded by gene located on chromosome 1q21-q31.Analysing the enzyme activity in the carriers is unreliable because there is an overlap between carriers and non-carriers. The test is a fluoromrtric assay and used the substrate 4-methylumbelliferyl-β-D-glucopyranoside. In affected individuals, glucosylceramidase enzyme activity in peripheral blood leukocytes is 0%-15% of normal activity, although the results of biochemical testing do not reliably enable prediction of severity or subtype. Affected individuals may first be suspected of having Gaucher disease following bone marrow examination for Gaucher disease –related manifestations (hepatosplenomegaly, pancytopenia). Bone marrow examination shows the presence of lipid-engorged macrophages (Gaucher





Left: Gaucher macrophages, showing the crumpled tissue paper appearance,
Right: Electron micrograph of a Gaucher tysosome, circled in red, showing depends of undigested lipids (arrow)





cells).BMA is not a reliable diagnostic test. Gaucher disease is caused by mutation in the GBA.

Identify two alleles which cause disease in GBA, the only gene that mutations in that are known to cause Gaucher disease additionally confirms the diagnosis but should not be used instead of biochemical testing.

The gene cause very low levels of glucosylceramidase. A person who has Gaucher disease inherits a mutated copy of the GBA gene from each of parents. In each pregnancy there is 25% chance of having an affected fetus, a 50%chance of having an asymptomatic carrier baby and a 25%chance of having a no affected and non-carrier baby.

Genetic counseling is recommended for the parents who have a familial history of Gaucher disease. Genetic tests can determine whether on the Gaucher disease. The parents carry the gene of Gaucher disease. It can also show if the fetus has Gaucher disease. Prenatal testing for pregnancies at increase risk is possible using assay of glucosylceramidase enzymatic activity and molecular genetic testing when both disease –causing mutations in a family are known.

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Article received on: 02/12/2011 Accepted for Publication: 25/12/2011 Received after proof reading: 22/02/2012

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Article Citation:
Ghorbani MH, Abdollazadeh M, Blourchian MJ, Joshari SP, Ramasanian M. Gaucher disease; a case report. Professional Med J Apr 2012;19(2): 272-275.

"Good people do not need laws to tell them to act responsibly, while bad people will find a way around the laws."

Plato (427-347 B.C.)