

In the name of God

**Shiraz E-Medical Journal**  
**Vol. 11, No. 2, April 2010**

<http://semj.sums.ac.ir/vol11/apr2010/88045.htm>

**A Case of Type 1 Gaucher's Disease Associated with Nonhodgkin Lymphoma.**

Eishi Oskuie A\*, Valizadeh N\*, Ilkhanizadeh B\*\*.

\*Assistant Professor, Section of Hematology and Medical Oncology, Department of Medicine, \*\*Associate Professor, Department of Pathology Urmia University of Medical Sciences, Urmia, Iran.

Correspondence: Dr. N. Valizadeh, Department of Medicine, Urmia University of Medical sciences, Urmia, Iran, Telephone: +98(441) 337-0234, Fax: +98(441) 346-9935, E-mail: nsedaha0@gmail.com.

Received for Publication: January 13, 2010, Accepted for Publication: March 5, 2010.

---

**Abstract:**

Gaucher's disease is rare and is the most common lysosomal storage disease. There are only a few case reports that show association between Gaucher's disease and lymphoproliferative disorders. Pseudo-Gaucher's cells are reported in patients with leukemia and lymphomas. Here we present a case of adult type 1 Gaucher's disease associated with lymphoma.

---

**Keywords: Gaucher's disease, Lymphoma**

**Introduction:**

Gaucher's disease is an autosomal recessive metabolic disorder. It is the most common glycogen storage disease which is more prevalent in Ashkenazi Jewish.<sup>(1,2)</sup> Lack of Glucocerebrosidase leads to accumulation of glucocerebroside and other glycolipids in lysosomes of macrophages.<sup>(3)</sup> Gaucher's disease includes three clinical subtypes. Visceral organ,

bone and bone marrow involvement may be seen in all of them.

Clinical manifestations are different and includes organomegaly, cytopenia, anemia, bleeding tendency, bone pain, osteopenia and pathologic fractures. Central nervous system involvement is seen only in type 2 and 3, but not in type 1. Due to high costs of enzyme replacement therapy (with Cerezyme), it is adminis-

tered only in neuropathic forms and in selected patients with clinically significant non-neuropathic forms<sup>(4)</sup> including symptomatic children and Patients with severe disease (platelet count <60,000/ $\mu$ L, liver size >2.5 times of normal, spleen size >15 times of normal, existence of skeletal involvement in radiography).<sup>(5)</sup>

Review of the literature shows that there are a few reports regarding an association between Gaucher's disease and Non-hodgkin lymphoma.<sup>(6,7,8,10)</sup> Landgren in 2007 studied risk of cancer in 1525 adult male US veterans with Gaucher's disease. They showed a non significant 2-3 times increase in risk of Non Hodgkin lymphoma, melanoma and pancreatic cancer.<sup>(9)</sup> Castelli in 2006 reported unusual development of severe common B-lymphoblastic leukemia in Gaucher's disease type 1.<sup>(11)</sup>

Pseudo-Gaucher's cells were reported in bone marrow and lymph nodes of patients with lymphoproliferative disorders.<sup>(12,13,14)</sup> Knox-Macaulay reported pseudo-Gaucher's cells in association with common acute lymphoblastic leukemia.<sup>(12)</sup> Padamalatha reported pseudo-Gaucher's cell in lymph node biopsy of IgM-k plasmacytoid lymphoma. They said macrophages containing the crystal-like inclusions that probably represent altered immunoglobulin are very similar to Gaucher's cells.<sup>(13)</sup> Alterini reported pseudo-Gaucher's cells in bone marrow of a case with non-hodgkin lymphoma.<sup>(14)</sup>

#### Case Report:

A 27 year old male was admitted to hospital due to with fatigue, myalgia and weakness since 2 years ago. Past medical

history was positive for jaundice and elevated liver enzyme (4-5 times above normal) with negative results for viral serologic studies, normal CBC and differential count. Erythrocyte sedimentation rate was elevated (ESR=64). He refused further evaluation and had left hospital without especial diagnosis at that time. Due to bone pain, arthralgia and wrist and knee joints arthritis, he had been visited by an internist. Pelvic X-ray showed bilateral sclerosis and joint space narrowing especially in left side compatible with bilateral severe sacroileitis. Serologic test was reported positive for human leukocyte antigen HLA B27. After starting Sulfasalazine the arthralgia was resolved. The physical examination revealed fever, tachycardia, pallor and huge splenomegaly.

Results of the blood works:

White blood cell (WBC) count=1100/ $\mu$ L, Hemoglobin=5.4 gr/dl, MCV=95 fl, Platelet counts=15,000/ $\mu$ l.

Aspartate aminotransferase (AST)=11 U/L, Alanine aminotransferase (ALT)=12U/L, Alkaline phosphatase (AlkP)=127 U/L, Lactate dehydrogenase (LDH)=558 U/L, Total Billirubin=1.9 mg/dl, Direct billirubin=0.32 mg/dl.

Hepatitis B surface antigen (HBS Ag), Hepatitis C antibody (HCV Ab), Antinuclear antibody (ANA), Anti-Double stranded DNA antibody (anti-Ds DNA), Human T-lymphotropic virus (HTLV) type-1&2 Antibodies all were negative.

Serum protein electrophoresis revealed polyclonal gammopathy. Prothrombin time (PT)=17.5 second, Partial thromboplastin time (PTT)=32 second, Ferritin=323 ng/ml. Coomb's test (both direct and indirect) were negative. Cal-

cium=7.3 mg/dl, Potassium=3.3 meq/L, Albumin=3.5g/dl. Iron and total iron binding capacity (TIBC) were normal. Abdominal CT Scan showed hepatosplenomegaly. Bone marrow aspiration was dry tap initially, so was repeated and revealed a dilute marrow with many lymphoid blasts with basophilic cytoplasm and cleaved nucleus in some of them. Bone marrow biopsy revealed cluster of Gaucher's cells compatible with Gaucher's disease. PAS staining was done on bone marrow and was positive. Immunohistochemistry (IHC) was positive for S100.

### Results:

We found a case of Gaucher's disease which was presented in adulthood and had been transformed to lymphoma. Also we found a new association between Gaucher's disease and positive serology for HLA-B27 in this patient for the first time.

### Discussion:

Literature review shows that the risk of malignancy is high in patients with Gaucher's disease, but there are only a few reports exist about association of Gaucher's disease with lymphoproliferative disorders.<sup>(6,7,8,9,10,11)</sup> Because the pseudo-Gaucher's cell had been reported in bone marrow of patients with lymphoproliferative disorders<sup>(12,13,14)</sup>, it is necessary to confirm diagnosis of Gaucher's disease with enzymatic analysis and finding reduced glucocerebrosidase activity in peripheral leucocytes and differentiate between these two conditions: Gaucher's disease associated with lymphoma, and pseudo-Gaucher's cells

which may be seen in patients with lymphoma. Enzymatic analysis for glucocerebrosidase activity is not available in Iran. It seems that there is a potential association between lymphoma and Gaucher's disease. Early diagnosis and treatment not only prevents disease progression but also may decrease of development of lymphoproliferative disorder.

### References:

1. Meikle, PJ, Hopwood, JJ, Clague, AE, Carey, WF. Prevalence of lysosomal storage disorders. (1999) JAMA; 281: 249.
2. Grabowski, GA. Recent clinical progress in Gaucher's disease. (2005) Curr Opin Pediatr; 17: 519.
3. Beutler, E, Grabowski, GA. Gaucher's Disease. In: Metabolic and Molecular Bases of Inherited Disease (2001), Scriver, CR, Beaudet, AL, Sly, WS, Valle, D (Eds), McGraw-Hill, New York, p. 3635.
4. Charrow, J, Andersson, HC, Kaplan, P, et al. Enzyme replacement therapy and monitoring for children with type 1 Gaucher's disease: consensus recommendations. J Pediatr 2004; 144: 112.
5. Up to date.2009,Version: 17-2.
6. Sanchez. R, et al. (2005). Pediatric malignancies. Case 2. Peripheral Tcell Lymphoma in an adolescent with unsuspected Gaucher's disease. J clin Oncol23 (21): 4792-3.
7. Perales. M, Cervantes. F, et al. (1998). Non Hodgkin lymphoma associated with Gaucher's disease. Leuk Lymphoma 31 (5-6): 609-12.
8. Shvidel. L, Sigler. E, et al (2007). Parotid gland involvement, the presenting sign of high-grade non Hodgkin lymphoma in 2 patients with Gaucher's disease and Sicca syndrome. J Inherit Metab Dis 30 (5): 825.
9. Landrogen. O, Turesson. I, et al (2007). Risk of malignant disease among 1525 adult male US veterans with Gaucher's disease. Arch Int Med167 (11): 1189-94.
10. Brody. J. D, Advani. R, et al (2006). Splenic diffuse large B-cell lymphoma in a patient with type-1 Gaucher's disease: Diag-

nostic and therapeutic challenges. *Ann Hematol* 85 (11): 817-20.

11. Castelli, R., Cassinero, E. (2006). Unusual severe development of common B lymphoblastic leukemia in Gaucher's disease type I. *Am J Hematol.* 81 (5): 383-4.

12. Knox-Macaulay, H. Bhusnurmath, S. Alwaily, A (1997). Pseudo-Gaucher's cells in association with common acute lymphoblastic leukemia. *South Med J* 90 (1): 69-71.

13. Pdamalta. C, Warner T. F, et al. (1981). PseudoGaucher's cell in Igmk Plasmacytoid lymphoma. *Am J surg Pathol.* 5 (5): 501-5.

14. Alterini, R. Rigacci, L. Stefanacci, S. (1996) Pseudo-Gaucher's cells in the bone marrow of a patient with centrocytic nodular non-Hodgkin's lymphoma. *Haematologica* 81(3): 282-3.