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DOI: 10.2478/folmed-2018-0043

CASE REPORT

Gaucher Disease Involving Virchow's Lymph Node: a Case Report

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Received: 27 Feb 2018
Accepted: 22 May 2018
Published online: 06 Aug 2018
Published: 29 Nov 2018

Key words: Gaucher disease, Gaucher cells, N370S, CD68, Virchow's lymph node

Citation: Zinovkin DA, Pranjol ZI, Kravchenko D, Kravchenko O, Kudryashov V. Gaucher disease involving Virchow's lymph node: a case report. Folia Med (Plovdiv) 2018;60(4): 647-50.
doi: 10.2478/folmed-2018-0043

Gaucher disease is a metabolic storage disorder caused by a mutation in the lysosomal enzyme B-glucocerebrosidase. This disease is usually manifested in new born infants, however, an exceptional case of this disease in adult has been recently reported. A 21-year-old Caucasian patient was diagnosed with Gaucher disease, demonstrating Virchow's lymphatic node enlargement and mild splenomegaly. A familial link to this disease was also found. Macrophage infiltration was observed in the affected Virchow's lymph node which is not a classic sign of Gaucher disease. DNA analysis and a whole blood count also suggested a manifestation of this disease. In summary, this is the first study to report such case of Gaucher disease in an adult female patient, which may suggest an asymptomatic characteristic of this condition and an importance of the presence of Gaucher cells in the enlarged Virchow's lymph node

INTRODUCTION

Gaucher disease is one of the most common glycolipid storage disorders, caused by an inherited deficiency of the lysosomal enzyme β-glucocerebrosidase, leading to accumulation of the substrate glucocerebroside in the cells of the monocyte-macrophage system. Pancytopenia, hepatosplenomegaly and skeletal complications are hallmarks of Gaucher disease. This disease is traditionally classified into three broad phenotypic categories: type 1 (non-neuronopathic disease); type 2, fulminant neuronopathic disease that is fatal during infancy; and type 3, chronic neuronopathic disease, that usually results in death in childhood or early adult life.[1]

CASE REPORT

A 21-year-old female Caucasian patient was admitted with symptoms of malaise, fatigue and pain in bones. Family history revealed that two relatives (father and sister) suffered from Gaucher disease. Physical examination demonstrated an enlarged Virchow's lymphatic node and mild splenomegaly. Complete blood count results are as follows: RBC – 3.31×10^6/μl, MCV – 86.1 fl, RDW –17.2%, HCT – 28.5%, hemoglobin – 91.9 g/l, MCHC – 27.7 g/l, PLT – 320×10^3/μl, thrombocrit – 0.29%, MPV – 9.3 fl, PDW – 17.2%; WBC – 9.41×10^3/μl, granulocytes: band forms – 2%, neutrophils – 46%, eosinophils – 1%, basophils – 1%; lymphocytes – 47%, and monocytes – 3%. The assessment of Virchow's node biopsy revealed areas of normal lymph node efface-

ment by large round cells ***(Fig. 1A)*** *with lattice-like cytoplasm and eccentric nuclei, which characterize Gaucher cells* ***(Fig. 1B)****. To differentiate between Gaucher disease, Hodgkin's lymphoma and signet-cell carcinoma, an immunohistochemical study was performed using anti-pCK, anti-CD15, anti-CD30, anti-fascin, anti-Epstein-Barr virus and anti-CD68 antibodies. Only CD68 staining was positive in cells with foamy cytoplasm* ***(Fig. 1C)****, suggesting a presence of macrophages.*

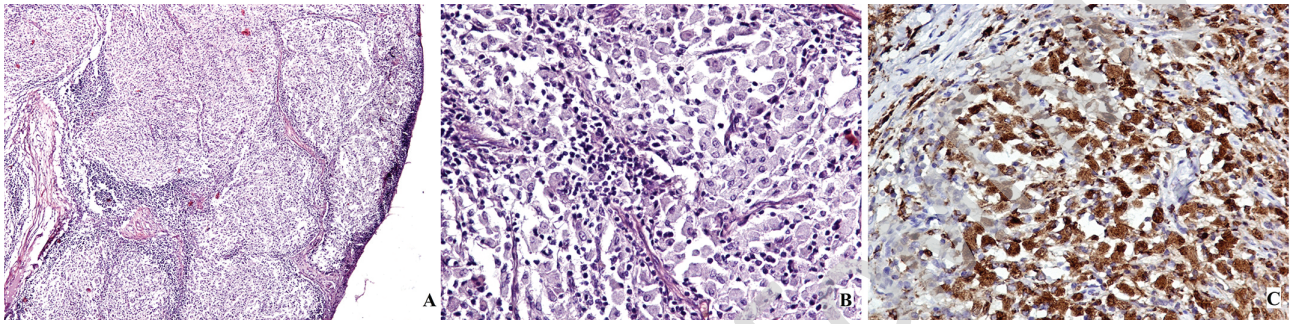

Figure 1. Biopsy of Virchow's lymph node. **A**: Lymph node structure is completely effaced by a diffuse Gaucher cells infiltration of lymphoid tissue at the big area. Stain: hematoxylin and eosin. Magnification: ×40; **B**: Gaucher histiocytes with foamy cytoplasm and eccentric situated nuclei. Stain: hematoxylin and eosin. Magnification: ×200; **C**: CD68 strong expression by Gaucher cells infiltrating lymph node structures. Immunohistochemistry: anti-CD68 primary antibody. Magnification: ×200.

DNA sequence analysis displayed mutation of glucocerebrosidase gene located in chromosome 1q21 and homozygous for the N370S mutation. Interestingly, PCR data did not present homozygous L444P mutations in the glucosylceramidase β gene, which is a marker of Gaucher disease. Glucocerebrosidase enzyme activity in the peripheral blood leukocytes was 29%, which is higher than the normal range: 0%-15%. Concluding all the data, the patient was diagnosed with type 1 Gaucher disease and was prescribed Cerezyme® as a therapy. Patient was discharged from hospital afterwards with significant clinical improvement.

DISCUSSION

Type 1 (non-neuronopathic) Gaucher disease accounts for more than 90% all Gaucher disease patients. Its prevalence worldwide is 1 in 50,000 to 100,000, but it is as high as ~1 in 850 in individuals of Ashkenazi heritage.[2] The broadest phenotypic spectrum in Gaucher disease with respect to age of onset, rate of progression, and organs affected occurs in type 1 Gaucher disease. Many manifestations of Gaucher disease, some not uncommon and others very rare, cannot be explained by storage per se; examples include immunologic abnormalities, increased prevalence of certain malignancies with relative paucity of others, neurologic comorbidities (peripheral neuropathy and Parkinsonism), calcification of cardiac valves, and pulmonary hypertension.[3-5]

Gaucher-like cells also can be found in some hematologic abnormalities, such as chronic lymphocytic leukemia and Hodgkin's lymphoma. However, we did not observe specific histopathological and immunohistochemical criteria of Hodgkin's lymphoma, which manifests in the neck where Gaucher disease was diagnosed in our case. In addition, our blood analysis data did not reveal any character for chronic lymphocytic leukemia specific lymphocytosis.

Homozygosity for the N370S mutation is the most common genotype in the Ashkenazim population, in whom it accounts for ~70% of all Gaucher disease-causing causes alleles. It is associated with atypical presentation in adults or the older patients and is notable for significant skeletal disease, such as deformity, fragility fractures and osteomyelitis, despite inconspicuous classical manifestations (splenomegaly, hepatomegaly, anemia, and thrombocytopenia).[2]

According to Feng et al., L444P was the most prevalent mutation and L444P homozygote genotype was associated with severe type 1 Gaucher disease.[6] The study reported that L444P homozygote genotype was associated with severe type 1 Gaucher disease phenotype.[6]

There is only one description of manifestation of old male patients in the literature. As hepatomegaly

was not observed in the present case study, we assume that it could be a specific characterization for manifestation of Gaucher disease in adult patients.[7] Nevertheless, in this case thrombocytopenia was not presented at diagnosis, which is a symptom of Gaucher disease. We agree with the suggestion that Gaucher disease presented by extraosseous conditions in adult age may be a prognostic factor of this disease.[8]

CONCLUSION

To our knowledge, this is the first study to report an involvement of the Virchow's node by Gaucher disease. Gaucher disease may remain asymptomatic for a long period of time and ultimately be diagnosed in adult age. Therefore, adult patients with foamy macrophages infiltration of lymph nodes and family history of Gaucher disease must be diagnosed with this disease condition and treated.

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Болезнь Гоше, поражающая железу Вирхова: клинический случай

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Дата получения: 27 февраля 2018
Дата приемки: 22 мая 2018
Дата онлайн публикации: 06 августа 2018
Дата публикации: 20 ноября 2018

Ключевые слова: болезнь Гоше, клетки Гоше N370S, CD68, железа Вирхова

Образец цитирования:
Zinovkin DA, Pranjol ZI, Kravchenko D, Kravchenko O, Kudryashov V. Gaucher disease involving Virchow's lymph node: a case report. Folia Med (Plovdiv) 2018;60(4): 647-50.

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Болезнь Гоше является заболеванием матаболического накопления, вызванное мутацией в лизосомальном ферменте β-глюкоцереброзидазы. Эта болезнь обычно встречается у новорожденных, но сообщается о крайне редком случае заболевания взрослого человека. 21-летнему пациенту белой расы был поставлен диагноз болезни Гоше, проявляющейся увеличением железы Вирхова и лёгкой формой спленомегалии. Установлена также наследственная связь заболевания. Инфильтрация макрофагами наблюдалась в поражённой железе Вирхова, что не является классическим признаком болезни Гоше. Анализ ДНК и полный анализ крови тоже показали проявление данного заболевания. В целом, это первое исследование, в котором сообщается о таком случае болезни Гоше у взрослой женщины, что может говорить о бессимптомной особенности этого заболевания и о важности наличия клеток Гоше в увеличенной железе Вирхова.