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CASE REPORT Open Access

Improvement of Niemann Pick (B) Disease: Report of a Case Treated with Iranian Traditional Medicine

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ABSTRACT

Background: Niemann-Pick Disease (NPD) is a rare autosomal recessive disorder associated with intracellular deposition of sphingomyelin and cholesterol storage within the lysosome. There are mainly three types of NPD namely types A, B, and C. NPD type B is generally later in onset with a good prognosis for survival into adulthood and usually with no neurological abnormalities.

Case Presentation: The patient, male, was born in 35 weeks of pregnancy. Failure to thrive started at around 4 months and the diagnosis of type B Niemann-Pick disease was made approximately at the age of 2 years. Currently, the patient is 10 years old and having undergone 3 years of Traditional Persian Diet, has had obvious improvement in growth and laboratory tests.

Conclusion: The NPD is no specific treatment, especially in modern medicine. Considering the significant improvement in the patient's condition after an appropriate diet and traditional medicines, it seems that traditional medicinal therapies have great results in the treatment of NPD. In this study, we presented an innovation for NPD treatment by the use of a Traditional Persian diet.

Keywords: Niemann-Pick Disease; Iranian Traditional Medicine; diet; Treatment

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Introduction

Niemann-Pick Disease (NPD) is a disorder of infancy characterized by failure to thrive, hepatosplenomegaly and neurodegenerative changes that lead to sphingomyelin and cholesterol storage within the lysosome [1]. The disease affects the metabolism of sphingolipids, and causes various dysfunctions in the patient's body. There are mainly three types of NPD namely types A, B, and C. NPD type B is generally later in onset with a good prognosis for survival into adulthood and usually with no neurological abnormalities [2].

Case presentation

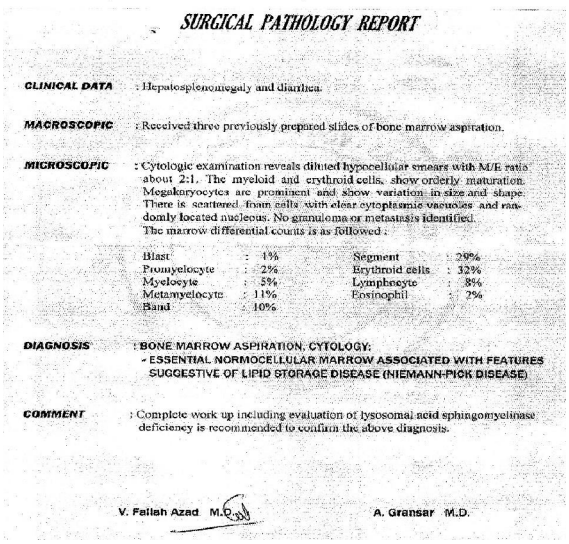
History and Examination according to Modern Medicine

The patient, male, was born in 35 weeks of pregnancy. Failure to thrive started at around 4 months of age and the diagnosis was made approximately at the age of 2 years with type B Niemann-Pick disease. Parents did not have a history of genetic disease.

The patient was evaluated periodically by physical exam; laboratory tests: hematologic indices, lipid profile, hepatic function tests; radiologic studies: chest X-ray, abdominal ultrasound, cranial computed tomography scan, and echocardiogram; and histologic exams: hepatic biopsy and bone marrow aspiration. There was significant abdominal distension with hepatosplenomegaly and diarrhea. Cytologic examination revealed diluted hypocellular smears with an M/E ratio of about 2:1. The myeloid and erythroid cells showed orderly maturation. Megakaryocytes were prominent with variation in size and shape. There were scattered foam cells with clear cytoplasmic vacuoles and randomly located nucleus. Initially, regarding results of bone marrow aspiration and cytology, essential normocellular marrow associated with features suggestive of lipid storage disease was confirmed. Finally, evaluation of Lysosomal enzyme studies confirmed the diagnosis of Niemann Pick disease type B (Fig.1a.Fig.1b).

Therapeutic Intervention

Generally, there is no specific treatment for NPD. Management of disease is based on surveillance and supportive care. Lipid-Lowering treatment was started by Ursodeoxycholic acid (Ursodiol) and then Atorvastatin. The patient was advised for regular follow up and hematology test evaluation was performed. Blood lipid levels were somewhat lower with the drug treatment. However, he did not respond to current treatments well. The patient visited the Traditional Medicine Health Center when 7 years old. The diagnosis of cold temperament was taken as the most important reason for the child's development. In traditional Iranian medicine, the process of growing up in children is a process that is carried out with the help of heat and humidity. The patient maintained regular visits to the Traditional Medicine Health Center to receive a regimen of Iranian Traditional Medicine. Remedial measures were started on 08/05/2016. These measures were along with nutritional and lifestyle recommendations. Along with chemical drugs, a program including the nutrition practices was given to the patient to help with the treatment so that the patient could learn the manners and nutrition principles in traditional medicine. Given that the patient had a dominant cold and dry temperament, he was prohibited from eating sour foods and beverages and also fatty foods,



SURGICAL PATHOLOGY REPORT

CLINICAL DATA : Hepatosplenomegaly and diarrhea.

MACROSCOPIC : Received three previously prepared slides of bone marrow aspiration.

MICROSCOPIC : Cytologic examination reveals diluted hypocellular smears with M/E ratio about 2:1. The myeloid and erythroid cells, show orderly maturation. Megakaryocytes are prominent and show variation in size and shape. There is scattered, foam cells with clear cytoplasmic vacuoles and randomly located nucleous. No granuloma or metastasis identified.
The marrow differential counts is as followed :

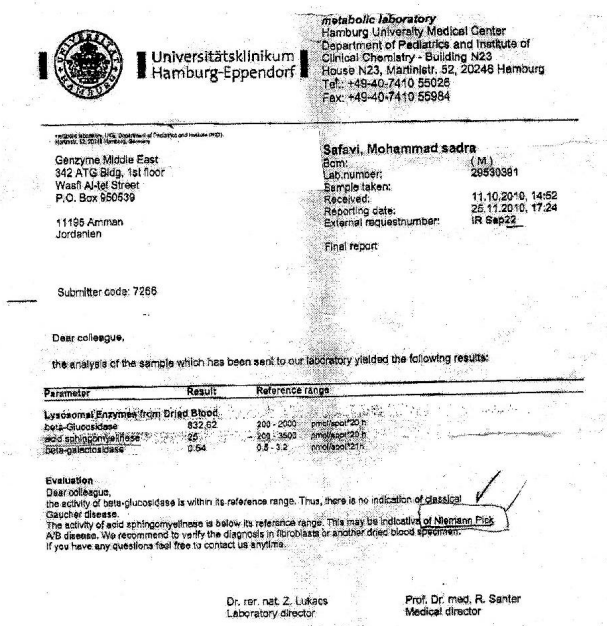
Blast	: 1%	Segment	: 29%
Promyelocyte	: 2%	Erythroid cells	: 32%
Myelocyte	: 5%	Lymphocyte	: 8%
Metamyelocyte	: 11%	Eosinophil	: 2%
Band	: 10%		

DIAGNOSIS : BONE MARROW ASPIRATION, CYTOLOGY:
- ESSENTIAL NORMOCELLULAR MARROW ASSOCIATED WITH FEATURES SUGGESTIVE OF LIPID STORAGE DISEASE (NIEMANN-PICK DISEASE)

COMMENT : Complete work up including evaluation of lysosomal acid sphingomyelinase deficiency is recommended to confirm the above diagnosis.

V. Fallah Azad M.D. A. Gransar M.D.

Figure 1a: Pathology report of Niemann Pick disease type B



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Safavi, Mohammad sadra
Bem: (M.)
Lab.number: 29530361
Sample taken:
Received: 11.10.2010, 14:52
Reporting date: 25.11.2010, 17:24
External requestnumber: IR Sep22

Final report

Submitter code: 7266

Dear colleague,

the analysis of the sample which has been sent to our laboratory yielded the following results:

Parameter	Result	Reference range	
Lysosomal Enzymes from Dried Blood			
beta-Glucosidase	832,62	200 - 2000	pmol/spot*20 h
acid sphingomyelinase	25	100 - 3500	pmol/spot*20 h
beta-galactosidase	0.64	0.8 - 3.2	nmol/spot*21h

Evaluation
Dear colleague,
the activity of beta-glucosidase is within its reference range. Thus, there is no indication of classical Gaucher disease.
The activity of acid sphingomyelinase is below its reference range. This may be indicative of Niemann Pick A/B disease. We recommend to verify the diagnosis in fibroblasts or another dried blood specimen.
If you have any questions feel free to contact us anytime.

Dr. rer. nat. Z. Lukacs
Laboratory director

Prof. Dr. med. R. Santer
Medical director

Figure 1b: Verification testing of Niemann Pick disease type B

Table 1. Laboratory exams before (12/19/2010) and after (12/1/2016) intervention.

Laboratory parameter	Result (before intervention)	Result (after intervention)	Unit	Reference Intervals
Cholesterol	295*	157	mg/dL	Desirable : <200 Borderline : 200-240 High : >240
Triglycerides	535*	194	mg/dL	Desirable : < 200 Moderate risk : 200 - 400 High risk : > 400
S.G.O.T. (AST)	109*	69*	U/L	Up to 38
S.G.P.T. (ALT)	73*	64*	U/L	Up to 41

*High

Table 2: A summary of dietary recommendation to patient due to traditional Persian medicine

- Cumin (Cuminum cyminum L.)	- Fatty foods,
- Apple (Malus pumila L)	- Ice water
- Low salt olive (Olea europaea L.)	- Ice cream.
- Ripe Banana (Musa acuminata)	- Junk foods
- Mango (Mangifera indica)	
- Pear (Pyrus communis)	
- Grape (Vitis vinifera)	
- Lamb muscle or Chicken	
- Well fermented bread [1-2].	

According to the table above, the patient is on a treatment regimen.
The patient has accepted the principles of dietary therapy.

ice water, and ice cream. The patient was advised to be gentle exercising due to his physical state. No traditional drugs and herbs were given. A summary of the treatment is explained in the Table 1.

Follow-up and outcomes

After applying therapies intermittently, the lipid's blood serum levels were better in comparison to previous examinations. The hematology tests showed the enzymes of SGOT, SGPT, LDL, and TG decreased and HDL increased. The blood biochemistry results before and after intervention are listed in Table 2. The weight of the patient was measured and record at each visit and the growth curve was obtained (Figure 2). The last hematology examination showed normal functional liver tests related to lipids blood. For the moment there is no need for the supplementary product but the patient will be re-evaluated periodically. The patient maintained regular visits to the Traditional Medicine Health

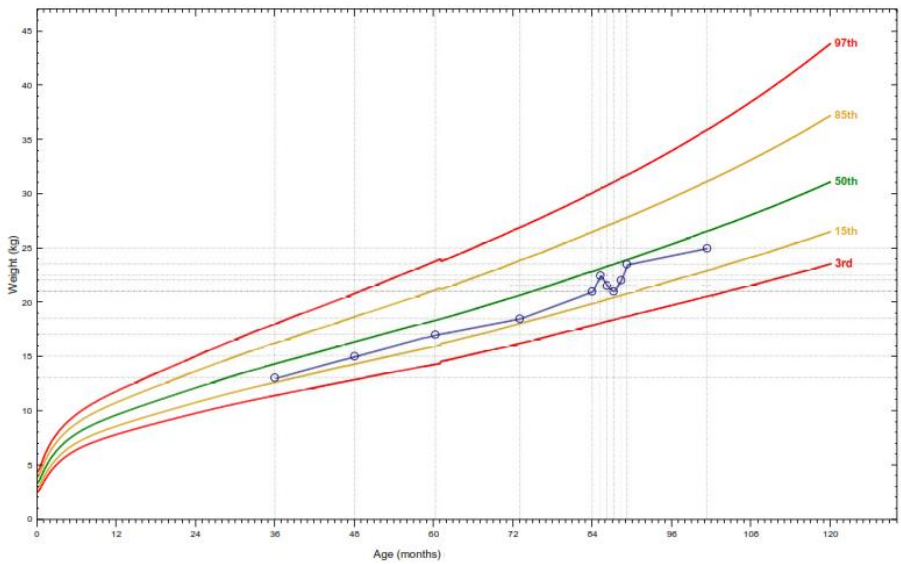

Figure 2: The body weight history of patient with Niemann-pick type B

Center. The patient followed the treatment completely.

Discussion

Niemann-Pick Disease is a disorder of infancy characterized by failure to thrive, hepatosplenomegaly and neurodegenerative changes that lead to sphingomyelin and cholesterol storage within the lysosome [3-4]. The disease affects the metabolism of sphingolipids. These dysfunctions cause different changes in the patient's body. It has been described as a very rare disease in childhood [5]. NPD is a lysosomal storage disease caused by deficient activity of acid sphingomyelinase (ASM) and the accumulation of sphingomyelin within cells of the monocyte-macrophage system [6]. The accumulation of sphingomyelin may result from a variety of biochemical derangements, including enzyme deficiency and altered intracellular cholesterol processing, which are associated with the accumulation of 'foam cells'. The overall prevalence of acid sphingomyelinase deficiency (types A and B combined) is estimated to be 1:250 000 [7]. NPD type B is generally later in onset and less severe, with a good prognosis for survival into adulthood [8]. NPD disease type B begins at 3-4 months of age with feeding difficulties and failure to thrive. Neurologic function is gradually deteriorated and ultimately development is retarded. It is characterized by hepatosplenomegaly with progressive hypersplenism, worsening atherogenic lipid profile, and stable liver dysfunction [7]. The main path to diagnosis, the combination of signs and symptoms, which can be similar to many other diseases, may raise suspicion and lead to diagnosis. The diagnosis of acid sphingomyelinase is confirmed when residual ASM activity in peripheral blood leucocytes is less

than 10% of that of controls [9,10]. Bone marrow examination indicates sea-blue histiocytes and lipid-laden macrophages. There is no specific treatment for NPD that has been proven to modify the onset of neurological progression of the disease or to prolong lifespan [9]. Therefore, the management of the patient is based on surveillance and supportive care. Patient with NPD type B should be evaluated at least yearly for history (growth and weight (in children), fatigue, bleeding, dyspnea, abdominal pain, headaches, extremity pain, any change in social, domestic, school-related or work-related activities); also, physical examination, blood tests (including liver enzymes, platelet count, and fasting lipid profile), pulmonary function testing and chest radiograph, skeletal, and nutrition assessment are needed. An individual who has splenomegaly should avoid contact sports [7]. Genetic counseling and prenatal testing must be offered. In NPD, the extent of abnormality may vary considerably even between affected siblings, but our case had some of the cardinals features including presentation in early months of life, huge hepatosplenomegaly, failure to thrive, diarrhea and foam cells in the bone marrow. However, these conditions in our case were controlled with food and physical activity. In Iranian Traditional Medicine, food has a major role in the prevention and treatment of disease [2]. Also, Some food have a warm temperament like grapes, mangos, apples and food that was selected in this intervention, while others have a cold temperament like watermelon, lettuce, ice cream and ice water [1] that the patient in this study was prohibited from eating due dry and cold dominance. We assumed the use of diet including food with warm temperament can improve the function of the liver and regulate liver enzymes and lipid profiles. Finally, the results of clinical exams and the general status of the patient confirmed our assumption.

The efficacy of different dietary strategies on control or treatment of this disease has been demonstrated in some studies. Although, there are limited studies on Niemann-Pick Type B, findings provide some evidence to support improvement in other types of NPD through diet and plants. In a clinical trial, a diet without disaccharides for two patients with Niemann-Pick Type C lead to a complete halt in gastrointestinal side effects during treatment with miglustat [11]. In another study, curcumin supplementation inhibited cholesterol absorption in hamsters by suppressing sterol regulatory element-binding protein-2 (SREBP-2) and subsequently, down-regulating Niemann-Pick C1-like 1 expression [12].

The abnormal growth curve is common in children and adolescents with NPD type B [13]. Despite this, our case except in the beginning had normal growth during the intervention until now.

Conclusion

Overall, given the patient's healing process, it seems that combining modern and Iranian Traditional Medicine as a 'Traditional Persian Diet ' May be beneficial in lipid and liver enzyme improvement in patients with Niemann Pick and cold dry traditional Mizaj, which should be confirmed with more studies. It is essential to perform a wide range of assessments and studies in different diseases based on the teachings of medicine. Therefore, it is necessary to evaluate the new combination of drugs and traditional methods to have the highest therapeutic effect in the shortest time and report them scientifically.

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