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(CASE REPORT)

Exploring Gaucher disease: A pediatric case of severe dyslipidemia and unique symptoms

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Abstract

Introduction: Gaucher disease is a rare inherited lysosomal storage disorder caused by mutations in the GBA gene, leading to glucocerebrosidase deficiency. This results in the accumulation of glucocerebroside in macrophages, forming "Gaucher cells" that infiltrate various tissues, primarily affecting the liver, spleen, bone marrow, and nervous system. The disease manifests in three types, with Type 1 being the most common and devoid of neurological symptoms. Diagnosis involves enzyme level testing, genetic screening, and imaging, while treatment primarily consists of enzyme replacement therapy (ERT) and substrate reduction therapy (SRT).

Case-Report: A one-year-old girl presented with weakness, irritability, and recurrent fever over six months, previously misdiagnosed with malaria and respiratory infections. Physical examination revealed pallor, hepatosplenomegaly, and cherry-red spots on fundoscopy. Laboratory findings indicated anemia, leukocytosis, and severe dyslipidemia, highlighting atypical features for Gaucher disease.

Discussion: This case emphasizes the diagnostic challenges in pediatric Gaucher disease, especially with nonspecific symptoms. The combination of cherry-red spots and dyslipidemia suggests a unique variant or severity of the disease, underlining the necessity for heightened awareness among healthcare providers for prompt diagnosis.

Conclusion: Gaucher disease should be considered in pediatric patients with unexplained systemic symptoms. Early detection and ERT initiation can significantly improve clinical outcomes. The case illustrates the variability in clinical presentations, emphasizing the need for comprehensive diagnostic evaluation.

Keywords: Gaucher disease; Lysosomal Storage Disorder; Glucocerebrosidase Deficiency; Hepatosplenomegaly; Enzyme Replacement Therapy; Dyslipidemia.

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1. Introduction

Gaucher disease is a type of lysosomal storage disorder that is inherited and rare, resulting from mutations in the GBA gene that lead to a lack of the enzyme glucocerebrosidase. A lack of this enzyme causes glucocerebroside to build up in macrophages, forming "Gaucher cells" that gather in different tissues like the liver, spleen, bone marrow, and nervous system. (1) Gaucher disease is the most prevalent lysosomal storage disorder, particularly common among the Ashkenazi Jewish community. It is passed down in an autosomal recessive manner, requiring both parents to have the mutated gene for their child to be impacted. (2) The buildup of glucocerebroside in Gaucher cells results in enlarged organs, bone issues, and bone marrow infiltration, potentially causing anemia and thrombocytopenia. (3)

There are three types of Gaucher disease categorized according to the presence and development of neurological symptoms. Type 1 is the most prevalent and not related to nerve damage, whereas types 2 and 3 involve nerve damage to different extents. Frequent symptoms consist of low red blood cell count, low platelet count, enlargement of the liver and spleen, and abnormalities in the bones. (4) Diagnosing usually includes testing enzyme levels to measure glucocerebrosidase activity, genetic screening for GBA mutations, and imaging scans such as MRI to evaluate organ impact. A bone marrow biopsy can show Gaucher cells, confirming the diagnosis. (5) The main treatment for types 1 and 3 of Gaucher disease is enzyme replacement therapy (ERT). Substrate reduction therapy (SRT) is additionally employed to lessen the buildup of glucocerebroside. In extreme situations, especially when the nervous system is affected, hematopoietic stem cell transplantation (HSCT) could be an option.

2. Case Report

A one-year-old girl presented to emergency department with complaints of weakness irritability, fever on and off for six months. according to the patient attendant she was alright before that. The fever was mild in intensity and was relieved by medication. Attendant is also complaining of excessive cry of the baby. The patient was taken to multiple doctors for the same complaint in hospital for Malaria, Upper respiratory tract infection and HIE related complications.

Family history was insignificant other than the history of her mother having TB at 6 years of age. The patient vaccination record was unavailable. BCG vaccination scar was present on right arm. She was breast fed till date and has not started weaning yet. Past history was significant for malaria, and repeated chest infections.

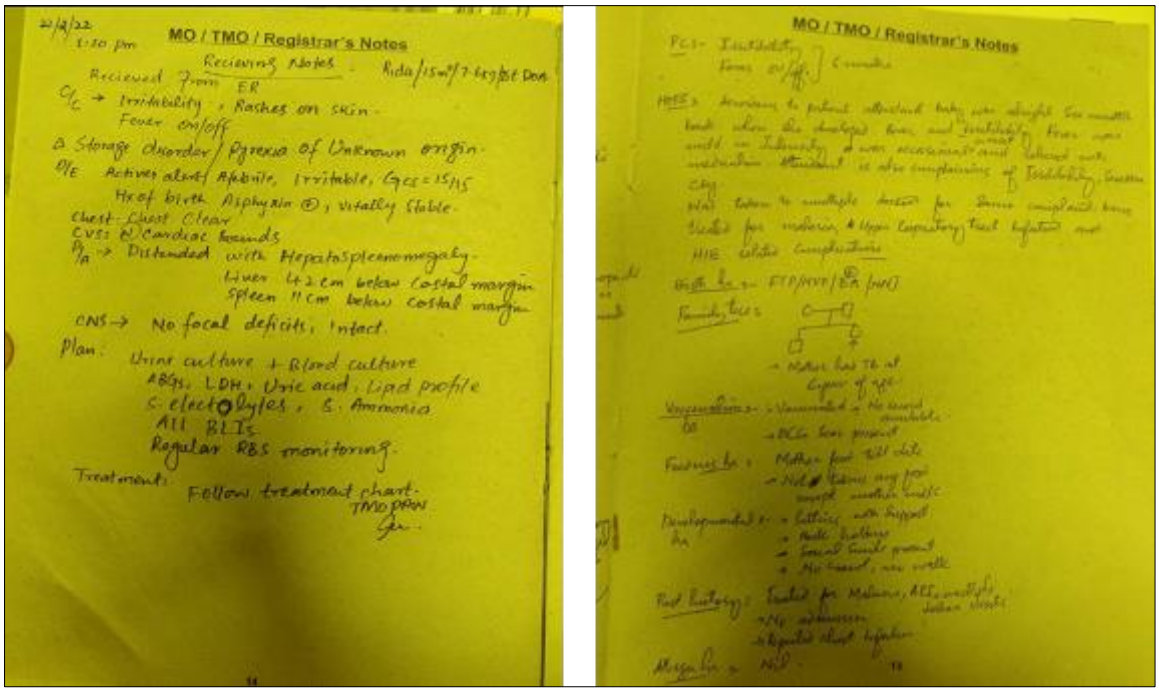

Figure 1 The Patient History on initial presentation

On physical examination she is pale looking and has distended abdomen with hepatosplenomegaly. Liver was palpable 4.2 cm below costal margins and spleen was palpable 11 cm below costal margins. No focal deficits were present. On fundoscopy dull fundal reflection and cherry red Spots were seen bilaterally.

Table 1 Lab Reports of the Patient

Test	**Patient Value**	**Normal Range**
Complete Blood Count (CBC)		
White Blood Cell (WBC)	14,000 cells/μL	4,000 - 11,000 cells/μL
Red Blood Cell (RBC)	4.43 million cells/μL	4.7 - 6.1 million cells/μL (men)
		4.2 - 5.4 million cells/μL (women)
Haemoglobin (Hb)	11 g/dL	13.8 - 17.2 g/dL (men)
		12.1 - 15.1 g/dL (women)
Haematocrit (Hct)	32%	40.7% - 50.3% (men)
		36.1% - 44.3% (women)
Platelets	800,000/μL	150,000 - 450,000/μL
Mean Corpuscular Volume (MCV)	86 fL	80 - 100 fL
Basic Metabolic Panel (BMP)		
Sodium (Na)	138 mEq/L	135 - 145 mEq/L
Potassium (K)	4.5 mEq/L	3.5 - 5.0 mEq/L
Chloride (Cl)	109 mEq/L	98 - 106 mEq/L
Calcium (Ca)	8.5 mg/dL	8.5 - 10.2 mg/d
Bicarbonate (HCO3)	24 mEq/L	22 - 28 mEq/L
Blood Urea Nitrogen (BUN)	10 mg/dL	7 - 20 mg/dL
Creatinine	0.9 mg/dL	0.6 - 1.3 mg/dL
Glucose	92 mg/dL (fasting)	70 - 99 mg/dL (fasting)
Liver Function Tests (LFTs)		
Alanine Aminotransferase (ALT)	27 U/L	7 - 56 U/L
Aspartate Aminotransferase (AST)	36 U/L	10 - 40 U/L
Alkaline Phosphatase (ALP)	166 U/L	<281 U/L
Total Bilirubin	1.3 mg/dL	0.1 - 1.2 mg/dL
Lipid Panel		
Total Cholesterol	137 mg/dL	< 200 mg/dL
LDL Cholesterol	10 mg/dL	< 100 mg/dL
HDL Cholesterol	14 mg/dL	> 40 mg/dL (men)
		> 50 mg/dL (women)
Triglycerides	639 mg/dL	< 150 mg/dL
LDH	353 U/L	80-253 U/L

The findings from the lab results in Table-1 of this patient suspected to have Gaucher disease are significant. Significantly, there is an increased white blood cell count of 14,000 cells/μL, suggesting possible inflammation or infection, as a result of chronic macrophage activation in Gaucher disease. The presence of anemia is confirmed,

indicated by a hemoglobin level of 11 g/dL and a hematocrit of 32%, possibly caused by Gaucher cells infiltrating the bone marrow and affecting the production of red blood cells. Interestingly, there is an unusual high platelet count of 800,000/μL in Gaucher disease, where thrombocytopenia is more frequent; this might indicate reactive thrombocytosis.

The lipid panel indicates noteworthy dyslipidemia, with unusually low levels of LDL cholesterol (10 mg/dL) and HDL cholesterol (14 mg/dL), which are uncommon results in Gaucher disease. The significantly high triglycerides (639 mg/dL) contribute to this atypical lipid profile, indicating a unique metabolic reaction. The high LDH (353 U/L) suggests cell renewal and tissue damage often observed in individuals with Gaucher disease. A slightly increased bilirubin level (1.3 mg/dL) could suggest liver issues or destruction of red blood cells. This case stands out due to the elevated platelet count and severe dyslipidemia, which could indicate a more intricate or different form of Gaucher disease.

3. Discussion

This case has various distinctive features that set it apart from the typical Gaucher disease cases documented in the literature. The one-year-old girl showed prolonged symptoms like weakness, irritability, and intermittent fever for six months, which initially resulted in misdiagnoses of malaria, upper respiratory tract infection, and complications related to hypoxic-ischemic encephalopathy (HIE). Identifying Gaucher disease in pediatric patients can be challenging due to the wide range of possible diagnoses, particularly when the symptoms are unusual. The combination of enlarged liver and spleen, low red blood cell count, and decreased platelet count is indicative of Gaucher disease, but the discovery of cherry-red spots during eye examination and severe dyslipidemia with high triglycerides and low HDL cholesterol levels is noteworthy. Red spots that are cherry-red in color are usually seen in other lysosomal storage diseases like Tay-Sachs, and while they can also be found in Gaucher disease, it is uncommon and can make diagnosis more challenging.(6) Furthermore, the significant dyslipidemia observed in this patient is atypical and might suggest a variant or more severe form of Gaucher disease. From a diagnostic standpoint, the delayed identification of Gaucher disease in these individuals underlines the difficulties presented by the vague and similar symptoms that it shares with other childhood illnesses. The infrequency of the illness, especially in areas with low occurrence, can also lead to a delayed detection. (7) This situation highlights the importance of healthcare providers being more aware of the various ways that Gaucher disease can present in order to prevent delays in diagnosis.

Table 2 Patients Demographics, Presentation, Treatment, and Outcomes in Different Gaucher Disease cases:

Patient	Age/Sex	Presentation	Type	Treatment	Outcome	References
Case 1	18/F	Abdominal pain, hepatospleno megaly	Type 1	ERT	Stable, managed symptoms	Valdés-Díaz K, Fariña-Lamadrid R, Artiles-Martínez D, López JA. Gaucher disease. Presentation of a clinical case and literature review. Hematol Transfus Cell Ther. 2022 Jan-Mar;44(1):104-107. doi: 10.1016/j.htct.2020.04.006. Epub 2020 Jun 6. PMID: 32536534; PMCID: PMC8885392.
Case 2	7/F	Hepatospleno megaly, bone pain, anaemia	Type 1	ERT	Improved, no new complications	Stirnemann J, Belmatoug N, Camou F, Serratrice C, Froissart R, Caillaud C, Levade T, Astudillo L, Serratrice J, Brassier A, Rose C, Billette de Villemeur T, Berger MG. A Review of Gaucher Disease Pathophysiology, Clinical Presentation and Treatments. Int J Mol Sci. 2017 Feb 17;18(2):441. doi: 10.3390/ijms18020441. PMID: 28218669; PMCID: PMC5343975.
Case 3	5/M	Severe bone disease, hepatospleno megaly, neurological symptoms	Type 3	ERT, supportive care	Progressive neurological decline	Turyalai Hakimi, Omran Omar Amarkhil, Muhammad Arif Zamani, Mansoor Aslamzai, Salmai Turial, Mohammad Tareq Rahimi, Mohammad Anwar Jawed,

						Gaucher's disease in children: Case report from Afghanistan with literature review, Global Pediatrics, Volume 5, 2023, 100072, ISSN 2667-0097, https://doi.org/10.1016/j.gpeds.2023.100072.
Case 4 (Current Case)	1/F	Weakness, irritability, fever, hepatosplenomegaly, anemia, thrombocytopenia	Type 1?	ERT (planned)	Awaiting treatment, prognosis depends on early intervention	(Current Case)
Case 5	25/M	Bone pain, hepatosplenomegaly, anemia	Type 1	ERT, bisphosphonates	Improved bone density, stable hematological parameters	Zimran A, Belmatoug N, Bembi B, et al. Demographics and patient characteristics of 1209 patients with Gaucher disease: Descriptive analysis from the Gaucher Outcome Survey (GOS). *Am J Hematol*. 2018; 93: 205–212. https://doi.org/10.1002/ajh.24957

The table offers a detailed comparison of five instances of Gaucher disease, highlighting various demographics, symptoms, therapies, and results. An in-depth examination uncovers the effects of age, disease type, and treatment approaches on the clinical course of Gaucher disease. Patients aged between 1 and 25 years show diversity in the onset of Gaucher disease. The majority of the patients are youthful, with a slightly greater proportion of females (3 out of 5 cases). Prompt identification is essential in influencing the medical prognosis, as demonstrated in Case 1 (1/F) and Case 2 (7/F), where timely treatment is vital. Typical symptoms include enlarged liver and spleen, low red blood cell count, and discomfort in bones. Case 3 (5/M) is notable for displaying more severe neurological symptoms, typical of Type 3 Gaucher disease, leading to more significant complications. The present situation displays a wide range of symptoms such as fatigue, crankiness, high body temperature, enlarged liver and spleen, low red blood cell count, and low platelet count. This diverse display indicates an initial phase of Type 1 Gaucher disease, with confirmation still pending. ERT is a popular and successful treatment for Type 1 Gaucher disease that enhances symptoms and quality of life for the majority of patients. Case 1 (18-year-old female) and Case 5 (25-year-old male) both demonstrated consistent improvements following ERT. In certain situations, such as Case 5, bisphosphonates were employed for alleviating bone pain and enhancing bone density. Despite receiving enzyme replacement therapy (ERT), the patient in Case 3 (Type 3) required supportive care due to experiencing ongoing neurological decline, which can be particularly challenging to address in the advanced stages of Gaucher disease. The majority of patients diagnosed with Type 1 Gaucher disease showed stable results with ERT, as demonstrated in Case 1, Case 2, and Case 5. Case 4 (Current Case) is waiting for treatment, and the outcome depends on the prompt initiation of ERT. On the other hand, the outlook for Type 3 (Case 3) is more severe because of neurological complications, even with ERT treatment. The significance of early detection and treatment with ERT is emphasized in the table, as it has the potential to stabilize the condition in patients with Type 1. Nonetheless, patients with Type 3 and neurological symptoms may face a more difficult outlook, even with comparable treatment methods. The existing situation highlights the importance of immediate care to prevent lasting issues.

4. Conclusion

This case underscores the importance of considering Gaucher disease in the differential diagnosis of pediatric patients presenting with nonspecific symptoms such as prolonged fever, hepatosplenomegaly, and cytopenia. Early recognition and diagnosis are critical, as they allow for timely initiation of enzyme replacement therapy, which can significantly

improve outcomes. The presence of atypical findings, such as cherry-red spots and severe dyslipidemia, in this case, highlights the variability in clinical presentations and the potential for diagnostic challenges. This case illustrates the need for a high index of suspicion and comprehensive diagnostic evaluation in suspected cases of Gaucher disease, particularly in young children with unexplained systemic symptoms.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest among authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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