**Case Presentation**
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# A Case of A 12-Year-Old Female with Type 1 Gaucher's Disease. A Rare Genetic Lipid Metabolic Disorder

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## Abstract

**Introduction:** Gaucher's disease is a rare autosomal recessive lysosomal storage disease with unknown prevalence in Africa and no record of the disease exists in Uganda.

**Case presentation:** We report a case of a 12-year-old female, the last born of 6 from a family with no known familial disease who presented with non-neuropathic Gaucher's disease and superimposed malaria. The disease was initially misdiagnosed as hyper reactive malarial splenomegaly but was subsequently confirmed by examination of the bone marrow smear and core. The disease was managed supportively and because of the worsening hematological parameters, a splenectomy was done. She currently takes morphine for bone pains in addition to physiotherapy.

**Conclusion:** Clinicians must always exclude other possible causes of hepatosplenomegaly before diagnosis of HMS. Treatment and management of patients with rare conditions like GD need to improve. Although splenectomy is indicated in GD, it should only be done when it is absolutely necessary.

**Keywords:** Type 1 Gaucher's disease • Case report • Lysosomal Storage Disease (LSD)

## Introduction

Gaucher's Disease (GD) is an autosomal recessive Lysosomal Storage Disease (LSD), caused by over 300 mutations in the *GBA1* gene located on the long arm of chromosome 1, region 2 band 1 [1,2]. This causes a deficiency of a key lysosomal enzyme called β-glucosidase (also known as glucocerebrosidase) in the leukocytes. This enzyme is critical in the metabolic conversion of glucosylceramides (sugar-containing fat) to glucose and ceramide. Because of its deficiency, glucosylceramides accumulate in the lysosomes (digestive machinery of macrophages), transforming the macrophages into Gaucher cells that characterize Gaucher's disease [3]. This material/substrate (glucosylcerebroside) is continuously produced by the body but the lysosomes cannot break it down, it gets "stored" in the macrophages, hence its name, LSD. Therefore, these transformed macrophages accumulate in the body's organs like bone marrow, spleen, liver, and nerves, impairing these organs' functions [4].

GD has no sex predilection and is the second most common lipid storage disease after Fabry disease [5].

It is a rare disease with a prevalence of 1 in 100,000 and an incidence of 1 to 60,000 births in the general population. The incidence drastically rises to about 1 in 450 births among Ashkenazi Jews [6]. In Africa, data is limited, however, a number of cases have been reported by several authors, from South Africa, Morocco, Mali, and Kenya [2,6-8]. In Uganda, data about the condition is lacking. To the best of our knowledge, this is the first case of Gaucher's disease to be reported in the country.

The disease can present in either of the 3 forms. The non-neuronopathic form (Gaucher's disease type 1) and the neuronopathic forms (Gaucher's disease type 2 and 3) [3,9]. Type 1 disease is characterized by the absence of neurological involvement and may present with pancytopenia, organomegaly (hepatosplenomegaly), skeletal lesions, and lung and renal involvement. It's the commonest form of the disease. Type 2 is

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characterized by central nervous system involvement and is rapidly fatal. It is more common among infants and newborns and is also known as the acute neuropathic form. Type 3 disease also causes central nervous system involvement, however, it takes a more chronic form and also causes hematological and skeletal involvement. Sufferers can live up to 40 years and the disease is known as the chronic neuropathic form [1,5].

## Case Presentation

She was a 12-year-old female, a referral from a peripheral health center with 2 years history of on and off spontaneous epistaxis worsening over time, associated with an 8/12 history of progressive abdominal distension, and mild pain but no other GI symptoms. The bleeding was always preceded by a sharp frontal throbbing headache. Two weeks prior to admission, epistaxis worsened with up to 4 episodes per day with an increase in abdominal distension and pain. In the same period, she developed on-and-off low-grade fevers, associated with severe headaches, palpitations, dizziness, and general malaise. She had had 3 admissions last year for which she was managed for malaria, with no blood transfusion.

She is the last born of 6 children, was delivered by SVD, and needed no resuscitation at birth. Had normal development in early childhood and currently in school had been progressing well. Her other siblings and the parents are normal, and there is no known familial illness.

She was weighing 34 kg, with a height of 141.4 cm, had moderate anemia, was mildly jaundiced, and had a non-tender swollen submandibular lymph node. Capillary refill was reassuring, with an axillary temperature of 38.4°C, SBP of 120 mmHg, DBP of 60 mmHg, tachycardia of 120 bpm, saturating at 98% on room air, and tachypnea at 20 breaths/min.

The abdomen was moderately distended, and non-tender, with a palpable spleen 8 cm below the coastal margin, and palpable liver 12 cm below the coastal margin. Other organ systems were unremarkable. A complete blood count showed pancytopenia. Table 1 for details. Peripheral blood film revealed ring forms of plasmodium falciparum with marked thrombocytopenia. An abdominal ultrasound scan revealed gross hepatosplenomegaly and scanty mesenteric lymph node enlargement. A clinical diagnosis of malaria with Hyper Reactive Malarial Splenomegaly (HMS) was made with a differential diagnosis of hematological malignancy. She was managed for malaria with 3 doses of intravenous artesunate, dihydroartemisinin and piperaquine, paracetamol, and folic acid. Subsequently, a bone marrow biopsy and aspirate were done. Smears were stained with Giemsa while trephine biopsy was stained with H and E and these revealed Gaucher cells (Figures 1 and 2) which are weakly Periodic Acid Schiff (PAS) positive (Figure 3). Therefore, a diagnosis of Gaucher's disease was made although enzyme assay for glucocerebrosidase could not be done. Because of the lack of definitive treatment for Gaucher's disease, the family was counseled and discharged on tranexamic acid per required need, fansidar two tablets monthly, and to be reviewed once every month. After 6 months of follow-up, splenectomy was done due to worsening hematological parameters. The procedure was successful, the spleen weighed 695 g and was firm solid with no infarcts or discrete nodules seen.

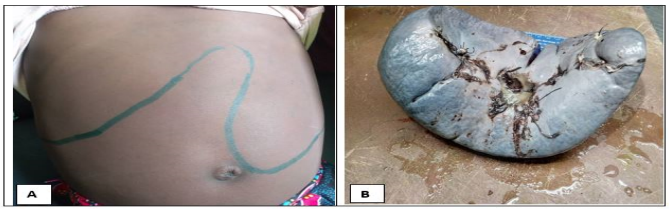


**Figure 1.** Panel A shows gross hepatomegaly and splenomegaly. Panel B shows the spleen after splenectomy was done.

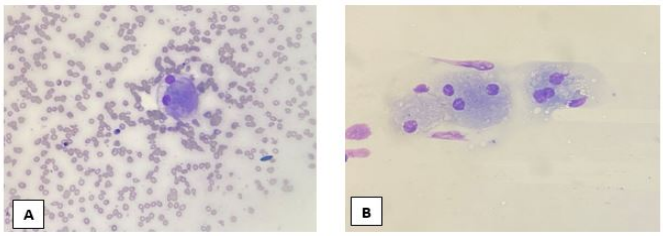


**Figure 2.** Both panels are peripheral blood smears show large cells (macrophages) with multiple hyperchromatic eccentric and nuclei with abundant bluish cytoplasm (Gaucher cells) (X400, Giemsa stain).

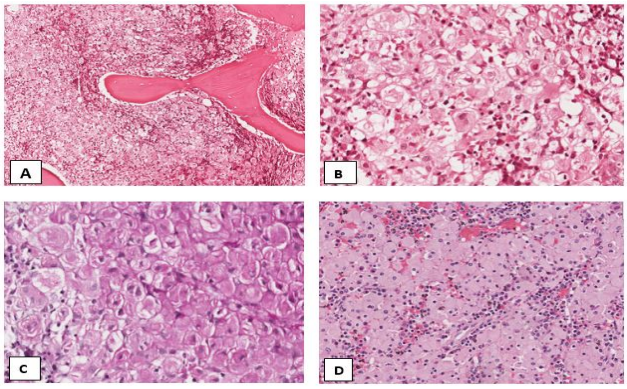


**Figure 3.** Panel A: Low power Images of the trephine biopsy showing a hypercellular marrow (100% cellularity) with numerous large cells with abundant pink cytoplasm crowding out all the hematopoietic cells. Panel B: high power view (x400) of the same marrow showing Gaucher cells with wrinkled tissue paper cytoplasm. Panel C: High power view of the trephine biopsy showing Gaucher cells weakly positive for Periodic Acid Schiff (PAS). Panel D: Histology section of the spleen showing sheets of macrophages (Gaucher cells) with abundant amphophilic cytoplasm and scattered residual lymphocytes.

After splenectomy, the subsequent CBCs initially revealed an upsurge in the leukocytes (14400/µl), platelets (666000/µl), and near-normal hemoglobin (10.0 g/dl) (done on day 2 weeks post-operatively). Five weeks postoperatively, she was still running a leukocytosis (18700/µl), a normal hemoglobin (11.4 g/dl), but had developed a thrombocytopenia (28000/µl) (Table 1). She also had developed severe bone pain involving the pelvis and lower limbs and episodic fevers. Lower limb x-ray revealed early skeletal deformities (Erlenmeyer flask deformity) involving the metaphysis of the femur. Her pain was managed by morphine in addition to physiotherapy. She currently attends monthly reviews at pediatric oncology clinic and physiotherapy although the prognosis is bad (Figure 4).

| Date | Parameters | Results | Normal ranges |
|---|---|---|---|
| 3/February/2023 (On admission) | White blood cells | 2.10 ($10^3$/µl) | 3.10-15.00 ($10^3$/µl) |
| | Hemoglobin | 5.9 (g/dl) | 9.5-15.8 (g/dl) |
| | Mean corpuscle volume | 78.1 (fL) | 68.0-98 (fL) |
| | Platelets | 76 ($10^3$/µl) | 126-438 ($10^3$/µl) |
| 22/February/2023 (After blood transfusion) | White blood cells | 2.52 ($10^3$/µl) | 5.50-17.00 ($10^3$/µl) |
| | Hemoglobin | 10.1 (g/dl) | 9.5-13.5 (g/dl) |
| | Mean corpuscle volume | 77.3 (fL) | 76.0-92.0 (fL) |
| | Platelets | 63 ($10^3$/µl) | 150-400 ($10^3$/µl) |
| | Creatinine | 20.0 mg/dl | 10-50 mg/dl |
| | Urea | | |
| | Liver enzymes | | |
| | ASAT/GOT | 23 U/L | 0-37 U/L |
| | ALAT/GPT | 20 U/L | 0-42 U/L |
| | Alkaline phosphatase | 152 U/L | 64-306 U/L |
| | Peripheral blood | Malaria parasites (++ seen) | -- |
| | Electrolytes | 137.8 mmol/L | |
| | Sodium | 5.01 mmol/L | 135-145 mmol/L |
| | Potassium | 107.2 mmol/L | 3.5-5.5 mmol/L |
| | Chloride | | 98-108 mmol/L |
| 7/July/2023 (15 days' post-splenectomy) | White blood cells | 14.4 ($10^3$/µl) | 4.00-10.00 ($10^3$/µl) |
| | Hemoglobin | 10.0 (g/dl) | 11.0-15.0 (g/dl) |
| | MCV | 74.5 (fL) | 86.0-98.0 (fL) |
| | Platelets | 666 ($10^3$/µl) | 126-438 ($10^3$/µl) |
| 31/July/2023 (39 days' post splenectomy) | White blood cells | 18.7 ($10^3$/µl) | 4.00-10.00 ($10^3$/µl) |
| | Hemoglobin | 11.4 (g/dl) | 11.0-15.0 (g/dl) |
| | Mean corpuscle volume | 70.3 (fL) | 86.0-98.0 (fL) |
| | Platelets | 28 ($10^3$/µl) | 126-438 ($10^3$/µl) |

**Table 1.** Shows some of the complete blood count parameters and other blood tests done on admission and how they varied during the follow-up period.

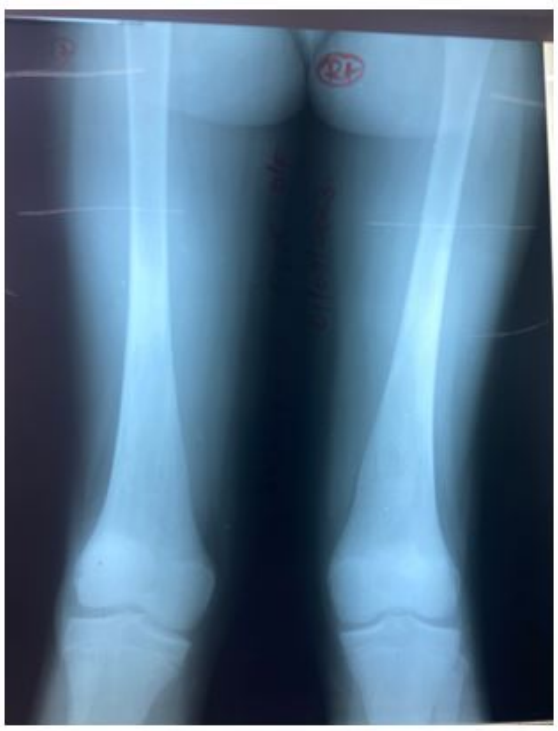

**Figure 4.** X-ray of the femur taken 5 weeks after splenectomy showing early musculoskeletal changes in the bones (Erlenmeyer flask deformity in the right femur).

## Discussion

GD type 1 is the commonest form of the disease with variable age of onset but is common before 20 years of age [10,11]. Patients have some residual activity of the enzyme glucocerebrosidase. It is characterized by the involvement of the bone marrow, spleen, liver, and kidneys, and spares the central nervous system. Patients, therefore, present with bleeding diathesis, anemia, increased risk of infections, and abdominal distension due to organomegaly. In our case, the patient had worsening epistaxis, recurrent malaria infections, and abdominal distension. The initial CBC revealed pancytopenia with Hemoglobin (Hb) of 5.6 g/dl, WBC count of 1670/µl, and Platelet count of only 63000/µl. Because of the low Hb, she had tachypnea, tachycardia, palpitations, and dizziness. These could also have been caused by the high fever of 38.4°C that she presented with because of malaria. She also had epistaxis at presentation which is attributed to thrombocytopenia. Thrombocytopenia can occur in severe malaria and this can easily confound the diagnosis [12]. However, in her case, she had been having these episodes of spontaneous epistaxis for the last two years and had reportedly worsened with up to 4 episodes of epistaxis per day. Therefore, malaria infection could not solely explain the worsening epistaxis over the 2 years' period.

As reported in all cases of type 1 GD, she had the characteristic hepatomegaly and splenomegaly of 12 cm and 8 cm below the coastal margin respectively as in Figure 1 above. Because we are in a malaria-endemic region, splenomegaly with a positive malaria test is always thought to be Hyper Reactive Malarial Splenomegaly (HMS). A recent systemic review revealed that up to 76% of splenomegaly in African Countries is caused by HMS as was also suspected in this case clinically [13]. Because hepatosplenomegaly is not exclusive to HMS, other causes of hepatosplenomegaly need to be excluded to avoid misdiagnosis as it could easily have happened in this case.

Gaucher's disease can be clinically suspected by the presence of clinical signs and symptoms and the identification of Gaucher-like cells on histological examination of either splenic, liver, or bone marrow biopsy. These investigations are usually done to investigate other suspected conditions like hematological malignancies as was suspected in this case. In our case, a bone marrow aspirate was done for suspected leukemia. Giemsa stained smears revealed large cells with small eccentric nuclei with basophilic cytoplasmic inclusions which were suspected to be Gaucher cells. Examination of the H and E stained trephine biopsy showed abundant accumulation of macrophages crowding out all hematopoietic cells. The macrophages had eccentric condensed chromatin and abundant cytoplasm with wrinkled paper-like accumulations which were weakly PAS positive. Based on the presence of these cells and the clinical picture, a diagnosis of GD type 1 was reached at. However, although Gaucher cells are pathognomonic for the disease, pseudogaucher cells have been reported in several other conditions. Pseudogaucher cells are seen in chronic myeloid leukemia, acute myeloblastic leukemia, chronic lymphocytic leukemia, Pompe disease, Niemann-Pick disease, Tay-Sachs disease, and Hurler syndrome.

The diagnosis is confirmed by laboratory demonstration of deficiency of glucocerebrosidase enzyme activity in the white blood cells (Beta-glucosidase leukocyte blood test). Patients with type 1 GD usually have some residual activity of the enzyme. Also, the test may not be helpful in carriers for which genetic testing is required to detect variants in the *GBA1* gene. In our case, enzyme testing is not available in the country. Attempts were made to have it done but the only available option was shipping the sample to India at a cost that the family could not afford.

Enzyme Replacement Therapy (ERT) is the mainstay treatment strategy, especially for type 1 GD. Recombinant glucocerebrosidase enzymes (imiglucerase, velalglucerase alfa, and taliglucerase alfa) are currently in use, however, these are not available in most underdeveloped countries. In our setting, treatment is largely supportive as indicated in the case above and in several cases reported in Kenya. After 6 months of supportive care, there was worsening cytopenia and organomegaly for which a total splenectomy was done. Splenectomy is indicated as one of the treatment options in patients not receiving ERT but the prognosis after the procedure is still debatable. There may be an improvement in hematological abnormalities [14], however, the disease tends to worsen in other organs with an increased risk of pulmonary hypertension and malignancy [15] as seen in the case above. After splenectomy, the hematological parameters showed an improvement with hemoglobin in the normal range. The white blood cells improved beyond the normal upper limit and this coincided with a fever although there were no other features of possible infection. Contrary to hemoglobin and white blood cells, platelets remained consistently low, lower than the

pre-splenectomy values. Additionally, she started experiencing bone pains with evidence of Erlenmeyer flask deformity which signifies worsening of the disease in the bones. Ultimately, we predict that she will suffer pathological fractures. Other recommended treatment options include substrate reduction using either eliglustat or imiglustat. These block the production of glucocerebrosides thus preventing their accumulation in the macrophages.

## Conclusion

This case should alert clinicians of possibility of other causes of hepatosplenomegaly other than HMS malaria endemic areas. Patients with hepatosplenomegaly and pancytopenia should always be investigated for other possible causes of hepatosplenomegaly before the diagnosis of HMS is made. There is a need to improve the diagnosis and treatment of rare genetic conditions like GD in low-resource settings because these may not be as rare as they are depicted in literature. Although splenectomy may result in an improvement of the hematological parameters, it should only be done if it is absolutely necessary because of the deterioration that follows it as seen in this case.

## Limitations

Confirmation of GD requires enzyme assay to establish deficiency of glucocerebrosidase. In our setting, the test could only be done from India and it required us to ship the blood sample which was expensive for the patient to afford and so it was not done.

## Consent and Ethical Approval

We obtained consent from the patient's mother to allow us to use images from her daughter's specimens and publish them in this case report for the purposes of creating awareness of the disease. She also gave consent to use the remaining specimens for any further research purposes in the future. The head of the pathology department also provided us with clearance to use the laboratory and the specimen. Institutional approval was not required.

## Patient Perspective

This being a rare genetic condition, the family was really worried and concerned about their daughter's condition. What was even more disturbing was the fact that it had no definitive cure and the recommended drugs were not available in the country. The family was counseled and educated about the pattern of inheritance and the type of care that can be provided to them. Fortunately, they are very adherent to treatment and have followed the follow-up schedule to the dot and so far they are satisfied with the care given despite the dismal outcome that the condition bears.

## Acknowledgment

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## Author Contribution

All the authors significantly contributed to this manuscript.

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## Availability of Material and Data

The data and materials of this case report are available from the corresponding author upon request after approval from the Pathology Department and Mbarara Regional Referral Hospital.

## References

1. Pastores GM, Hughes DA. Gaucher Disease. In: Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, et al., editors. GeneReviews(®). Seattle (WA): University of Washington, Seattle Copyright © 1993-2023, University of Washington, Seattle. GeneReviews is a registered trademark of the University of Washington, Seattle. All rights reserved.; 1993.
2. Sevitz H, F Laher, ST Varughese, and M Nel, et al. "Baseline characteristics of 32 patients with Gaucher disease who were treated with imiglucerase: South African data from the International Collaborative Gaucher Group (ICGG) Gaucher Registry." *S Afr Med J* 112 (2022): 21-26.
3. Stirnemann, Jerome, Nadia Belmatoug, Fabrice Camou, and Christine Serratrice, et al. "A review of Gaucher disease pathophysiology, clinical presentation and treatments." *Int J Mol Sc*i 18 (2017): 441.
4. Stone WL BH, Master SR. Gaucher Disease. 2022.
5. Disorders. NNOfR. Gaucher Disease: National Organization for Rare Disorders. 2018 updated March 03, 2020.
6. Murila, F, JA Rajab, and JM Ireri. "Gaucher's disease at a national referral hospital." *East Afr Med J* 85 (2008): 455-458.
7. Traore, Moussa, Mariam Sylla, Jeannette Traore, and Toumani Sidibe, et al. "Type 2 Gaucher's disease in a Malian family." *Afr J Health Sci* 11 (2004): 67-69.
8. Essabar, Laila, Toufik Meskini, Najat Lamalmi, and Said Ettair, et al. "Gaucher's disease: report of 11 cases with review of literature." *Pan Afr Med J* 20 (2015).
9. Weinreb, Neal J, Jose Simon Camelo Jr, Joel Charrow, and Monica R McClain, et al. "Gaucher disease type 1 patients from the ICGG Gaucher Registry sustain initial clinical improvements during twenty years of imiglucerase treatment." *Mol Genet Metab* 132 (2021): 100-111.

10. Dardis A, Helen Michelakakis, P Rozenfeld, and Ksenija Fumic, et al. "Patient centered guidelines for the laboratory diagnosis of Gaucher disease type 1." *Orphanet J Rare Dis* 17 (2022): 442.

11. Chaabouni M, H Aoulou, N Tebib, and M Hachicha, et al. "Gaucher's disease in Tunisia (multicenter study)." *La Revue de Medecine Interne* 25 (2004): 104-110.

12. Chiabi, Andreas, Seraphin Nguefack, Isabelle Kewe, and Ritha Mbono, et al. "Massive Epistaxis due to Profound Malaria-Induced Thrombocytopenia in an Adolescent: A Case Report at the Yaounde Gynaeco-Obstetric and Pediatric Hospital, Cameroon." *Health Sci Dis* 15 (2014).

13. Leoni, Stefania, Dora Buonfrate, Andrea Angheben, and Federico Gobbi, et al. "The hyper-reactive malarial splenomegaly: a systematic review of the literature." *Malar J* 14 (2015): 1-11.

14. Adas, Mine, Gokhan Adas, Oguzhan Karatepe, and Merih Altiok, et al. "Gaucher's disease diagnosed by splenectomy." *N Am J Med Sci* 1 (2009): 134.

15. Thomas, Alison S, Atul Mehta, and Derralynn A. Hughes. "Gaucher disease: haematological presentations and complications." *British J Haematol* 165 (2014): 427-440.

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