Case Report

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# Non-neuronopathic Gaucher disease (Type I) in an elderly female: a case report

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**Introduction and importance:** Gaucher disease is a rare autosomal recessive lysosomal storage disorder marked by a substantial reduction in beta-glucocerebrosidase activity. Historically, supportive treatments such as splenectomy and orthopedic interventions were employed, whereas recent advances have led to the approval of Enzyme Replacement Therapy (ERT) and Substrate Reduction Therapy (SRT) as therapeutic options.

**Case presentation:** The authors present the case of a 61-year-old female with chronic abdominal pain, abdominal fullness, pancytopenia, and hepatosplenomegaly, all indicative of Gaucher's disease, later confirmed by histopathological examination. The patient was informed about newer treatment options like ERT and SRT, as well as the traditional approach of splenectomy. However, due to financial constraints, she opted for splenectomy in conjunction with conservative management.

**Discussion:** Gaucher disease is defined by a deficiency of glucocerebrosidase, leading to the accumulation of Gaucher cells (pathognomonic of the disease), particularly in the spleen, liver, bone marrow, and lungs. Type 1 Gaucher disease (GD1) can manifest at any age, from childhood to late adulthood. Definitive diagnosis is confirmed by reduced beta-glucocerebrosidase activity. Traditionally, treatment options for GD1 have been supportive, including splenectomy, blood transfusions, and orthopedic procedures. However, SRT and ERT, though effective, remain prohibitively expensive and often inaccessible in low-resource settings.

**Conclusion:** Early diagnosis of Gaucher disease is challenging due to its rarity and should be considered in patients presenting with hepatosplenomegaly, pancytopenia, and low glucocerebrosidase activity.

**Keywords:** case report, Gaucher disease, lysosomal storage disorder, Nepal, splenectomy

## Introduction

Gaucher disease (GD, *OMIM #230800, ORPHA355*) is a rare autosomal recessive lysosomal storage disorder with a birth incidence of ~0.39–5.38 per 100 000 general population, but as high as 1 per 850 among the Ashkenazi Jewish population[1–3]. It is the most frequent multisystemic sphingolipidosis involving the liver, spleen, bone marrow, as well as lymph nodes. Gaucher disease is characterized by a significant reduction in the activity of the lysosomal enzyme, glucocerebrosidase, which hydrolyzes glucosylceramide (GlcCer) into ceramide and glucose due to mutations in the GBA1 gene located on chromosome 1(1q21). Consequently, substrate infiltration occurs in the cytoplasm of macrophage-monocyte system cells, such as those in the liver, spleen, bone marrow, and lymph nodes, presenting a character istic 'crumpled tissue paper' appearance[1,2].

GD exhibits variable phenotypes and is clinically classified into three subtypes based on the presence or absence of neurological involvement; (i) Type 1- non-neuropathic form (ii) Type 2- acute neuropathic form; infantile-onset (iii) Type 3- a neuronopathic form of juvenile-onset[4]. Previously, splenectomy and orthopedic intervention were the supportive treatments for GD1. However, recent advances have led to the approval of Enzyme Replacement Therapy (ERT) and Substrate Reduction Therapy (SRT) for therapeutic management in both children and adults, significantly

### HIGHLIGHTS

- Gaucher disease is a rare lysosomal disorder of autosomal recessive inheritance.
- Substrate infiltration in the macrophage-monocyte system presents a characteristic 'crumpled tissue paper' appearance.
- Splenectomy remains an alternative approach to substrate reduction therapy and enzyme replacement therapy.

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altering the natural history of the disease[5].

We present the case of an elderly female with chronic abdominal pain, abdominal fullness, pancytopenia, and hepatosplenomegaly, along with decreased beta-glucocerebrosidase activity, diagnosed as Gaucher's disease, and later confirmed through histopathological examination. This case report has been reported in line with the SCARE Criteria.

## Case presentation

A 61-year-old woman from the hilly region of Nepal, a farmer by occupation with type 2 diabetes mellitus under medication, presented to our center with complaints of unbearable pain in her left abdomen, along with a history of chronic right upper quadrant abdominal pain. The pain started 6 months prior and gradually worsened, with no identifiable aggravating or relieving factor, scoring 5/10 on the universal pain scale. The patient reported decreased appetite and a progressively enlarging mass in the left upper quadrant. She visited a tertiary medical care center, where blood tests revealed pancytopenia. She was, then, referred to the surgery department for a suspected surgical abdomen, imaging revealed a massive spleen. Consultation with the interventional radiology team considered the possibility of embolizing the splenic artery to prevent further enlargement due to abnormal scavenging of blood cells by the spleen. The patient had a history of hysterectomy 1 year prior. There is no history of recurrent infection, recurrent history of blood transfusion, bone pain, petechial rashes, or recent travel history to the endemic region. There were no similar or other significant illnesses in the past or in the family. She did not smoke or drink alcohol. Her menstrual history was normal.

On physical examination, all vitals were within normal limits, and the general examination revealed pallor; however, there was no koilonychia, flapping tremors, or jaundice. Abdominal examination revealed a palpable spleen just below the left subcostal margin and mild hepatomegaly. Similarly, neurological examination and other systemic findings were unremarkable. Her laboratory investigations (Table 1) revealed leukopenia, anemia, thrombocytopenia, and elevated LDH levels. Likewise, serology for HIV, syphilis, and hepatitis B and C were negative. Also, the test for sputum acid-fast smear was negative with no growth of organisms on the sputum culture. Similarly, stool routine and microscopy showed normal gastrointestinal flora.

Computed tomography (CT) of the abdomen and pelvis revealed massive splenomegaly and mild hepatomegaly, along with hypertrophied splenic arteries. A contrast-enhanced CT of the abdomen showed a dilated main portal vein, splenic vein, and superior mesenteric vein; a few enlarged periportal and celiac lymph nodes, multiple sub-centimeter aortocaval and left paraaortic lymph nodes; and mildly calcified plaques in the abdominal aorta and bilateral common iliac arteries (Fig. 1).

Considering the rare pathology, we decided to measure beta-glucocerebrosidase activity, which was found to be low at 0.82 nmol/h/mg protein (normal: 8.7 nmol/h/mg protein). Thus, in the background of the absence of neurological components, clinical spectrum, and laboratory findings, Gaucher type I was diagnosed. The patient was informed about the newer treatment modalities such as ERT and SRT, along with the traditional treatment option of splenectomy, for managing her condition and its potential complications if left untreated. Due to the patient's financial constraints, she opted for splenectomy along with conservative treatment modalities.

**Table 1**

**Laboratory investigation profile of the patient**

| Parameters | Units | Reference normal range | Reported |
|---|---|---|---|
| Lactate dehydrogenase (LDH), serum | U/l | 120–246 | 312.00 |
| Total protein, serum | g/dl | 6.3–8.2 | 7.60 |
| Albumin, serum | g/dl | 3.5–5.0 | 4.40 |
| Alanine amino transferase (ALT) | U/l | < 35 | 14 |
| Aspartate amino transferase (AST/SGOT) | U/l | 14–36 | 25 |
| Bilirubin (Total), serum | mg/dl | 0.2–1.3 | 1.30 |
| Bilirubin conjugated | mg/dl | 0.0–0.3 | 0.2 |
| Bilirubin unconjugated | mg/dl | 0–1.1 | 1.1 |
| Alkaline phosphatase | U/l | 38–126 | 89 |
| Serum urea | mg/dl | 15–45 | 46 |
| Serum creatinine | mg/dl | 0.52–1.04 | 0.6 |
| Serum sodium | mmol/l | 137–145 | 143 |
| Total leukocyte count | cells/cumm | 4000–11 000 | 3220 |
| Red blood cells | $10^6$ cells/cumm | 4.5–5.5 | 4.51 |
| Packed cell volume (PCV) | % | 40–50 | 32.9 |
| Hemoglobin | gm% | 11.9–14.6 | 10.8 |
| Platelet count | $10^3$ cells/cumm | 150–450 | 146 |

Preoperatively vaccinations for Pneumococci, Meningococcal, and H influenza were provided. It was then decided to undergo a splenectomy with biopsy by a multidisciplinary team. The gross specimen of the spleen measured 23×22×11 cm. The spleen was markedly enlarged, and the capsule was intact. The cross-section showed areas of congestion. Likewise, the microscopy report of the specimen revealed autolytic and ischemic changes along with the marked expansion of the red pulp with a large number of histiocytic cells with finely fibrillary cytoplasm, particularly in the splenic cords. The white pulp was intact and preserved (Fig. 2).

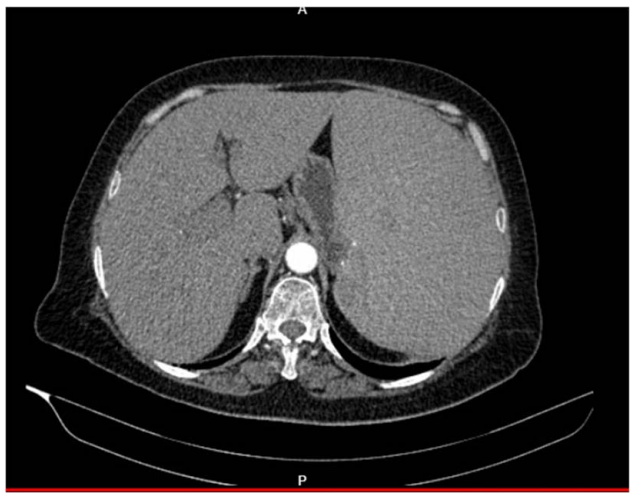


**Figure 1.** Contrast-enhanced computed tomography showing grossly enlarged liver and spleen.

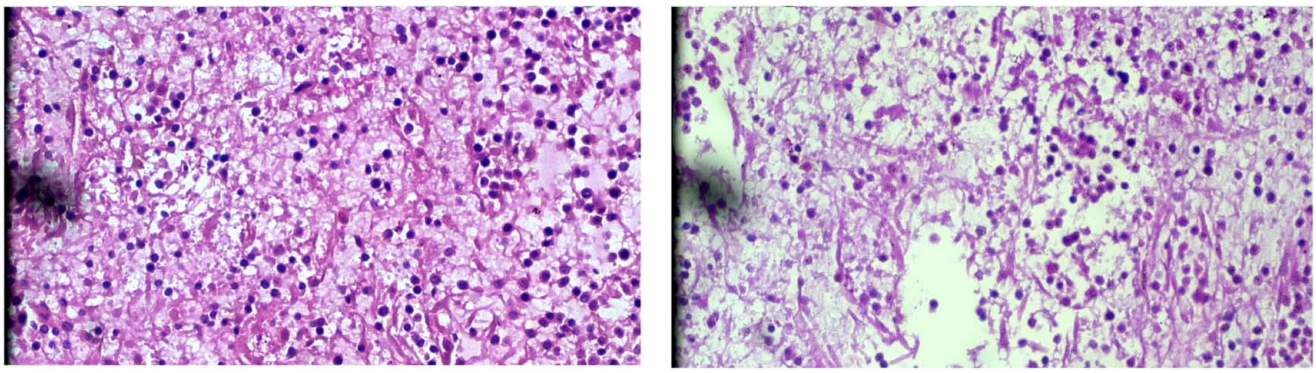

**Figure 2.** Histopathological images of the spleen showing a large number of histiocytic cells with finely fibrillary cytoplasm suggestive of Gaucher's disease.

Then differential diagnosis was discussed again with the multidisciplinary team, and the team of pathologists decided it was consistent with Gaucher's disease, type 1, with ischemic changes. Postoperatively, recovery was uneventful, and there were no complications during follow-up at 2 and 4 weeks.

## Discussion

Gaucher disease is a rare autosomal recessive lysosomal storage disorder, characterized by a deficiency of glucocerebrosidase (a lysosomal enzyme), which breaks down glucosylceramide into glucose and ceramide[6,7]. Deficiency of glucocerebrosidase enzyme results in the accumulation of glycolipids in macrophages (Gaucher cells), especially in the spleen, liver, bone marrow, and lungs[6]. The Gaucher cell is the pathognomonic feature of Gaucher disease, which was first recognized in 1882 by CPE Gaucher in a woman with an enlarged spleen[6,8,9].

Based on early-onset neurological involvement, Gaucher disease can be classified into neuronopathic Type 1 and non-neuronopathic Types 2 and 3[8,10]. Type 2 is an acute form manifesting in early childhood while type 3 is a subacute form that manifests in adolescence[11]. Type 1 Gaucher disease is the most common form among the three types, accounting for ~94% of all cases followed by type 3 (5%) and type 2 (1%)[8]. Here, we report a case of Type 1 Gaucher disease.

In the Gaucher registry, the mean age of diagnosis was 17.4 years, the majority (49%) receiving a diagnosis before 10 years of age, and Jews were the most commonly affected ethnic group[12]. In contrast to the data from the Gaucher registry, our case involved a 61-year-old Asian woman, indicating that Gaucher disease can occur at any age regardless of ethnicity as supported by a case of Gaucher disease reported in a 75-year-old Korean woman[7]. Type 1 GD can present at any age from child hood to old age and can have near-normal to normally expected survival[13].

It can be asymptomatic in mild cases. Patients can present with massive organomegaly (splenomegaly more common than hepatomegaly), cytopenia, and bone lesions[6,8,10]. Symptomatic splenomegaly with associated pain, early satiety, and cytopenia can be the presenting features of Gaucher disease[13], as observed in our case. Splenomegaly and hepatomegaly, in our case, could be attributed to the infiltration of Gaucher cells in the spleen and liver, while pancytopenia could be due to splenic sequestration or bone marrow infiltration by Gaucher cells, leading to bone mar row failure[10]. Early satiety and abdominal pain, in our case, could be attributed to splenomegaly[13]. Skeletal involvement in Gaucher disease can manifest as an acute painful bone crisis (due to infarcts) and chronic pain due to avascular necrosis[10,13]. However, the bone changes noticed in our case, lumbar spondy losis could also be age-related.

The definitive diagnosis of Gaucher disease is confirmed by reduced beta-glucocerebrosidase activity[14]. The enzyme level was reduced in our case too. Radiological imaging in Gaucher disease assesses liver and spleen morphology, and effects on bone[10]. Abnormal liver function tests may indicate cholestasis; however, they are typically normal in Gaucher disease, as observed in our case. The most common hematological abnorm ality in Gaucher disease is thrombocytopenia, followed by ane mia and leukopenia[10]. Our case also exhibited pancytopenia. Gaucher cells can be identified in bone marrow aspiration, how ever, it is not done routinely for the diagnosis of GD[10].

Previously, the treatment options for GD1 were supportive, including splenectomy, blood transfusions, and orthopedic procedures[15,16]. However, the approach has now shifted to enzyme replacement therapy (ERT) and substrate reduction therapy (SRT)[13,15]. ERT functions by hydrolyzing glycolipids accumulated in macrophages, while SRT (miglustat, eliglustat) reduces glycolipid synthesis by inhibiting the glucosylceramide synthase enzyme[13,15]. Our case was managed with splenectomy since advanced treatments such as ERT and SRT are expensive and unavailable in our setting.

## Conclusion

Gaucher's disease can be overlooked clinically due to its rarity; therefore, it should be considered if a patient presents with hepatosplenomegaly, pancytopenia, and low glucocerebrosidase enzyme activity. Splenectomy remains a viable alternative to substrate reduction therapy and enzyme replacement therapy.

## Ethical approval

Not applicable.

## Consent

Written informed consent was obtained from the patient for the

publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.


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## Author contribution

S.B.1, S.B.2, M.K.: conceptualization, resources, writing – original draft, and writing – review and editing; D.G. and G.A.: writing – review and editing and data curation; N.P. and S.K.: resources, writing – review, and editing; S.S.D,: writing – review and editing and supervision.

## Conflicts of interest disclosure

The authors declare no conflicts of interest.

## Guarantor

Sujan Bohara.

## Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

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