Molecular Genetics and Metabolism Reports 39 (2024) 101075

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

Case Report

A case of gaucher disease with a rare complication of gaucheroma and protein-losing enteropathy

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ARTICLE INFO

Keywords:
Gaucher disease
Gaucheroma
Protein-losing enteropathy
Lymphadenopathy

ABSTRACT

This case report describes a patient initially diagnosed with Gaucher disease (GD) with type I with homozygous mutation c.1448T > C p. (Leu483Pro) at age of 2, presenting with hepatosplenomegaly and cytopenia. Imiglucerase replacement therapy was initiated. At age 17, bilateral hearing loss developed, with subsequent Cranial MRI revealing thalamic damage, leading to a reclassification as type 3 GD. By age of 20, the patient presented with a range of symptoms, including abdominal pain, diarrhea, hypoproteinemia, multiple lymphadenopathy, edema, and Gaucher cell infiltration in the lymph nodes. Comprehensive diagnosis identifies Gaucher tumor and protein-losing enteropathy. Imiglucerase therapy at 90-120 U/kg every 2 weeks significantly improved clinical symptoms, emphasizing the importance of tailored interventions for managing GD manifestations.

1. Introduction

Gaucher disease (GD) is a rare autosomal recessive lysosomal storage disease, with a global incidence of about 1/40,000 to 1/100,000 [1]. Its pathogenesis revolves around mutations within the glucocerebrosidase (*GBA1*) gene. Gaucheroma with protein-losing enteropathy (PLE) is an extremely rare complication of GD. The main clinical manifestations are multiple lymphadenopathies, more commonly in mesenteric lymph nodes, accompanied by abdominal pain, diarrhea, hypoproteinemia and/or lower limb edema [2]. In this context, we illuminate the case of a patient diagnosed with GD type 3, concurrently grappling with a Gaucher tumor and PLE. The patient was initially thought to have Gaucher type 1, but as she aged, developed additional symptoms. Case Report: A 20-year-old female with type 3 GD at our hospital, with complaints of diarrhea characterized by yellow watery stools occurring 4 to 8 times daily, accompanied by abdominal pain, abdominal distention, tenesmus persisting for one year, and a six-month history of weight loss. There was no reported history of fever, bleeding, or loss of appetite. At the age of 2, she was diagnosed GD (type 1) owing to hepatosplenomegaly, cytopenia, deficient acid β-glucosidase activity and *GBA* homozygous mutation c.1488T > C p. (Leu483Pro) in exon 11. Early intervention ensued with imiglucerase replacement therapy, initiated at the age of 3, administered at a regular interval of 20–30 U/kg every 2 weeks. At the age of 17, the patient developed bilateral hearing loss. Further investigations through cranial MRI revealed patchy long T1 and long T2 signal shadows in the bilateral thalamus, indicative of involvement of the nervous system[3,4]. Subsequent reevaluation led to the reclassification of the disease as type 3 GD.

The admission examination revealed multiple palpable enlarged lymph nodes (maximum size: 3.1 cm × 2.4 cm) in the bilateral neck and supraclavicular region, the spleen was positioned 11.5cm below the left subcostal margin along the right spinoumbilical line, and mild pitting edema was observed in the bilateral lower limbs. Examination of Central vascular system, Central nervous system did not reveal any abnormality.

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https://doi.org/10.1016/j.ymgmr.2024.101075
Received 12 October 2023; Received in revised form 18 March 2024; Accepted 18 March 2024

No abnormalities were detected in the central vascular or nervous systems upon examination.

Auxiliary examinations yielded the following results: blood routine showed WBC 3.8 × 10^9/L, Hb 100 g/L, PLT 130 × 10^9/L; serum albumin 23.4 g/L; weakly positive occult blood was found in stool; stool culture showed no abnormality. Whole-body CT revealed multiple enlarged lymph nodes with calcification at the root of left neck and abdominal cavity, along with retroperitoneal lymph node enlargement. Other findings included an increased spleen volume, enlarged medullary cavities in bilateral humerus, tibia, and fibula with associated bone destruction, perisplenic and pelvic effusion, and diffuse interstitial edema in both lungs. Pathology examination of left neck lymph nodes unveiled revealed numerous Gaucher cells expressing CD163 (+), CD68 (+), and Ki-67 (approximately 10% +), suggesting Gaucher cell infiltration (see Figs 1 and 2).

Considering the non-infectious gastrointestinal symptoms, persistent hypoproteinemia, abdominal lymphadenopathy and lymph node pathology, the patient was diagnosed with Gaucher tumor and PLE. The patient was treated with imiglucerase (90-120 U/kg every 2 weeks) for 3 months. Encouragingly, the patient experienced resolution of abdominal pain, substantial improvement in diarrhea, and a return of serum albumin levels to normal.

2. Discussion

At present, only a few cases of gaucheroma with PLE have been reported [5]. Gaucher tumor, deemed a "pseudotumor", predominantly comprises Gaucher cells and typically manifests in lymph nodes within the mesenteric and mediastinal regions [6]. Occurrences have also been noted in the spleen, liver, abdomen, retina, and skin soft tissue, with an incidence rate of approximately 5%[5,7]. Biopsies typically showed Gaucher cell characterized by histiocytosis and expression of CD163, CD68, and vascular endothelial growth factor (VEGF) [8]. The disease usually progresses slowly and is closely associated with its severity. Because Gaucher tumor or involved lymph nodes vary in size and extent, the clinical manifestations vary greatly, and patients with mild disease may be asymptomatic, while severe cases can lead to PLE and even intestinal obstruction [9]. PLE is defined by a continual decrease in serum albumin (< 3.0 g/dL), excluding other causes,with or without elevated fecal alpha-1 trypsin. Patients typically exhibit symptoms like abdominal pain, abdominal distention, diarrhea, hypoproteinemia, edema. Additionally, complications may arise, including calcification, thrombosis, ascites, and electrolyte disturbances in lymph nodes [2]. PLE often signals disease advancement, predicts a challenging prognosis, and is associated with a heightened risk of early mortality. The pathogenesis of Gaucher tumor with PLE remains unclear. It is speculated to be related to mesenteric lymphadenopathy, secondary lymphatic obstruction, inadequate enzyme replacement therapy (ERT) dosage, splenectomy, and the development of neutralizing antibodies against ERT[10,11]. Currently there is no effective and targeted treatment for Gaucher tumor with PLE. Some studies propose that increasing the dose of ERT or combining substrate inhibitors (SRT) might be effective [12–14]. Consequently, the patient's imiglucerase dosage was adjusted to 90-120 U/kg every two weeks, resulting in a notable improvement in diarrhea symptoms during follow-up.

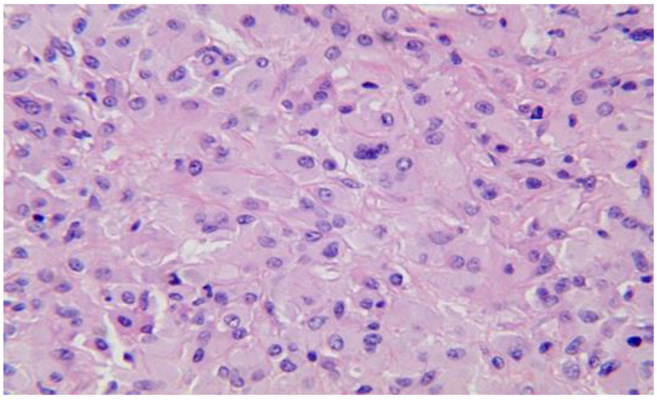

Fig. 1. Pathology of left neck lymph nodes revealed numerous Gaucher cells (HE × 400).

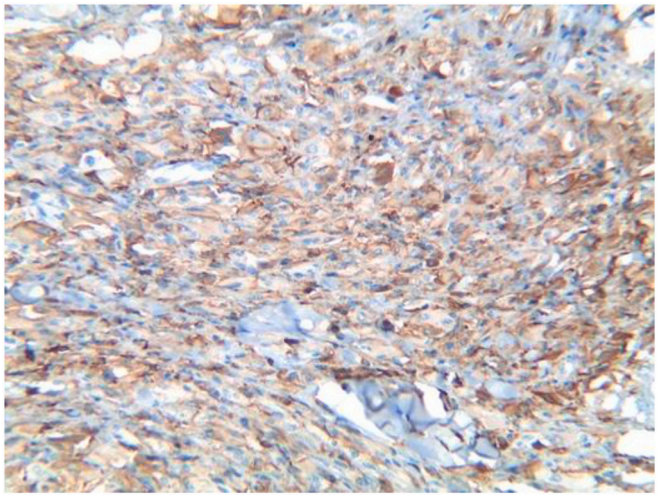

Fig. 2. Pathological immunohistochemistry of lymph nodes (CD163 staining × 200).

3. Conclusion

In conclusion, we present a case highlighting neurologic involvement and PLE in a patient carrying a homozygous L483P mutation. Notably, these complications persisted despite more than a decade of ERT. This underscores the importance of vigilance for potential neurological issues in individuals with L483P mutations and the need for timely adjustments in ERT dosage, particularly in the context of addressing the possibility of undertreating known neuronopathic Gaucher patients.

Enhancing awareness of rare complications is crucial to impede disease progression. Notably, our findings suggest that higher doses of ERT may offer partial efficacy in managing Gaucheroma with associated PLE. This insight contributes to a more comprehensive understanding of potential complications, aiding in the development of tailored treatment approaches.

Funding

The Study was Supported by Fundamental Research Program of Shanxi Province (202303021221201); Shanxi Bethune Talent Foundation Project (2021RC038) and (2021RC017).

CRediT authorship contribution statement

Tianbo Zhang: Writing – review & editing, Writing – original draft. **Xialin Zhang:** Writing – review & editing, Resources, Funding acquisition. **Ningning Zhang:** Resources. **Junrong Yan:** Resources. **Lina Wang:** Resources. **Weihong Yan:** Resources. **Zhuanzhuan Yu:** Resources. **Yonghong Zhang:** Resources. **Yanlong Duan:** Resources. **Ruijuan Zhang:** Writing – review & editing, Resources, Funding acquisition.

Declaration of competing interest

Ruijuan Zhang and Yanlong Duan are co-correspondence authors for

this study. All authors declare that there is no conflict of interest in this study.

Data availability

No data was used for the research described in the article.

Acknowledgements

We are grateful to MS. Yingying Meng of the Rare Disease Office at China Charity Federation (CCF) for follow-up management. We thank the CCF-Sanofi- Genzyme charitable aid projects for long-term free drug donation to patients.

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