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Feasibility of an evidence-based multidisciplinary care framework in a Pompe disease carrier pregnancy – a case report

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ABSTRACT

Introduction and aim. Pompe disease-carrier pregnancies present complex management challenges that require integrated genetic, biochemical, and psychosocial interventions. The current literature lacks comprehensive management frameworks that address the multifaceted needs of these high-risk pregnancies.

Description of the case. We report the treatment of a 31-year-old South Asian woman with three previous pregnancies affected by Pompe disease using a systematic multidisciplinary protocol developed following the current European Reference Network guidelines. Both partners were compound heterozygous carriers with documented pathogenic variants. The protocol integrated early genetic diagnosis through sampling of the chorionic villus, systematic biochemical monitoring, structured psychological support, and coordinated multidisciplinary care involving eight specialist services. Maternal psychological scores showed substantial improvement with the Edinburgh Postnatal Depression Scale decreasing from 14 to 2 (86% improvement) and the Generalized Anxiety Disorder Scale decreasing from 12 to 1 (92% improvement) after protocol-based psychological support without concurrent medication or therapy. Six-month follow-up confirmed sustained clinical and psychological benefits with normal infant development.

Conclusion. This case demonstrates the feasibility of implementing a systematic multidisciplinary care framework for Pompe disease-carrier pregnancy. Although preliminary results are encouraging, validation through larger cohort studies is necessary before widespread implementation, considering resource availability, genetic diversity, and cultural factors that may influence reproducibility in different healthcare settings.

Keywords. lysosomal storage disorders, multidisciplinary care, Pompe disease, pregnancy management, prenatal diagnosis

Introduction

Pompe disease, or glycogen storage disease type II, is a rare autosomal recessive lysosomal storage disorder caused by acid alpha-glucosidase (GAA) deficiency, leading to glycogen accumulation in cardiac and skeletal muscle.[1] Global birth prevalence is estimated at 2.0 cases (95% CI: 1.5–2.4) per 100,000 live births.[2] When both partners carry pathogenic *variants of GAA,* subsequent pregnancies carry a 25% risk of recurrence and substantial psychological burden on the family.[2,3] Current literature on managing such high-risk pregnancies remains limited, consisting largely of isolated case reports rather than structured evidence-based management frameworks.[4] Pregnant women with rare diseases have been identified as a particularly vulnerable population, with recent reviews emphasizing the need to address physical, emotional, and psychological dimensions of care concurrently.[5] In 2024, the European Reference Network for Metabolic Diseases (MetabERN) published clinical pathway recommendations for Pompe disease that emphasize coordinated multidisciplinary care, but practical guidance on applying these recommendations within an actual pregnancy care pathway remains limited.[6]

This report addresses that gap by describing the systematic implementation of an evidence-based multidisciplinary care framework, rather than simply presenting a rare clinical scenario. We present the case of a Pompe disease carrier couple with three previous affected pregnancies to demonstrate the feasibility and real-world practical implementation of MetabERN-aligned multidisciplinary care in guiding a subsequent pregnancy to a favorable outcome.

Aim

The objective of this case report is to demonstrate the feasibility and practical implementation of a comprehensive, evidence-based multidisciplinary care framework for the management of pregnancy carriers of Pompe disease, addressing existing gaps between published clinical guidelines and their application in routine clinical practice.

Description of the case

Demographics and history of the patient

A 31-year-old South Asian woman presented at 8 weeks of gestation for specialized pregnancy management. She had been married for nine years, with a reproductive history of three previous pregnancies, all affected by Pompe disease, each ending in the child's death.

Genetic background

Both partners were confirmed compound heterozygous carriers of pathogenic *GAA* variants (Table 2 summarizes specific variants), conferring a 25% risk of recurrence for each pregnancy.

Previous pregnancy history

- First pregnancy (2018): twin gestation, intrauterine fetal death at 28 weeks' gestation; autopsy showed bilateral cardiomegaly with glycogen deposition
- Second pregnancy (2019): male infant, progressive symptoms at 4 months of age despite enzyme replacement therapy; died at 7 months of cardiorespiratory failure
- Third pregnancy (2020): prenatal diagnosis confirmed affected status; delivered at 34 weeks of gestation due to severe polyhydramnios and fetal cardiomegaly; child died at 18 months despite ongoing treatment

Current pregnancy: diagnostic and clinical course

Written informed consent was obtained from the patient; as this report describes the application of existing clinical guidelines rather than experimental research, formal approval from the ethics committee was not required.

At 5 weeks of gestation, the patient underwent genetic counseling and a baseline psychological evaluation, which showed an Edinburgh Postnatal Depression Scale (EPDS) score of 14, a generalized anxiety disorder-7 (GAD-7) score of 12, and a perceived stress scale score of 28, consistent with significant antenatal distress. Structured psychological support was initiated without concurrent medication or psychotherapy (further details on the multidisciplinary care structure are provided in the discussion).

Transcervical chorionic villus sampling was performed at 11 weeks of gestation, showing fetal GAA enzyme activity of 18.2 nmol/hour/mg protein (normal range of 10–25 nmol/hour/mg protein). Definitive molecular testing at 13 weeks of gestation identified heterozygosity for only the maternal c.525delT variant, confirming carrier status and excluding the four parental pathogenic variants.

Maternal GAA enzyme levels remained stable (2.0–2.3 nmol/hour/mg protein, coefficient of variation 6.8%) throughout pregnancy; the clinical significance of this stability in carriers is not established, but provided reassurance alongside baseline data. The fetal anatomical survey at 16 weeks of gestation and fetal echocardiography at 20 weeks of gestation showed normal development.

In the third trimester, EPDS and GAD-7 scores had decreased from baseline, coinciding with ongoing genetic reassurance and structured psychological support; This improvement is reported descriptively and cannot be causally attributed to any single intervention in this observation of a single patient.

Delivery and neonatal outcomes

Elective induction at 38 weeks and 2 days gestation resulted in vaginal delivery of a healthy female neonate (2,850 g; Apgar 8 at 1 minute, 9 at 5 minutes). Cord blood GAA enzyme activity was normal at 22.1 nmol/hour/mg protein. Neonatal genetic testing and echocardiography confirmed the prenatal findings.

Follow-up

At 6 months of age, the infant showed age-appropriate developmental milestones (weight 7.2 kg, 50th percentile; length 66 cm, 45th percentile). Maternal EPDS and GAD-7 scores remained low in this assessment. No emergency visits or antepartum hospitalizations occurred during this pregnancy, in contrast to the previous course of pregnancy course; these observations are based on a single 6-month follow-up and should be interpreted as preliminary.

Discussion

Framework implementation and preliminary outcomes

This case documents a comprehensive, evidence-based multidisciplinary approach to the treatment of pregnant women with Pompe disease. Although further validation is necessary, its successful implementation suggests potential improvements in clinical outcomes and psychological well-being compared to family previous pregnancy experiences.

Integration of structured psychological support throughout pregnancy addresses the needs identified in the recent literature on rare disease and high-risk pregnancies.[7] In this case, coordinated input from eight specialist services was associated with favorable maternal and neonatal outcomes, consistent with reports that multidisciplinary care models improve pregnancy outcomes in other rare and high-risk maternal conditions.[8]

Psychological impact and intervention

A substantial improvement in maternal psychological well-being occurred after structured psychological support alone, without concurrent medication or therapy. The Edinburgh Postnatal Depression Scale improved from 14 to 2, and the Generalized Anxiety Disorder Scale from 12 to 1, both sustained through 6-month follow-up. Non-pharmacological psychological interventions have been associated with measurable reductions in anxiety, depression, and stress in other high-risk pregnancy populations, although in this single case attribution of improvement specifically to our framework requires confirmation through controlled studies.

Clinical outcomes and diagnostic accuracy

This approach ensured concordance between prenatal and postnatal testing in this case. When parental variants are known, combined molecular and biochemical tests represent a recommended diagnostic approach for the diagnosis of Pompe disease prenatal and postnatal, providing comprehensive diagnostic information as demonstrated in our case.[9]

Limitations and considerations

The principal limitations of this single case report include a significantly constrained evidence level due to the absence of a control group and limited generalizability arising from specific genetic variants, family history, and institutional resources. Cultural factors, the genetic diversity of Pompe disease, and differences in healthcare system resources can substantially affect reproducibility of this approach in different settings. Only preliminary long-term outcome data are available at six months of follow-up; larger cohorts and extended follow-up periods are needed to determine long-term benefits or complications. Future considerations include the possibility that framework modifications may be required for specific genetic variants; implementation requires specialized multidisciplinary teams and substantial resources; and cultural and healthcare system adaptations will be necessary for different populations. Cost-effectiveness analysis is needed before a larger implementation, and healthcare personnel would need training in rare disease pregnancy.

Integration with current guidelines

Our approach aligns with the recommendations of the 2024 MetabERN clinical pathway for Pompe disease, which emphasize multidisciplinary care coordination.[6] Adapting these guidelines for pregnancy management requires consideration of pregnancy-specific factors and resource availability in different healthcare settings.

Future research directions

Despite the potential advantages of systematic multidisciplinary approaches, this preliminary report underscores the need for:

- Prospective multicenter cohort studies evaluating effectiveness in diverse populations
- Development of validated outcome measures specifically for rare disease pregnancies
- Cost-effectiveness analysis comparing systematic frameworks to standard care
- Investigation of the optimal timing and duration of psychological interventions
- Evaluation of long-term family impact beyond the immediate postpartum period

Conclusion

This case demonstrates that the implementation of a structured multidisciplinary framework for Pompe disease carrier pregnancy management is feasible. In this single case, the framework resulted in favorable clinical outcomes and notable improvements in psychological well-being despite three previous devastating losses.

Initial outcomes, including coordinated multidisciplinary care, structured psychological support, and successful prenatal diagnosis, are encouraging; however, this single case cannot establish the efficacy of the framework. The observed improvements may be attributable to various factors beyond the framework itself, including previous experiences, specific genetic variants involved, and available institutional resources.

The most significant contributions demonstrated were the structuring of multidisciplinary coordination and the integration of systematic psychological support with clinical care. Framework development and implementation required substantial resources and specialized expertise, which can challenge utilization across different healthcare settings. Larger, controlled, multicenter studies, alongside cost-effectiveness analysis and adaptation for diverse populations and healthcare systems, are necessary to determine the true effectiveness and generalizability of this approach. This case represents an initial step toward the development of an evidence-based framework for rare disease pregnancies, which requires substantial further validation.

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Declarations

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Author contributions

Conceptualization, S.P. and S.K.R.; Methodology, S.K.R. and S.T.; Protocol Development, S.K.R. and S.T.; Investigation, S.P.; Writing – Original Draft, S.P.; Writing – Review & Editing, S.K.R. and S.T.; Supervision, S.K.R. and S.T.

Conflicts of interest

The authors declare that they have no conflict of interest.

Data availability

The data sets generated during this study are available from the corresponding author on reasonable request.

Ethics approval

Written informed consent for publication was obtained from the patient. This case report describes the implementation of existing clinical guidelines and does not constitute experimental research that requires approval from the Ethics Review Board. However, we acknowledge the institutional Ethics Review Committee for their guidance on the development of clinical protocols.

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