CASE REPORT

Spinal muscular atrophy carrier couple with normal child: Demonstrating Mendelian inheritance patterns

Anwita Shinde[1], Shradha Salunkhe[1], Shailaja Mane[1], Mahathi Reddy[1], Shruti Gaonkar[1], Adarsh Sahu[1]*

[1]Department of Paediatrics, Dr. D.Y. Patil Hospital and Research Centre, Pimpri, Pune- 411 018 (Maharashtra) India

Abstract

Spinal Muscular Atrophy (SMA) is an autosomal recessive neuromuscular disorder caused by mutations in the SMN1 gene, with a carrier frequency of approximately 1 in 40-60 individuals. When both parents are carriers, each pregnancy carries a 25% risk of producing an affected child, 50% chance of a carrier, and 25% probability of a completely unaffected offspring. We report the case of a 27-year-old primigravida and her 33-year-old husband, both confirmed SMA carriers through genetic testing. The wife had heterozygous deletions in SMN1 exons 7 and 8, while the husband showed heterozygous duplication with 3 copies. Despite having a family history of SMA (wife's sister died at 18 months with confirmed SMA), the couple elected to forego prenatal genetic testing after comprehensive genetic counseling. The pregnancy was monitored with serial ultrasounds, revealing bilateral renal pelvis dilatation but no other structural anomalies. The couple delivered a healthy male infant at term via normal vaginal delivery with appropriate growth parameters and normal neonatal examination findings. Postnatal genetic testing using Multiplex Ligation-Dependent Probe Amplification (MLPA) revealed normal copy numbers for both SMN1 and SMN2 genes in exons 7 and 8, with MLPA ratios within normal range (1.05-1.14), confirming the infant was neither affected nor a carrier of SMA. This case demonstrates the classical Mendelian inheritance pattern for autosomal recessive disorders, where two SMA carrier parents achieved the favourable 25% probability of having a completely unaffected child. The outcome emphasizes the importance of com-prehensive genetic counseling in supporting diverse reproductive choices and highlights that positive outcomes remain possible even in high-risk genetic scenarios.

Keywords: Spinal Muscular Atrophy; Genetic Counseling; Heterozygote; Prenatal Diagnosis; Inheritance Patterns; Survival Motor Neuron 1 Protein

Introduction

Spinal Muscular Atrophy (SMA) is a severe autosomal recessive neuromuscular disorder characterized by progressive degeneration of motor neurons in the spinal cord and brainstem, leading to muscle weakness and atrophy [1]. The condition is caused by homozygous deletions or mutations in the Survival Motor Neuron 1 (SMN1) gene located on chromosome 5q13, with an estimated incidence of 1 in 6,000 to 1 in 10,000 live births worldwide [1, 2]. The carrier frequency for SMA mutations varies significantly across different populations, with approximately 1 in 40 to 1 in 60 individuals being carriers in most populations [2]. When both parents are carriers of SMA mutations, each pregnancy carries a 25% risk of producing an affected child, a 50% chance of a carrier child, and a 25% probability of a completely unaffected offspring, following classic Mendelian autosomal recessive inheritance patterns [3]. However, the clinical outcome in any individual pregnancy can vary considerably due to

the complex genetic architecture of the SMN locus [3]. Genetic counseling and carrier screening for SMA have become increasingly important in reproductive medicine, particularly given the availability of preimplantation genetic diagnosis and emerging therapeutic interventions [4, 5]. Understanding the inheritance patterns and genetic counseling implications for SMA carrier couples is crucial for healthcare providers, as it enables informed reproductive decision-making and appropriate medical management [4]. This case report demonstrates the classical Mendelian inheritance pattern in a confirmed SMA carrier couple who had a genetically normal child, illustrating the 25% probability of an unaffected offspring and highlighting the importance of comprehensive genetic counseling in such scenarios.

Case Report

We present a case of a 27-year-old primigravida and her 33-year-old husband, both confirmed carriers of SMA mutations, who delivered a genetically normal male infant. The couple sought genetic counseling at Nityanand Clinic's Genetic Counseling Centre due to their carrier status and family history of SMA. Her family history was significant for her younger sister, who died at 18 months of age with a confirmed diagnosis of spinal muscular atrophy. Her previous genetic testing revealed heterozygous deletions in exons 7 and 8 of the SMN1 gene, confirming her carrier status for SMA. Her genetic analysis demonstrated heterozygous dup-lication in exons 7 and 8 of the SMN1 gene with 3 copies, also indicating SMA carrier status.

During her pregnancy, she underwent routine antenatal care with serial ultrasound monitoring. At 20+3 weeks gestation, fetal ultrasound revealed bilateral renal pelvis dilatation with an antero-posterior diameter of 6mm, though no other gross structural anomalies or soft markers of aneuploidy were detected. The mean uterine artery pulsatility index was greater than the 99th centile, suggesting increased risk for pregnancy complications. Given the 25% risk of having an affected child with both parents being SMA carriers, the couple elected not to undergo prenatal genetic testing, making an informed decision to continue the pregnancy. Comprehensive genetic counseling was provided in their preferred language (Marathi) to ensure complete understanding of inheritance patterns and recurrence risks. She delivered a male infant at term via normal vaginal delivery on March 13, 2025, at our hospital. The newborn had normal birth parameters with a weight of 2.820 kg, length of 49 cm, and head circumference of 34 cm. Apgar scores were 7 at 1 minute and 8 at 5 minutes. The infant cried immediately after birth and demonstrated normal neonatal reflexes and muscle tone.

Postnatal genetic testing was performed on the newborn using Multiplex Ligation-Dependent Probe Amplification (MLPA) analysis at MedGenome Labs. The results showed normal copy numbers for both SMN1 and SMN2 genes in exons 7 and 8, with MLPA ratios of 1.05 and 1.10 for SMN1 exons 7 and 8 respectively, and 1.08 and 1.14 for SMN2 exons 7 and 8 respectively. All values fell within the normal range (0.80-1.20), confirming that the infant was neither a carrier nor affected with SMA. The infant's clinical course was unremarkable with normal feeding patterns, appropriate weight gain, and achievement of expected developmental milestones. Family history documentation revealed that the couple had no consanguinity, and the father's sibling had expired at 2 days of age due to unknown causes, though this was not related to SMA.

This case exemplifies the classical Mendelian inheritance pattern for autosomal recessive disorders, where two carrier parents had a 25% chance

of having an unaffected child, 50% chance of having a carrier child, and 25% chance of having an affected child. The outcome demonstrates the favourable 25% probability of complete genetic normalcy, reinforcing the importance of comprehensive genetic counselling for at-risk couples and the value of postnatal genetic confirmation in such scenarios.

Result

No pathogenic or likely pathogenic variants causative of the suspected phenotype have been identified.

Discussion

This case report demonstrates the classical Mendelian inheritance pattern in a confirmed SMA carrier couple who had a genetically normal child, illustrating the 25% probability of an unaffected offspring. Our findings align with established genetic principles for autosomal recessive disorders and highlight the importance of comprehensive genetic counseling in reproductive decision-making. The carrier frequency observed in our case is consistent with published literature. Studies report SMA carrier frequencies of approximately 1 in 40 to 1 in 60 individuals in most populations [2], with approximately 95% of affected patients showing homozygous absence of SMN1 gene exon 7 [3]. The heterozygous deletion in the mother and heterozygous duplication in the father represent typical genetic variants seen in SMA carriers.

Our case differs from several published studies in the reproductive choices made by the carrier couple. While many studies report high uptake of prenatal diagnosis among at-risk couples, our couple elected to forego prenatal genetic testing. This decision contrasts with findings from various studies where carrier couples opted for comprehensive prenatal testing programs. Recent research on prenatal genetic counseling in India has demonstrated that cultural factors and individual family preferences significantly influence testing decisions.

The favourable outcome in our case represents the 25% probability of having a completely unaffected child, as confirmed by normal SMN1 and SMN2 copy numbers. This outcome demonstrates the

Table 1: Multiplex ligation-dependent probe amplification (MLPA) results showing normal SMN1 and SMN2 gene copy numbers in the newborn

Genes/ Exons	Deletions/ Duplications	MLPA probe ratio (Dosage quotient)	Copy number	Disease (OMIM)	Inheritance	Clasiification
SMN1 (Exon 7)	-	Exon 7 (1.05)	2	-	-	-
SMN1 (Exon 8)	-	Exon 8 (1.10)	2	-	-	-
SMN2 (Exon 7)	-	Exon 7 (1.08)	2	-	-	-
SMN2 (Exon 8)	-	Exon 8 (1.14)	2	-	-	-

SMN - Survival Motor Neuron; OMIM-Online Mendelian Inheritance in Man

importance of understanding that each pregnancy of a couple who are both SMA carriers has approximately 25% chance of producing an affected child, 50% chance of producing an asymptomatic carrier, and 25% chance of producing an unaffected child who is not a carrier [3,4]. Recent advances in SMA treatment have influenced reproductive decision-making patterns. The approval of disease-modifying therapies like nusinersen has transformed the landscape of SMA management [5, 6]. Studies indicate that the availability of effective treatments influences prenatal genetic counseling approaches and parental decision-making regarding testing and pregnancy management [6].

The genetic counseling approach in our case exemplifies best practices recommended in the literature. Formal genetic counseling services must be made available to anyone requesting testing, with counseling including description of the disorder and range of severity [4]. The provision of counseling in the couple's preferred language (Marathi) aligns with recommendations for culturally appropriate genetic services, which is particularly important in the Indian healthcare context. Our case also highlights the importance of postnatal genetic confirmation even when prenatal testing is declined. Carrier screening helps individuals make informed reproductive decisions and take appropriate steps to ensure the health of their future children. The normal genetic results provide valuable information for future reproductive planning and eliminate the need for ongoing SMA-related medical surveillance in this child. The family history of SMA in the maternal lineage, with the death of the mother's sister at 18 months, underscores the significance of cascade testing and family screening. Those who have a family member with SMA or a family member known to be a carrier are at increased risk to be carriers themselves [4], supporting the importance of genetic counseling and testing for at-risk family members. The evolution of genetic counseling approaches in the new treatment era has been documented extensively. With the availability of disease-modifying therapies, the landscape of reproductive decision-making has transformed significantly [6,7]. Studies show that prenatal genetic counselors are now aware of these treatments and feel that this information affects pregnancy management decisions [6].

Our case contributes to the growing body of literature demonstrating that successful outcomes are achievable in high-risk genetic scenarios. Large-scale carrier screening studies have shown the technical feasibility and clinical utility of population-based screening programs [8], emphasizing the need to routinely offer carrier screening in appropriate settings. The prenatal ultrasound findings of bilateral renal pelvis dilatation in our case, while concerning at the time, were ultimately unrelated to SMA and resolved without intervention. This highlights the importance of comprehensive fetal monitoring in high-risk pregnancies, even when genetic testing is declined. The decision-making process illustrated in our case reflects the complex considerations families face when dealing with genetic risk.

Recent research emphasizes that reproductive decisions are intensely personal and that families should have access to comprehensive information about all available options [7]. The support provided by genetic counseling services and the respect for autonomous decision-making demonstrated in this case align with current best practices in reproductive genetics.

Conclusion

This case report exemplifies the fundamental principles of Mendelian inheritance in autosomal recessive disorders, specifically demonstrating the 25% probability of having a genetically normal child when both parents are confirmed SMA carriers. The couple's decision to decline prenatal testing while proceeding with postnatal genetic confirmation illustrates the diverse reproductive choices available to at-risk families and emphasizes the critical role of comprehensive genetic counseling in supporting informed decision-making. The favorable outcome reinforces the importance of understanding inheritance probabilities and highlights that positive outcomes are possible even in high-risk scenarios. This case contributes valuable insights into reproductive decision-making patterns among SMA carrier couples and underscores the necessity of continued genetic counseling support throughout the reproductive journey, regardless of the testing choices made by families.

References

1. Lefebvre S, Bürglen L, Reboullet S, Clermont O, Burlet P, Viollet L, *et al*. Identification and characterization of a spinal muscular atrophy-determining gene. *Cell* 1995; 80(1):155-165.
2. Verhaart IEC, Robertson A, Wilson IJ, Aartsma-Rus A, Cameron S, Jones CC, *et al*. Prevalence, incidence and carrier frequency of 5q-linked spinal muscular atrophy - a literature review. *Orphanet J Rare Dis* 2017; 12(1):124.
3. Wirth B, Herz M, Wetter A, Moskau S, Hahnen E, Rudnik-Schöneborn S, *et al*. Quantitative analysis of survival motor neuron copies: identification of subtle SMN1 mutations in patients with spinal muscular atrophy, genotype-phenotype correlation, and implications for genetic counseling. *Am J Hum Genet* 1999; 64(5):1340-1356.
4. Prior TW, Leach ME, Finanger E. Spinal Muscular Atrophy. In: Adam MP, Feldman J, Mirzaa GM, *et al*., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
5. Finkel RS, Mercuri E, Darras BT, Connolly AM, Kuntz NL, Kirschner J, *et al*. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. *N Engl J Med* 2017; 377(18):1723-1732.
6. Zettler B, Estrella E, Liaquat K, Lichten L. Evolving approaches to prenatal genetic counseling for Spinal Muscular Atrophy in the new treatment era. *J Genet Couns* 2022; 31(3):803-814.
7. Serra-Juhe C, Tizzano EF. Perspectives in genetic counseling for spinal muscular atrophy in the new therapeutic era: early pre-symptomatic intervention and test in minors. *Eur J Hum Genet* 2019; 27(12):1774-1782.
8. Archibald AD, Smith MJ, Burgess T, Scarff KL, Elliott J, Hunt CE, *et al*. Reproductive genetic carrier screening for cystic fibrosis, fragile X syndrome, and spinal muscular atrophy in Australia: outcomes of 12,000 tests. *Genet Med* 2018; 20(5):513-523.

Author for Correspondence:

Dr. Anwita Shinde, Department of Paediatrics, Dr. D.Y. Patil Hospital and Research Centre, Pimpri, Pune-411018, Maharashtra,

Email: anvitashinde001@gmail.com

How to cite this article:

Shinde A, Salunkhe S, Mane S, Reddy M, Gaonkar S, Sahu A. Spinal muscular atrophy carrier couple with normal child: Demonstrating Mendelian inheritance patterns. *J Krishna Inst Med Sci Univ* 2025; 14(4): 200-204

Submitted: *01-July-2025* ***Accepted:*** *10-Sep-2025* ***Published:*** *01-Oct-2025*