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Unraveling the Enigmatic Profile of Niemann-Pick Disease-B in Pediatrics

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ABSTRACT

The case report presents a 3-year-old male diagnosed with Niemann-Pick Disease type B (NPDB). The child exhibited hepatosplenomegaly, abdominal distension, rickets, anemia, and associated symptoms. Clinical examination revealed significant organ enlargement and abnormal bone marrow findings. Genetic testing confirmed mutations in the SMPD1 gene, establishing the NPDB diagnosis. NPDB poses significant challenges due to its characteristic lysosomal storage disorder nature. Timely recognition, thorough evaluation, and multidisciplinary management are crucial for enhancing patient outcomes. Current management strategies primarily involve supportive care and pharmacological interventions such as vitamin supplementation to alleviate symptoms and address complications. Despite lacking a definitive cure, ongoing research focuses on promising avenues like enzyme replacement therapies and gene-based treatments. These innovative approaches offer hope for potential future interventions in NPD. However, further extensive studies are warranted to explore and refine these treatment modalities, aiming to improve the overall prognosis for individuals affected by Niemann-Pick Disease.

INTRODUCTION:

A collection of lysosomal lipid storage disorders known as the Niemann-Pick diseases are autosomal recessive conditions. Caused by a variant in the SMPD1 enzyme. Infancy-onset hepatosplenomegaly or newborn cholestatic jaundice are examples of systemic symptoms. [1] There are now two groups for these illnesses.1) Niemann-Pick disease type A (NP-A or NP-B), which is caused by mutations in the SMPD1 gene; and 2) Niemann-Pick disease type C (NP-C), which also includes type D, which is caused by mutations in either the NPC1 or NPC2 gene. Acid sphingomyelinase is a key enzyme in the body that produces sphingomyelin. [2] It is a unique hereditary condition brought on by faulty intracellular movement of cholesterol and secondary buildup of glycosphingolipids [3]. Type A disease is a severe neurological disease of infancy with an Ashkenazi Jewish preference. It is characterized by progressive psychomotor impairment, failure to thrive, hepatosplenomegaly, cherry-red macula, and death by the age of 2-3 years. Contrarily, type B disease, which is pan-ethnic, is characterized by hepatosplenomegaly, thrombocytopenia, interstitial lung disease, and dyslipidemia, with little to no neurologic involvement in most patients. Growth retardation, retinal stigmata, and liver failure are less consistent but possible symptoms. ASM activity levels have been linked to a disease spectrum, including intermediate neurologic aspects of the condition, according to more recent research [4,5]. Some patients with NP-B may live into adulthood because most individuals have minimal or no neurologic involvement. [6] Niemann-Pick disease type C is characterized by sea-blue histiocytes in the bone marrow and is caused by errors in intracellular cholesterol transport. Patients frequently appear with newborn jaundice or hepatitis and develop hepatosplenomegaly in the future. For Niemann-Pick disease type C, bone marrow transplantation has been tried.[7] Clinical evaluation, laboratory tests to measure specific enzymes or analyze chemicals, imaging scans to determine organ involvement, and genetic testing to find mutations in pertinent genes, such as SMPD1, NPC1, or NPC2, are all required for the diagnosis of Niemann-Pick disease. There is no known treatment for Niemann-Pick disease (NPD). The main emphasis is on supportive care, which includes blood lipid-lowering statins, monitoring of liver function, and blood transfusions to reduce bleeding risks. Lung problems are treated with oxygen treatment. Organ transplantation has a poor track record. Gene treatments and enzyme replacement therapies are being studied. Supportive care is the primary method for treating type C NPD. While pain is treated with drugs, physical therapy controls neurological symptoms. [8]

Case presentation:

A 3-year-old male patient was admitted to the pediatrics department with the following details: weight of 10 kg, height of 82 cm, MAC (Mid-Arm Circumference) of 14 cm, and HC (Head Circumference) of 46 cm. The patient presented with chief complaints of abdominal distension persisting for 2 years and abdominal pain for the past 2 months. It was noted that the abdominal distension was not related to food intake. Additionally, the child had a history of loose stools, high-colored urine, and a previous hospital admission for pneumonia, where oxygen inhalation was required. The child also had a history of gait abnormalities. Upon examination, the child appeared active, alert, and afebrile. The pulse rate was 96 beats per minute, and the respiratory rate was 26 breaths per minute. Cardiovascular examination revealed positive findings for S1 and S2 heart sounds. In the respiratory system, bronchial breath sounds were found to be positive. In the abdominal examination, the abdomen was soft and distended, with a liver span measuring 17.5 centimeters. The spleen was palpable Laboratory investigations yielded the following results: a bone marrow biopsy showed mild erythroid hyperplasia with increased megakaryopoiesis, displaying hypo and hyper lobated forms. Thyroid function tests indicated a TSH (thyroid-stimulating hormone) level of 3.17, T4 (thyroxine) level of 12.9, and a T3 (triiodothyronine) level of 0.93. An abdominal scan revealed partial distention of the urinary bladder. Serum samples indicated the presence of CMV (Cytomegalovirus) IgM antibodies at a level of 1.07 and HSV (Herpes Simplex Virus) 1 and 2 IgM antibodies at a level of 0.92. Considering the clinical features and laboratory findings, from the [Table1, Table2 and Table3] the child was diagnosed with Hepatosplenomegaly with Niemann-Pick Disease-B (NPDB). Genetic testing confirmed the presence of mutations in the SMPD1 gene, resulting in deficient acid sphingomyelinase activity. Additionally, the child was found to have rickets and anemia. To manage these conditions, the child underwent supportive therapy and received various pharmacological treatments. This included the administration of vitamin supplements such as syrup vitamin D3, capsule vitamin E, syrup vitamin A, injection vitamin K, syrup zinc, nebulization with 3% normal saline solution, syrup calcimax, syrup Tonoferon, and tablet B complex, among others.

Laboratory findings:

Table 1: Day-wise complete blood picture (CBP)

Days	Hb in gm%	RBC in mil/cm	WBC Mil/cm	MCV C.U	MCH r r.	MCHC %	PLT
Day1	8.3	4.42	7.7	68.8	18.8	27.3	49900
Day2	7.4	3.38	8.25	79.9	19.3	24.2	49900
Day3	7.1	3.71	8.18	71.7	19.1	26.7	68400
Day4	8.3	7.7	4.42	72	18.1	26.3	4.9lakhs
Day5	7.8	4.2	8.2	79	18	26.4	6.4lakhs

Table 2: Day-wise lipid profile values

Lipid profile	Day 1	Day 2	Day 3	Day 4	Day 5
Cholesterol	651	586	555	640	560
Triglycerides	708	723	723	723	740
High density lipoproteins (HDL)	48	45	45	44	46
Low density lipoproteins (LDL)	313	288	288	284	311
Very low-density lipoproteins (VLDL)	143	142	145	145	140

Table 3: Day-wise liver function test values

Liver function tests	Day 1	Day 2	Day 3	Day 4	Day 5
Urea	26	15	18	16	15
Creatinine	0.18	0.19	0.28	0.12	
Aspartate aminotransferase (AST)	984	784	833	363	720
Alkaline phosphatase (ALP)	387	389	390	425	425
Albumin (ALB)	3.88	3.73	3.99	4.3	431
Total Bilirubin	1.49	1.3	1.22	0.93	0.97
Total protein	733	6.84	7.2	7.61	7.67
Globulin	3.4	3.1	3.21	3.3	3.4
Na/k/calcium	132/4.7/97	129/3.9/93	132/3.9/98	132/4.8/101	132/34/97

DISCUSSION:

The presented case report describes a child with hepatosplenomegaly, abdominal distension, abdominal pain, loose stools, high-colored urine, gait abnormalities, and a history of pneumonia. Based on the clinical features, laboratory investigations, and genetic testing, the child was diagnosed with Hepatosplenomegaly with Niemann-Pick Disease type B (NPDB) caused by mutations in the SMPD1 gene [6]. NPDB is a subtype of Niemann-Pick disease, which is a group of rare autosomal recessive lysosomal lipid storage disorders [1]. Niemann-Pick diseases can be categorized into acid sphingomyelinase-deficient Niemann-Pick disease (NP-A or NP-B) and Niemann-Pick disease type C (NP-C) [2]. NPDB is characterized by hepatosplenomegaly, thrombocytopenia, interstitial lung disease, and dyslipidemia, with little or no neurologic involvement [6]. The clinical presentation of the child aligns with the features commonly seen in NPDB, including hepatosplenomegaly, abdominal symptoms, and gait abnormalities [4,5]. Genetic testing confirmed mutations in the SMPD1 gene, resulting in deficient acid sphingomyelinase activity. SMPD1 gene mutations are responsible for NPDB and NP-A, both of which are caused by acid sphingomyelinase deficiency [6]. Deficiency of this enzyme leads to the accumulation of sphingomyelin and other lipids within the lysosomes, contributing to the pathogenesis of NPDB [3]. The laboratory investigations in this case provided additional evidence supporting the diagnosis of NPDB. The bone marrow biopsy showed mild erythroid hyperplasia with increased megakaryopoiesis, which is consistent with NPDB. The presence of rickets and anemia further highlights the multi-system involvement of Niemann-Pick diseases. Management of NPDB primarily involves supportive care, as there is currently no cure for the disease. Supportive therapy aims to alleviate symptoms and manage complications associated with NPDB. In this case, the child received various pharmacological treatments and vitamin supplements to address specific deficiencies and symptoms. Research into potential treatments for Niemann-Pick diseases, including NPDB, is ongoing. Enzyme replacement therapies and gene therapies are being explored as potential therapeutic options for these disorders [6]. However, these treatments are still under investigation and not yet widely available.

CONCLUSION:

This case report highlights the clinical features, laboratory findings, and genetic diagnosis of Hepatosplenomegaly with Niemann-Pick Disease type B (NPDB) in a child. The diagnosis was confirmed by identifying mutations in the SMPD1 gene. NPDB is a rare lysosomal lipid

storage disorder characterized by hepatosplenomegaly, interstitial lung disease, dyslipidemia, and minimal neurologic involvement. Supportive care remains the mainstay of management for NPDB, while research into novel therapeutic approaches continues to offer hope for future treatments.

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REFERENCES:

1. Vélez Pinos, Paola Jacqueline, et al. “Niemann-Pick Disease: A Case Report and Literature Review.” Cureus vol. 15,1 e33534. 9 Jan. 2023, doi:10.7759/cureus.33534
2. Vanier MT. Chapter 176—Niemann-Pick diseases. In: Dulac O, Lassonde M, Sarnat HB, editors. Handbook of Clinical Neurology, vol. 113. Amsterdam: Elsevier; 2013. P. 1717–21.í
3. Patterson MC, Vanier MT, Suzuki K, et al. Niemann-Pick disease type C: a lipid trafficking disorder. In: Scriver CR, Beaudet AL, Sly WS, et al, eds. The metabolic and molecular basis of inherited disease, 8th ed. New York, NY: McGraw-Hill, 2001:3611 –3633 [Google Scholar] View Full Reference List Read More: https://www.ajronline.org/doi/10.2214/AJR.09.2871
4. Wasserstein MP, Aron A, Brodie SE, Simonaro C, Desnick RJ, McGovern MM. Acid sphingomyelinase deficiency: prevalence and characterization of an intermediate phenotype of Niemann-Pick disease. J Pediatr 2006; 149:554 –555Read More:https://www.ajronline.org/doi/10.2214/AJR.09.2871
5. Pavlu-Pereira H, Asfaw B, Poupctova H, et al. Acid sphingomyelinase deficiency: phenotype variability with prevalence of intermediate phenotype in a series of twenty-five Czech and Slovak patients—a multi-approach study. J Inherit Metab Dis 2005; 28:203–227 [Crossref] [Medline] [Google Scholar]
6. McGovern MM, Wasserstein MP, Giugliani R, Bembi B, Vanier MT, Mengel E, et al. A prospective, cross-sectional survey study of the natural history of Niemann-Pick disease type B. Pediatrics. 2008;122(2): e341..
7. Robert S. Venick et al, Transplantation for Metabolic Disease in Children, Transplantation of the Liver (Third Edition),2015, Pages 317-345,https://doi.org/10.1016/B978-1-4557-0268-8.00027-0
8. Pineda M, Walterfang M, Patterson MC. Miglustat in Niemann-Pick disease type C patients: a review. Orphanet J Rare Dis. 2018 Aug 15;13(1):140. [PMC free article] [PubMed]