Published by
Saidu Medical College

OPEN ACCESS

Case Report

A Rare Presentation of Biotinidase Deficiency Mimicking Acrodermatitis Enteropathica in a Toddler

Muneeba Qadus[1], Kulsoom Ali[1], Rahmat Ali[2]
Ayesha Sohail[1] & Nayab Akhtar[1]
[1]Saidu Group of Teaching Hospital, Swat, Pakistan
[2]Best Skin and Laser Clinic, Peshawar, Pakistan

https://doi.org/10.52206/jsmc.2025.15.4.1204

Abstract

Background: Biotinidase deficiency is a rare autosomal recessive metabolic disorder caused by defective recycling of biotin. This results in multisystem involvement, with dermatological, neurological, and immunological manifestations. Due to overlapping features with other conditions such as acrodermatitis enteropathica, diagnosis can be delayed or missed, especially in low-resource settings.

Case Presentation: We describe a 2.5-year-old male toddler who presented with persistent eczematous rash, alopecia, conjunctivitis, recurrent seizures, developmental delay, and progressive hearing loss. The child was initially misdiagnosed as having acrodermatitis enteropathica. Laboratory evaluation revealed markedly reduced biotinidase activity (1.8 nmol/min/mL; reference range: >4.4 nmol/min/mL), confirming biotinidase deficiency.

Results: The patient was treated with oral biotin supplementation (5 mg/day) alongside supportive topical therapies. Within one month, there was dramatic improvement in cutaneous lesions, hair regrowth, seizure control, and developmental milestones. However, sensorineural hearing loss persisted despite treatment initiation.

Conclusion: This case highlights the diagnostic challenges of biotinidase deficiency in resource-limited settings where metabolic screening is not routinely available. Early recognition and timely supplementation with biotin can lead to rapid and transformative clinical improvement, preventing irreversible complications such as hearing loss and neurodevelopmental delay.

Keywords: Acrodermatitis enteropathica, Biotinidase deficiency, Consanguinity; Developmental delay, Eczema, Pediatric metabolic disorder, Sensorineural hearing loss.

ISSN (P): 1819-4583
ISSN (E): 3007-9470

Copyright © Copyright (c) 2025 The authors retain the copyrights. Authors are permitted and encouraged to post their work online (e.g. in institutional repositories or on their website), as it can lead to productive exchanges, as well as greater citation of published work.

Citation:
Qadus M, Ali K, Ali R, Sohail A, Akhtar N. A Rare Presentation of Biotinidase Deficiency Mimicking Acrodermatitis Enteropathica in a Toddler. J Saidu Med Coll. 2025;15(4):708–713.

Corresponding Author:
Dr. Muneeba Qadus
Medical Specialty (B),
Saidu Group of Teaching Hospital,
Swat, Pakistan
munibaq8@gmail.com

Funding:
The authors received no external funding for this study.

Conflicts of Interests:
The authors have declared that no competing interests exist.

Data Sharing Statement:
The data that support the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Received: January 27, 2025
1st Revision: February 21, 2025
2nd Revision: April 20, 2025
Accepted: May 23, 2025

Check for updates

Journal of Saidu Medical College

Introduction

Biotinidase deficiency (BD) is a rare autosomal recessive metabolic disorder caused by mutations in the BTD gene, leading to defective recycling of biotin, an essential water-soluble vitamin that functions as a cofactor for carboxylase enzymes involved in gluconeogenesis, fatty acid synthesis, and amino acid metabolism [1]. First described by Wolf et al. in the 1980s, the estimated worldwide incidence is about 1 in 60,000 live births [2,3].

Clinically, BD manifests with a constellation of dermatological, neurological, and immunological features such as alopecia, eczema, developmental delay, seizures, hypotonia, hearing loss, and recurrent infections [4,5].

In countries like Pakistan, where neonatal screening is unavailable, delayed diagnosis is common, often resulting in irreversible complications [6-8]. This case highlights the diagnostic challenge of BD mimicking acrodermatitis enteropathica and emphasizes the significant therapeutic benefits of timely biotin supplementation.

Patient Information

A 2.5-year-old male toddler, born at term by spontaneous vaginal delivery with normal birth weight, was brought to the outpatient department with an 18-month history of recurrent itchy eczematous rash, alopecia, and eye irritation. He had also experienced hearing loss, delayed speech, gross motor delay, and a seizure episode. Vaccination status was up to date, with no previous hospitalizations or significant medical history. The family history revealed parental consanguinity, and a first cousin had been diagnosed with acrodermatitis enteropathica.

Diagnostic Assessment

Laboratory evaluation including CBC, LFTs, RFTs, serum electrolytes, coagulation profile, and viral serology were within normal limits (Table 1). Biotinidase enzyme activity was markedly reduced (1.8 nmol/min/mL; reference 4.5–7.5), confirming BD. Imaging was not performed. Genetic testing was recommended but not completed due to resource limitations.

Clinical Findings

On examination, the child was comfortable with stable vital signs. Dermatological evaluation revealed diffuse oozy, eczematous lesions on the periorificial regions, trunk, and flexures, associated with generalized alopecia and conjunctivitis (Figure 1). Neurological examination demonstrated delayed milestones, including inability to stand or walk independently, reduced speech development, and poor auditory responsiveness. ENT evaluation confirmed bilateral sensorineural hearing loss, and ophthalmology confirmed conjunctivitis.



Figure 1: conjunctivitis, Alopecia with scalp scaling and diffuse erythema of the neck flexure before therapy.

Timeline

- Birth: Normal spontaneous vaginal delivery, normal birth weight.
- 6–12 months: Onset of eczematous rash and alopecia, treated initially with topical agents.
- 18 months: Development of seizures, hearing impairment, and delayed speech.
- 2.5 years: Persistent symptoms despite zinc supplementation and moisturizers; presented for further evaluation.
- Post-diagnosis: Initiated on oral biotin 5 mg/day with topical therapy; marked clinical improvement within one month.

Therapeutic Intervention

The patient was started on oral biotin supplementation at 5 mg/day, along with topical zinc oxide paste, emollients, and intermittent corticosteroids for eczema management. Conjunctivitis was treated with ophthalmic drops as per ophthalmologist's advice. Although developmental therapy was suggested, it was not initiated during the follow-up period.

Follow-up and Outcomes

Within one month of treatment, the patient showed remarkable dermatological improvement, with resolution of eczematous rash and regrowth of hair (Figures 2, 3). Conjunctivitis subsided completely with restored visual clarity. Neurological development improved modestly, with better motor coordination and speech initiation. However, bilateral sensorineural hearing loss persisted, and the child was referred to ENT services for auditory rehabilitation.

Table 1: laboratory tests results of the patient

Laboratory test	Results	Reference value
Complete Blood Count		
Hemoglobin	11 gm/dL	9.5-14 g/dL
WBCs	5 x 10 3/ µL	4-12 x103/µL
Platelets	250 x109/L	150-450 x 109/L
Liver Function Tests		
GGT	9.8 U/L	7.6-29.1 U/L
ALP	103 U/L	81-335 U/L
ALT	6.4 U/L	3.9-41.4 U/L
AST	20.7 U/L	15.9-64.1 U/L
Total Bilirubin	0.7 µmol/L	1-7 µmol/L
Serum Electrolytes		
Sodium	142 mEq/L	136-145 mEq/L
Potassium	4.0 mEq/L	3.4-4.7 mEq
Chloride	100 mEq/L	102- 112 mEq/L
Coagulation Profile		
PT	12 s	11-13 s
INR	1	< 1
APTT	29 s	26-36 s
Serum Virology		
HBs antigen (HBsAg)	Negative	-
Anti HCV Antibody	Negative	-
Anti HIV Antibody	Negative	-
Biotinidase Enzyme Level	1.8 nmol/min/mole	4.5-7.5 nmol/min/L



Figure 2: Restoration of normal hair growth and resolution of neck flexure rash with scalp scaling following treatment.



Figure 3: Resolution of conjunctivitis and normal hair growth after therapy.

Discussion

Biotinidase deficiency (BD) is an autosomal recessive metabolic disorder caused by mutations in the BTD gene, resulting in defective recycling of biotin—an essential cofactor for multiple carboxylase enzymes involved in gluconeogenesis, fatty acid synthesis, and amino acid metabolism [1]. The disorder manifests primarily in childhood, with multisystem involvement, including dermatological, neurological, and immunological features. Common clinical presentations include seizures, developmental delays, alopecia, hearing loss, and chronic eczematous skin lesions [8-9].

We report the case of a 2.5-year-old child with alopecia, developmental delays, chronic eczematous skin lesions, and sensorineural hearing loss, illustrating the diagnostic challenges of BD in resource-limited settings. The patient was initially misdiagnosed with acrodermatitis enteropathica, delaying appropriate management. Definitive diagnosis was established based on markedly decreased biotinidase activity, leading to the initiation of oral biotin supplementation. The child showed significant improvement in dermatological symptoms and developmental milestones within one month of therapy, consistent with prior research demonstrating that biotin supplementation can reverse clinical manifestations when started promptly [10-11].

This case highlights the importance of clinical vigilance in populations with high rates of consanguinity, where autosomal recessive disorders are more prevalent. In such contexts, BD should be considered in children presenting with unexplained eczematous rashes, alopecia, seizures, and developmental regression [8]. Early recognition is crucial, as untreated BD can result in irreversible complications such as sensorineural hearing loss and cognitive impairment [12].

Limited awareness and the absence of routine newborn screening in many countries, including Pakistan, contribute to delayed diagnosis. Integration of BD into newborn screening programs and improved physician education on its clinical presentation could significantly enhance early detection [13]. Neurological involvement in BD is attributed to the accumulation of lactate and other toxic metabolites in the cerebrospinal fluid, leading to seizures, developmental delay, and sensorineural hearing loss. Irreversible hearing loss occurs in up to 76% of untreated cases of profound BD, underscoring the necessity of early intervention [14].

In our patient, treatment with oral biotin (5 mg/day) led to substantial recovery of dermatological features and developmental progress within a month, reflecting the rapid therapeutic response described in previous studies [15]. Nonetheless, hearing loss and certain neurodevelopmental deficits may remain partially irreversible if treatment is delayed, further emphasizing the value of timely intervention.

Long-term management of BD requires a multidisciplinary approach, including annual ophthalmologic and auditory assessments, regular metabolic monitoring, and genetic testing for definitive diagnosis and severity classification [16].

Conclusion

This case illustrates the diagnostic challenge of BD presenting as refractory eczema and developmental delay. Early suspicion, timely diagnostic testing, and initiation of biotin therapy can reverse most clinical manifestations and prevent long-term disability. However, delayed diagnosis may result in irreversible complications, particularly hearing loss, as observed in this patient.

Learning Points

- Biotinidase deficiency (BD) should be considered in infants or toddlers presenting with persistent eczematous rashes, alopecia, developmental delay, and seizures—especially in regions with high consanguinity.
- Early enzymatic testing for biotinidase activity can confirm diagnosis and enable timely initiation of therapy, preventing irreversible neurological and auditory complications.
- Biotin supplementation (5 mg/day) leads to rapid clinical recovery and is both safe and effective, even in resource-limited settings.
- Delayed diagnosis may result in permanent sensorineural hearing loss and neurodevelopmental delay, underscoring the need for increased clinician awareness.
- Integration of biotinidase screening into neonatal metabolic programs can drastically improve outcomes and reduce lifelong disability in affected children.
- Multidisciplinary care, including dermatology, neurology, and audiology follow-up, is vital for long-term management and developmental monitoring.

Authors' Contributions

All authors meet the ICMJE criteria for authorship. They have reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Author 1: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 2: Substantial contribution to conception and design, data acquisition, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 3: Analysis and interpretation of data, drafting the manuscript, final approval, agreed to be accountable for all the work.
Author 4: Analysis and interpretation of data, critical revision, final approval, agreed to be accountable for all the work.
Author 5: Substantial contribution to conception and design, drafting the manuscript, final approval, agreed to be accountable for all the work.

References

1. Tardy AL, Pouteau E, Marquez D, Yilmaz C, Scholey A: Vitamins and Minerals for Energy, Fatigue and Cognition: A Narrative Review of the Biochemical and Clinical Evidence. *Nutrients.* 2020121, 228-2020. https://doi.org/10.3390/nu12010228

2. Wolf B: Worldwide survey of neonatal screening for biotinidase deficiency. *J Inherit Metab Dis.* 1991, 14:923-927. https://doi.org/10.1007/BF01800475
3. Wolf B. Biotinidase Deficiency. 2000 Mar 24 [updated 2023 May 25]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, *Seattle;* 1993–2025. https://www.ncbi.nlm.nih.gov/books/NBK1322/
4. Ahmed S, Ni M, DeBerardinis RJ, Habib A, Akbar F, Afroze B: Clinico-Pathological and Molecular Spectrum of Biotinidase Deficiency- Experience from a Lower Middle-Income Country. *Clin Lab.* 2021, 67:10-7754. https://doi.org/10.7754/Clin.Lab.2020.200937
5. Saleem H, Simpson B: Biotinidase Deficiency. In. StatPearls, Treasure Island (FL): StatPearls Publishing; February 9; 2023.
6. Tomar R, Vashisth D, Vasudevan R: Biotinidase deficiency. *Med J Armed Forces India.* 2012, 68:81-83. https://doi.org/10.1016/S0377-1237(11)60118-4
7. Asgari A, Rouhi Dehnabeh S, Zargari M. Clinical, Biochemical and Genetic Analysis of Biotinidase Deficiency in Iranian Population. *Arch Iran Med.* 2016, 19:774-778.
8. Wolf B, Grier RE, Secor McVoy JR, Heard GS: Biotinidase deficiency: a novel vitamin recycling defect. *J Inherit Metab Dis.* 19858, 1:53-58. https://doi.org/10.1007/BF01800660
9. Kannan B, Navamani HK, Jayaseelan VP, Arumugam P: A Rare Biotinidase Deficiency in the Pediatrics Population: Genotype-Phenotype Analysis. *J Pediatr Genet.* 2022:1-15. https://doi.org/10.1055/s-0042-1757887
10. László A, Schuler EA, Sallay E, et al.: Neonatal screening for biotinidase deficiency in Hungary: clinical, biochemical and molecular studies. *J Inherit Metab Dis.* 2003, 26:693-698. https://doi.org/10.1023/b:boli.0000005622.89660.59
11. Szymańska E, Średzińska M, Ługowska A, Pajdowska M, Rokicki D, Tylki-Szymańska A: Outcomes of oral biotin treatment in patients with biotinidase deficiency - Twenty years follow-up. Mol Genet Metab Rep. 20155, 33-35. https://doi.org/10.1016/j.ymgmr.2015.09.004
12. Gaspar HB, Hammarström L, Mahlaoui N, Borte M, Borte S: The case for mandatory newborn screening for severe combined immunodeficiency (SCID). *J Clin Immunol.* 2014, 34:393-397. https://doi.org/10.1007/s10875-014-0029-0
13. Reynolds E, Potter SN, Scott S, Bailey DB: Parent Reports of Developmental Service Utilization After Newborn Screening. *International Journal of Neonatal Screening.* 2025, 11:3. http://doi.org/10.3390/ijns11010003
14. Wolf B, Hsia YE, Sweetman L, et al.: Multiple carboxylase deficiency: clinical and biochemical improvement following neonatal biotin treatment. *Pediatrics.* 1981, 68:113-118. https://doi.org/10.3390/ijns11010003
15. Wolf B: Biotinidase deficiency should be considered in individuals exhibiting myelopathy with or without and vision loss. *Mol Genet Metab.* 2015, 116:113-118. https://doi.org/10.1016/j.ymgme.2015.08.012
16. Cowan TM, Blitzer MG, Wolf B; Working Group of the American College of Medical Genetics Laboratory Quality Assurance Committee: Technical standards and guidelines for the diagnosis of biotinidase deficiency. *Genet Med.* 2010, 12:464-470. https://doi.org/10.1097/GIM.0b013e3181e4cc0f