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A Case of Carbonic Anhydrase Deficiency and Renal Tubular Acidosis Type 3 in a Pediatric Patient: Clinical Presentation and Management

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Abstract

Renal tubular acidosis (RTA) type 3 is a rare genetic disorder characterized by impaired bicarbonate reabsorption in the proximal renal tubules, leading to metabolic acidosis. Here, we present a case of a 6-year-old male Saudi child who was diagnosed with RTA type 3 associated with carbonic anhydrase deficiency. The patient presented with symptoms of metabolic acidosis, electrolyte abnormalities, and a family history of renal tubular acidosis. Laboratory investigations revealed metabolic acidosis, hypokalemia, and hypophosphatemia, consistent with the diagnosis of RTA type 3. Genetic testing confirmed the presence of mutations in the CA2 gene encoding carbonic anhydrase II, corroborating the diagnosis of carbonic anhydrase deficiency. The patient was managed with oral alkali supplementation and electrolyte replacement therapy to correct acidosis and restore electrolyte balance. This case underscores the importance of recognizing the rare association between RTA type 3 and carbonic anhydrase deficiency, highlighting the role of genetic testing in diagnosis and personalized management strategies for affected individuals. Further research is warranted to elucidate the underlying molecular mechanisms and optimize therapeutic interventions for this rare disorder.

Keywords: Carbonic Anhydrase Deficiency, Renal Tubular Acidosis Type 3, Pediatric Patient, Case Report, Clinical Presentation.

BACKGROUND

Renal tubular acidosis (RTA) is a group of heterogeneous disorders characterized by the impaired acid-base regulation of the kidneys, leading to metabolic acidosis [1,2]. Among the various types of RTA, type 3 (RTA type 3) is associated with carbonic anhydrase deficiency, a rare genetic condition that affects the proximal renal tubules [3]. Understanding the pathophysiology of RTA type 3 requires insight into the role of carbonic anhydrase and the mechanisms underlying renal acid-base regulation.

Carbonic anhydrase is an enzyme that catalyzes the reversible hydration of carbon dioxide to bicarbonate and protons [4]. This reaction occurs in various tissues, including the kidneys, lungs, and red blood cells, and is essential for maintaining acid-base homeostasis. In the kidneys, carbonic anhydrase plays a crucial role in bicarbonate reabsorption along the renal tubules, particularly in the proximal tubules [5]. By facilitating the conversion of filtered carbon dioxide into bicarbonate ions, carbonic anhydrase contributes to the reabsorption of bicarbonate and the secretion of protons, thereby regulating urinary pH and acid-base balance [4,6].

RTA type 3 is a subtype of RTA characterized by impaired bicarbonate reabsorption in the proximal renal tubules, resulting in urinary wasting of bicarbonate and metabolic acidosis [1]. This defect is primarily attributed to mutations in the gene encoding carbonic anhydrase II (CAII), located on chromosome 8q21. CAII deficiency leads to reduced enzyme activity and impaired bicarbonate reabsorption, contributing to the pathogenesis of RTA type 3 [7,8].

In individuals with RTA type 3, defective bicarbonate reabsorption in the proximal tubules impairs the kidneys' ability to excrete acid and maintain systemic pH within normal limits [1,9]. Consequently, there is an accumulation of acid in the body, leading to metabolic

acidosis. The urinary wasting of bicarbonate further exacerbates acidosis and disrupts electrolyte balance, resulting in secondary effects such as hypokalemia, hypophosphatemia, and hypercalciuria [10,11].

The clinical presentation of RTA type 3 can vary widely and may include nonspecific symptoms such as fatigue, weakness, and failure to thrive, particularly in pediatric patients [2]. Metabolic acidosis may manifest with symptoms such as anorexia, vomiting, growth failure, and developmental delay. Electrolyte disturbances, including hypokalemia and hypophosphatemia, can lead to muscle weakness, bone demineralization, and renal calcifications. Long-term complications of untreated RTA type 3 may include nephrocalcinosis, renal stones, and bone deformities [2,3].

Diagnosis of RTA type 3 involves a comprehensive evaluation of acid-base status, urinary electrolytes, and renal function tests. Laboratory findings typically reveal metabolic acidosis with normal anion gap, hyperchloremia, urinary bicarbonate wasting, and electrolyte abnormalities such as hypokalemia and hypophosphatemia [1,2]. Genetic testing for mutations in the CA2 gene can confirm the diagnosis of carbonic anhydrase deficiency [12].

Management of RTA type 3 aims to correct metabolic acidosis, restore electrolyte balance, and prevent long-term complications. Treatment strategies may include oral alkali supplementation with bicarbonate or citrate salts to correct acidosis, potassium and phosphate replacement for electrolyte imbalances, and monitoring of renal function and bone health. In severe cases, patients may require renal transplantation to restore normal renal function and acid-base regulation [12-14].

CASE PRESENTATION

Patient History and Initial Presentation

A 6-year-old Saudi male, previously healthy, presented to the Pediatric Consultant Clinic with a chief complaint of bleeding following a recent tooth extraction. Notably, the patient's medical history included a familial occurrence of renal tubular acidosis (RTA) in his brother. Laboratory investigations on 15-01-2023 revealed significant electrolyte abnormalities, including hypokalemia (K: 0.88 mmol/L), hyponatremia (Na: 3.7 mmol/L), and metabolic acidosis (pH 7.21, HCO3 14 mmol/L).

Clinical Examination and Diagnostic Workup

Upon examination, the patient appeared well and conscious, with stable vital signs. However, laboratory findings raised concerns about a potential metabolic disorder. Further investigations on 15-02-2023, including blood gas analysis and electrolyte assays, confirmed persistent acidosis (pH 7.25, HCO3 15.2 mmol/L) despite conservative measures. Notably, the patient's brother had been diagnosed with osteoporosis renal tubular acidosis at a young age.

Genetic and Imaging Studies

Given the familial history of RTA and metabolic abnormalities, genetic testing was pursued to explore potential genetic mutations associated with renal tubular dysfunction. Imaging studies, including skeletal surveys and CT brain, were performed, revealing skeletal anomalies consistent with osteopetrosis and cerebral calcifications, suggestive of a broader metabolic disorder.

Diagnosis and Management

The culmination of clinical, laboratory, genetic, and imaging data led to the diagnosis of carbonic anhydrase deficiency (CAD), a rare metabolic disorder characterized by impaired bicarbonate reabsorption in the renal tubules. The patient was commenced on a multidisciplinary management plan, including electrolyte supplementation, alkalinizing agents, and close monitoring of metabolic parameters. Regular follow-up appointments were scheduled to track disease progression and treatment response.

Clinical Course and Follow-up

Despite initial stabilization, the patient experienced intermittent episodes of metabolic decompensation, necessitating ongoing adjustments to his treatment regimen. Serial laboratory evaluations, including blood gas analysis and electrolyte monitoring, were conducted to guide therapeutic interventions and assess treatment efficacy. Long-term management involved close collaboration between various healthcare providers, including pediatricians, nephrologists, and genetic counselors, to optimize patient outcomes and quality of life.

In conclusion, the case exemplifies the intricate interplay between clinical presentation, diagnostic evaluation, and therapeutic management in unraveling the complexities of rare metabolic disorders such as carbonic anhydrase deficiency. Through meticulous assessment and multidisciplinary collaboration, clinicians can navigate the diagnostic odyssey and formulate tailored treatment strategies to mitigate long-term complications and improve patient prognosis. Continued research and advancements in the field are imperative to enhance our understanding and management of these intriguing disorders.

DISCUSSION

Carbonic anhydrase deficiency is a rare autosomal recessive disorder caused by mutations in the carbonic anhydrase II (CAII) gene (CA2) [15]. This enzyme plays a crucial role in catalyzing the reversible hydration of carbon dioxide to bicarbonate and protons in various tissues, including the kidneys, lungs, and red blood cells [2,16]. Deficient activity of carbonic anhydrase II leads to impaired bicarbonate reabsorption

in the proximal renal tubules, resulting in renal tubular acidosis (RTA), a condition characterized by metabolic acidosis due to impaired urinary acid excretion despite normal glomerular filtration rate (GFR) [17].

RTA type 3, also known as proximal RTA or carbonic anhydrase deficiency syndrome, represents a subtype of RTA characterized by defective bicarbonate reabsorption in the proximal tubules of the kidney [3]. This defect results in urinary wasting of bicarbonate, leading to metabolic acidosis with normal anion gap. In addition to acidosis, patients with RTA type 3 may exhibit electrolyte abnormalities, including hypokalemia, hypophosphatemia, and hypercalciuria [1,3]. The clinical presentation of RTA type 3 is variable and may include failure to thrive, polyuria, nephrocalcinosis, rickets, and developmental delay.

The case presented herein describes a 6-year-old male patient with a known diagnosis of RTA type 3 secondary to carbonic anhydrase deficiency. The patient presented with a history of tooth extraction and subsequent bleeding, prompting medical evaluation. Laboratory investigations revealed metabolic acidosis, electrolyte imbalances, and urinary abnormalities consistent with RTA type 3. Notably, the patient's brother had been previously diagnosed with the same condition at an early age, suggesting a familial predisposition to CA deficiency and RTA type 3.

Comparison of the presented case with existing literature highlights several key aspects of RTA type 3 and carbonic anhydrase deficiency syndrome. Firstly, the clinical presentation of metabolic acidosis, electrolyte disturbances, and urinary abnormalities aligns with the classical features of RTA type 3 reported in previous studies [17,18]. Additionally, the familial occurrence of CA deficiency underscores the genetic basis of the disorder, emphasizing the importance of genetic counseling and screening in affected families [18].

The patient's clinical presentation, laboratory findings, genetic testing, and imaging studies were pivotal in establishing the diagnosis and guiding management. Notably, the patient's medical history, familial occurrence of RTA, and clinical manifestations provided valuable insights into the underlying pathophysiology of the disease [19,20].

The presented case underscores the importance of early recognition and diagnosis of rare metabolic disorders such as carbonic anhydrase deficiency [2]. Despite its rarity, prompt identification and appropriate management are essential to prevent long-term complications and optimize patient outcomes. The utilization of a multidisciplinary approach involving pediatricians, nephrologists, geneticists, and other specialists is crucial for comprehensive evaluation and tailored management strategies [21,22].

Comparing our case with existing literature, several similarities and differences emerge. Consistent with previous reports, our patient exhibited typical features of carbonic anhydrase deficiency, including metabolic acidosis, electrolyte abnormalities, and a family history of renal tubular acidosis. Laboratory investigations revealed hypokalemia, hyponatremia, and metabolic acidosis, corroborating previous studies highlighting the characteristic biochemical profile of the condition [17,19]. Additionally, genetic testing confirmed mutations in the CA2 gene, consistent with the underlying pathophysiology of carbonic anhydrase deficiency [18].

However, certain aspects of our case deviate from the classical presentation described in literature. For instance, the patient's age at diagnosis and the severity of symptoms may vary, reflecting the heterogeneous nature of the disease. Moreover, the presence of associated complications, such as osteopetrosis and cerebral calcifications, further complicates the clinical picture, necessitating a comprehensive evaluation and tailored management approach [21-23].

The management of RTA type 3 in the presented case involved a multidisciplinary approach, including fluid rehydration, alkali supplementation, and monitoring of electrolyte balance [19]. These interventions aim to correct metabolic acidosis, prevent electrolyte imbalances, and optimize growth and development. Importantly, long-term management may require ongoing monitoring of renal function, electrolyte status, and bone health to mitigate complications such as nephrocalcinosis and rickets [17,20].

The presentation and reporting of this case contribute to the growing body of literature on RTA type 3 and carbonic anhydrase deficiency syndrome. Case reports play a crucial role in elucidating rare or atypical manifestations of diseases, providing insights into pathophysiology, diagnosis, and management [3,20]. By sharing clinical experiences and observations, case reports facilitate knowledge dissemination, promote early recognition of rare conditions, and inform clinical practice.

Moreover, the documentation of familial cases, such as the one presented here, underscores the genetic basis of RTA type 3 and highlights the importance of genetic counseling and testing in affected families. Recognizing familial predisposition allows for early identification of at-risk individuals and implementation of preventive measures to mitigate disease burden and improve outcomes [17,20,22].

CONCLUSION

In conclusion, the presented case underscores the clinical manifestations, diagnostic challenges, and management strategies associated with RTA type 3

secondary to carbonic anhydrase deficiency. By elucidating the clinical course and outcomes of this rare disorder, the case contributes to the existing literature and enhances our understanding of RTA type 3 pathophysiology. Furthermore, the familial occurrence of CA deficiency emphasizes the genetic basis of the disorder and underscores the importance of genetic counseling and screening in affected families. Moving forward, continued documentation and dissemination of clinical experiences through case reports are essential for advancing knowledge, improving diagnostic accuracy, and optimizing management strategies for rare genetic disorders such as RTA type 3.

REFERENCES

1. Palmer BF, Kelepouris E, Clegg DJ. Renal tubular acidosis and management strategies: a narrative review. Advances in Therapy. 2021 Feb; 38:949-68.
2. Santos F, Ordóñez FA, Claramunt-Taberner D, Gil-Peña H. Clinical and laboratory approaches in the diagnosis of renal tubular acidosis. Pediatric nephrology. 2015 Dec; 30:2099-107.
3. Mohebbi N, Wagner CA. Pathophysiology, diagnosis and treatment of inherited distal renal tubular acidosis. Journal of nephrology. 2018 Aug;31(4):511-22.
4. Occhipinti R, Boron WF. Role of carbonic anhydrases and inhibitors in acid–base physiology: insights from mathematical modeling. International journal of molecular sciences. 2019 Aug 6;20(15):3841.
5. Deitmer JW, Theparambil SM, Ruminot I, Becker HM. The role of membrane acid/base transporters and carbonic anhydrases for cellular pH and metabolic processes. Frontiers in Neuroscience. 2015 Jan 5;8:430.
6. Caldwell HG, Carr JM, Minhas JS, Swenson ER, Ainslie PN. Acid–base balance and cerebrovascular regulation. The Journal of Physiology. 2021 Dec;599(24):5337-59.
7. Alexander RT, Bockenhauer D. Renal tubular acidosis. Pediatric kidney disease. 2023 Apr 7:1071-93.
8. Vallés PG, Batlle D. Hypokalemic distal renal tubular acidosis. Advances in chronic kidney disease. 2018 Jul 1;25(4):303-20.
9. Wagner CA, Silva PH, Bourgeois S. Molecular pathophysiology of acid-base disorders. InSeminars in nephrology 2019 Jul 1 (Vol. 39, No. 4, pp. 340-352). WB Saunders.
10. Yaxley J, Pirrone C. Review of the diagnostic evaluation of renal tubular acidosis. Ochsner Journal. 2016 Dec 21;16(4):525-30.
11. Tinawi M. Pathophysiology, Evaluation and Management of Metabolic Acidosis. Archives of Clinical and Biomedical Research. 2021;5(1):85-109.
12. Sharma S, Gupta A, Saxena S. Comprehensive clinical approach to renal tubular acidosis. Clinical and experimental nephrology. 2015 Aug; 19:556-61.
13. Yaxley J, Pirrone C. Review of the diagnostic evaluation of renal tubular acidosis. Ochsner Journal. 2016 Dec 21;16(4):525-30.
14. Soares SB, de Menezes Silva LA, de Carvalho Mrad FC, Simões e Silva AC. Distal renal tubular acidosis: genetic causes and management. World Journal of Pediatrics. 2019 Oct; 15:422-31.
15. Alsharidi A, Al-Hamed M, Alsuwaida A. Carbonic anhydrase II deficiency: report of a novel mutation. CEN case reports. 2016 May; 5:108-12.
16. Alsharidi A, Al-Hamed M, Alsuwaida A. Carbonic anhydrase II deficiency: report of a novel mutation. CEN case reports. 2016 May; 5:108-12.
17. Vasquez-Rios G, Westrich DJ, Philip I, Edwards JC, Shieh S. Distal renal tubular acidosis and severe hypokalemia: a case report and review of the literature. Journal of Medical Case Reports. 2019 Dec; 13:1-7.
18. Alsharidi A, Al-Hamed M, Alsuwaida A. Carbonic anhydrase II deficiency: report of a novel mutation. CEN case reports. 2016 May; 5:108-12.
19. Laway BA, Mubarik I. Renal tubular acidosis, osteopetrosis, and cerebral calcification: a rare syndrome caused by carbonic anhydrase II deficiency. Indian Journal of Nephrology. 2017 Jul 1;27(4):330-1.
20. Alayed Y, Alghamdi W, Alyousef R. Carbonic Anhydrase II Deficiency: Unusual Presentation of the Arabic Mutation. A Case Report. Global Pediatric Health. 2024 Feb; 11:2333794X241230873.
21. Naeem A, Kiblawi MA, Kar SS, Ahmed E, Mossad S, Goud BK. Familial renal tubular acidosis: Report of two cases from a single family. Ann Nigerian Med. 2015 Jan 1; 9:33-7.
22. Giglio S, Montini G, Trepiccione F, Gambaro G, Emma F. Distal renal tubular acidosis: a systematic approach from diagnosis to treatment. Journal of Nephrology. 2021 Dec 1:1-1.
23. Satapathy AK, Pandey S, Chaudhary MR, Bagga A, Kabra M, Uwe K, Gupta N. Report of another mutation proven case of carbonic anhydrase II deficiency. Journal of Pediatric Genetics. 2019 Jun;8(02):091-4.