STUDENTS' CORNER
CASE REPORT

Unforeseen severity in a case of neonatal cow milk protein allergy: A case report

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Abstract

Cow milk protein allergy (CMPA) is one of the most common childhood allergies that manifests with a range of digestive symptoms and skin reactions, which usually resolve with age. In this report, we present the case of a one-month-old male who presented with a rare and severe manifestation of neonatal CMPA. The neonate underwent numerous hospital admissions due to a presentation that closely mimicked symptoms of a metabolic disorder and sepsis. Our primary objective is to highlight the significance of systematically considering or excluding a CMPA diagnosis, irrespective of the severity of presentation. This proactive approach may potentially reduce future complications among the affected paediatric population, thereby preventing prolonged hospitalisation and the associated disease burden, as seen in this case.

Keywords: Cow milk protein allergy, Metabolic acidosis, Amino-acid based infant formula, Neonatal food allergy, CMPA.

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Introduction

Globally, neonates who are not breastfed are introduced to cow's milk-based formula as a primary source of nourishment. However, within the initial week of formula feeding, neonates are prone to develop symptoms indicative of cow milk protein allergy (CMPA). CMPA is a common immune-mediated response to specific proteins present in cow's milk. It is a prominent contributor to food allergy in children under the age of three years, in addition to being a prevailing cause of food induced anaphylaxis, affecting 4.5% of the paediatric population.[1] The prevalence of CMPA varies globally, particularly in developing countries where its occurrence ranges from 0.5% to 3% at age one year.[2] The usual clinical presentation includes an array of rapid and slow onset symptoms such as urticaria, cough, vomiting, and in severe cases, anaphylaxis. Over time, these may progress to chronic diarrhoea, haematochezia, and poor growth/failure to thrive.[3] The prevalence drastically reduces to less than 1% by the age of six.[4]

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Case Report

A one-month-old male presented to the emergency department of Dr. Ziauddin Hospital in Clifton, Karachi, on May 29, 2023, with recurrent vomiting and intermittent fever since the seventh day of life. He has had episodes of loose stools for the past 24 hours and multiple prior hospital admissions. He was delivered, at a hospital, via an emergency lower segment caesarean section at 37+4 weeks of gestation with a birth weight of 2.9kg. On the seventh day of life, he received the BCG (Bacille Calmette-Guérin) vaccination for tuberculosis, part of standard immunisation regimen in Pakistan. The next day he spiked a temperature coupled with episodes of vomiting and loose stools, marked drowsiness and dehydration, prompting swift transportation to the hospital. Initial lab tests were notable for marked metabolic acidosis with pH 7.06(normal 7.35 to 7.45), pCO_2 of 13.5mmHg (normal 35 to 45 mmHg), HCO_3 level of 3.7mmol/L (normal 21 to 28 mmol/L), and base excess of -24.6mmol/L (normal is -2 to +3mmol/L). CBC showed Hb of 11.4g/dL (normal 10.7 to 17 g/dL) and WBC count of 19200/mm^3 (normal 9000 to 30,000mm^3) while C-Reactive Protein (CRP) level was elevated to 50.96 mg/dl (normal 2 to 5 mg/L). He was treated for neonatal sepsis with IV antibiotics during a four to five-day hospital admission. His weight regressed to 2.2kg, amounting to a 24% decrease from the birth weight and he was, therefore, transferred to a tertiary care facility. The formula was changed from milk-based infant formula to lactose-free infant formula and treatment with IV antibiotics continued. His weight returned to 2.8kg along with a noteworthy reduction in CRP levels to 1mg/dl at the end of his nine-day hospital stay. He was discharged with a suspected diagnosis of Hirschsprung's disease, which had been considered by doctors during his previous admission at Valley hospital in Abbottabad, based on their clinical examination.

Figure-1: Symmetrical vesiculobullous, scaly rash on the upper and lower extremities along with abdominal distention.

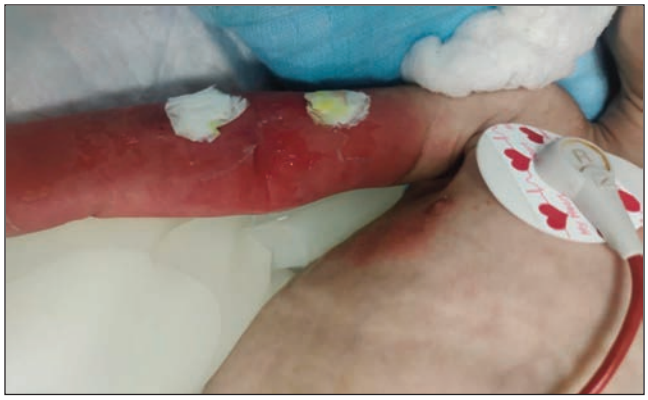

Figure-2: Erythematous, scaly rash on the arm.

A week later, the patient's vomiting and diarrhoea reappeared, and he was brought to the ER at Dr. Ziauddin Hospital and admitted to the neonatal ICU. He was managed with intravenous hydration, antibiotics, and oxygen supplementation. Laboratory tests showed raised CRP levels of 47.9mg/L and increased ammonia levels of 241.7 umol/L (normal 10 to 47umol/L). Arterial blood gas report showed pH 7.32, pCO_2 of 22.9mmHg, HCO3 level of 11.7mmol/L, and base excess of -12.1mmol/L, which prompted suspicion of inborn error of metabolism. A newborn metabolic and genetic screen and tests for urine organic acids and plasma amino acids were ordered, all of which were unremarkable. A gastroenterologist was consulted and the infant's nutrition was modified to a protein restricted diet. Treatment with sodium benzoate decreased ammonia levels to 33.4 umol/L. He developed a symmetrical vesiculobullous, scaly rash on the upper and lower extremities, as well as around the perianal area, which was managed with topical ointments (Figure 1 and Figure 2). After a two-week admission, the patient's clinical condition improved, he tolerated oral feeding well and was discharged on 50:50 combination feed with lactose-free and protein-free (Basic P) infant formula.

Despite following recommended out-patient treatment, the patient was readmitted to the NICU on June 20, 2023 with severe dehydration, reduced oral intake, abdominal distention, and failure to thrive. Investigations revealed a similar pattern with elevated leukocytes and CRP but with normal ammonia levels. A diagnosis of CMPA was suspected, prompting a formula change to Neocate, a hypoallergenic amino acid-based formula, followed by a dramatic improvement in the child's clinical condition and resolution of symptoms. Subsequent follow-ups in the next three months showed no return of previous symptoms with appropriate weight gain.

Discussion

Food allergies affect a significant proportion of adults and children alike. Some food allergies can often be confused with food intolerance, leading to misdiagnosis and mismanagement of the patient and subsequent degradation of their condition. CMPA presents in the first few months of life because cow milk proteins are the first proteins encountered by children who are fed either breast milk or any other form of milk. The presentation of CMPA is significantly milder in exclusively breastfed infants.[1]

Food allergens are identifiable components present in food or its ingredients. Upon subsequent exposure, they trigger either an IgE-mediated reaction, which constitutes 60% of cases, or a non-IgE-mediated response. In IgE-mediated reactions, patients exhibit symptoms within two hours of exposure, while in non-IgE-mediated reactions, symptoms may appear between three hours and one week after ingestion. Both types of reactions involve IgA antibody-mediated responses, specifically IgM and IgG-mediated type II and type III hypersensitivity reactions.[5]

The chemical constitution of cow's milk involves more than 20 different protein fractions. From these, casein proteins (α-s1-, α-s2-, ß- and k-casein) and whey proteins (α-lactalbumin and ß-lactoglobulin) are the cause of most allergies.[4] However, it is reported that individuals suffering from CMPA are allergic to both casein and whey proteins.

CMPA is known to be a self-limited and benign allergy, with reports that infants suffering from it can sustain a normal food diet by the end of the first year.[6] It develops after exposure to the allergen and does not manifest until weeks or even months after exposure. Hence, it is not instantly observed in neonates. It is important to note that this allergy does not only manifest due to oral post-birth exposure to milk but may also occur due to pre-birth exposure. It has been suggested that cow milk protein allergens may also pass through the placenta and amniotic fluid via vertical transmission to sensitise foetuses. The proliferative reactions of cord blood lymphocytes towards cow milk allergens such as α-lactalbumin, ß-lactoglobulin,

and α-casein were observed in full-term neonates. This discovery highlights the possibility of allergy manifestation in neonates prior to their first feed. However, this is often overlooked whilst diagnosing the disease, especially since there is no standardised testing and presentation is non-specific.[7] Diagnosis can only be ascertained by altering the feeding regimen and the infant's response to it. The allergens in cow milk are eliminated differently in formula fed and breastfed babies. Treatment using the method of elimination for breastfed infants can involve removal of all milk products from the mother's diet,[7] whereas formula fed infants can be given a substitute formula.[6] Substitute formulas such as extensively hydrolysed cow milk formula prove to be effective in over 90% children with CMPA and are considered first-line treatment. Hydrolysed rice formula, soy-based formulas and amino acid-based formulas are also beneficial alternatives; however, their cost, efficacy, and risks should be taken under consideration.[8]

Conclusion

CMPA is notably one of the most difficult allergies to diagnose, because it manifests in a variety of ways. Healthcare providers should be made aware of all possible presentations of this disease and an appropriate first-line response to prevent the use of invasive testing and unnecessary medication. Additionally, since the possibility of in-utero exposure to CMPA has been unearthed, asking about CMPA and other allergies should be included in routine history-taking questions asked to expectant mothers.

Informed Consent: Written informed consent to publish this case report was obtained from the patient's father.

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References

1. Miyuki Takata E, Gómez MS, Cohen Arazi L, Suárez PG, Villa Novac S. Cow's milk protein allergy, a rare case report in the neonatal period. Arch Argent Pediatr 2020;118:e554-7. doi: 10.5546/aap.2020.e554.
2. Flom JD, Sicherer SH. Epidemiology of Cow's Milk Allergy. Nutrients 2019;11:1051. doi: 10.3390/nu11051051
3. Caffarelli C, Baldi F, Bendandi B, Calzone L, Marani M, Pasquinelli P. Cow's milk protein allergy in children: a practical guide. Ital J Pediatr 2010;36:5. doi: 10.1186/1824-7288-36-5
4. Edwards CW, Younus MA. Cow Milk Allergy. Treasure Island, FL: StatPearls Publishing; 2024.
5. Baghlaf MA, Eid NM, Enani S, Kokandi S, Alhussaini B, Waked MS. Prevalence and Risk Factors for IgE and IgG Cow's Milk Protein Allergies in Saudi Arabia. Cureus 2023;15:e50812. doi: 10.7759/cureus.50812
6. Aktaş S, Ergenekon E, Ünal S, Türkyılmaz C, Hirfanoğlu İM, Atalay Y. Different presentations of cow`s milk protein allergy during neonatal period. Turk J Pediatr 2017;59:322-8. doi: 10.24953/turkjped.2017.03.015
7. Madala A, Lure AC, Cheng S, Cheng SX. Case Reports of Cow's Milk Protein Allergy Presenting as Delayed Passage of Meconium With Early Onset Infant Constipation. Front Pediatr 2022;10:858476. doi: 10.3389/fped.2022.858476
8. Kipfer S, Goldman RD. Formula choices in infants with cow's milk allergy. Can Fam Physician 2021;67:180-2. doi: 10.46747/cfp.6703180

Author Contribution:

AI: Concept, design, drafting, final approval and agreed to be accountable for all aspects of the work.
FML: Data acquisition, drafting, revision, final approval and agreed to be accountable for all aspects of the work.
SK: Supervised entire project, data interpretation, revision, final approval and agreed to be accountable for all aspects of the work.