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Case Report

Recurrent pulmonary infections as the first manifestation of cow milk intolerance: a rare case report from Syria

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Abstract

Cow milk protein intolerance is a common gastrointestinal condition in the first year of life. It is mainly manifested as gastrointestinal and dermatology symptoms. It rarely presents as a respiratory manifestation only without other accompanying symptoms. We report a case of a 5-month-old Syrian boy who presented with a history of recurrent acute bronchitis symptoms (cough, wheezing, tachypnea) for 3 months with no significant personal or family history. Hematological and radiographic investigations were normal. The diagnosis of cow milk intolerance was confirmed by clinical, endoscopically, and histological findings. The child was placed on amino acid hydrolysate milk with restricted cow products. The child improved significantly, and chest symptoms improved within a week of the treatment. Despite the rarity of cow milk intolerance in children with only respiratory symptoms, it should be kept in mind when the patient has recurrent pulmonary infections that are not improving on appropriate therapy.

INTRODUCTION

Cow's milk protein intolerance (CMPI) is the most common abnormal immunology response to cow milk protein that commonly occurs in infants less than 1 year [1]. Since 1970, CMPI has been well documented and estimated to occur between 8% and 17% of formula food, and 0.5% in breastfed infants [2]. The first exposure to cow milk develops an immunological response that takes weeks or months after birth. Cow milk allergens are not only transported orally but also through a mother's breast milk into the infant's circulation [3]. Some studies suggest that allergens can also pass through the placenta and amniotic fluid to sensitize fetuses and cause allergies [4]. The prevalence of CMPI in infants under the age of 12 months is approximately 3%. CMPI is often misdiagnosed as gastroesophageal reflux disease (GERD) or colic, which increases the risk of repeated exposure to antigens. Bear in mind that most infants outgrow CMPI by 12 months [5]. Multiple mechanisms of CMPI have been documented that include: (1) IgE immediate hypersensitivity reaction, histamine released through mast cell (2) non-mediated delayed hypersensitivity reaction, cytokine released from antigen-mediated T-cell stimulation or antigen-mediated IgA or IgG immune complex stimulation (3) mixed between immunological and non-immunological mechanism [3]. Symptoms of CMPI range from severe (Anaphylaxis, shock-like symptoms with severe metabolic acidosis which is very rare) to inconsolable crying which is very common in infants with CMPI. Gastrointestinal (dysphagia, diarrhea, vomiting, reflux, constipation, not feeding, or failure to thrive) and dermatology (urticarial, Atopic dermatitis, swelling of lips or eyelids) symptoms are the most common symptoms [2]. The less common symptoms are respiratory (wheezing, cough, recurrent pulmonary infections) [6].

CASE PRESENTATION

A 5-month-old child was admitted to the pediatric department in Tishreen University Hospital with a complaint of recurrent acute bronchitis symptoms (cough, wheezing, tachypnea) every two weeks for 3 months without any accompanying symptoms (digestive or skin). He was the first child of unrelated parents. He was a full-term infant delivered by spontaneous vaginal delivery. The birth weight was 3 kg. Also, there is no history of CMPI in the family or significant personnel. There was no recent travel or relocation of place. He was on formula since birth due to a lack of producing milk from his mother. His temperature of 37.1°C, Oxygen saturation (sO2) was 95%, blood pressure (BP) was

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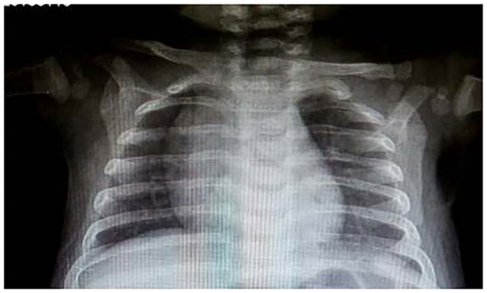

Figure 1. X-ray of the chest is normal.

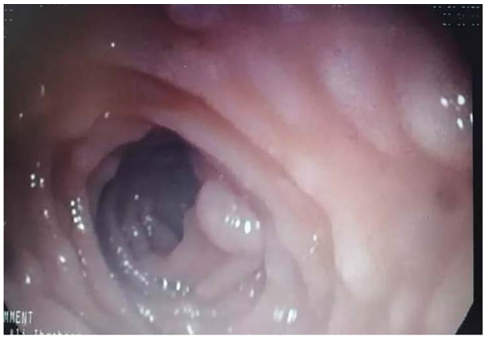

Figure 2. Diffuse nodules in the duodenum.

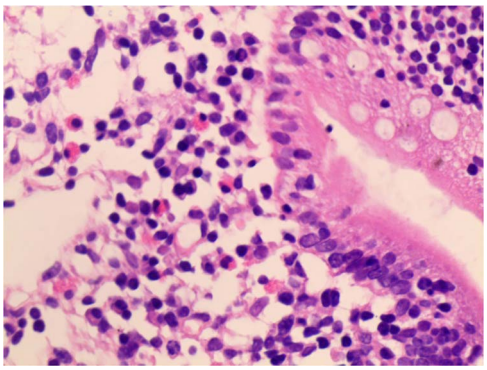

Figure 3. Histopathology biopsies showed mild focal gastritis with an increase in eosinophils infiltration.

80/60 mmHg, with a heart rate of 100 beats/min, a respiratory rate of 25 breaths/min. He had normal growth (weight 6 kg, length 65 cm, head circumference 43 cm) with a normal physical examination. Hematological [complete blood count (CBC), C- reactive protein (CRP), erythrocyte sedimentation rate (ESR)], liver function tests, kidney function tests, electrolytes, and immunoglobulins (IgE, IgD, IgG, IgA) and radiographic (Chest-X-Ray) (Fig. 1) investigations were performed within normal findings. His parents refused the bronchoscopy to evaluate the respiratory secretions of possible viral precipitants of bronchitis because they thought it was dangerous despite various attempts to convince them. Esophagogastroduodenoscopy (EGD) was performed to exclude GERD, which showed lower inflammation Grade (A), esophagus with diffuse nodules in the duodenum (Fig. 2). Histopathology biopsies showed mild focal gastritis with hyperplasia (villus/crypt ratio = 4:1) in the duodenal (Fig. 3). Intraepithelial lymphocytes (less than 20ILE/100) with an increase of eosinophils infiltration of more than 30/HPF in the duodenum (Fig. 4).

The child was placed on amino acid hydrolysate milk plus multivitamins with restricted cow's products. The child improved

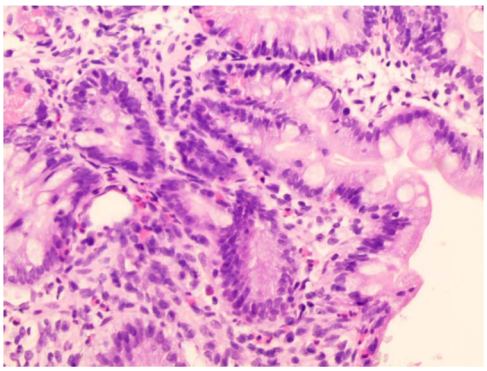

Figure 4. Hyperplasia (villus/crypt ratio = 4:1) in the duodenal, intraepithelial lymphocytes (less than 20ILE/100) with an increase of eosinophils infiltration of more than 30/HPF in the duodenum.

significantly, and chest symptoms improved within a week of the treatment. After about a week, the milk was returned as the symptoms returned. According to the clinical, endoscopically, and histological findings, CMPI was diagnosed. During 7 month follow-up, the patient was asymptomatic with normal weight gain. He is well until now and still on restricted cow's products and amino acid hydrolysate milk without any complaint.

DISCUSSION AND CONCLUSION

Recurrent respiratory infections (RRIs) are one of the most frequent reasons for pediatric visits and hospitalization [7]. According to (Gruppo di Studio), to diagnose RRI, at least one of the following criteria should be met. (1) six or more respiratory infections annually, (2) one or more respiratory infections per month involving the upper airways from September to April, (3) three or more respiratory infections annually involving the lower airways [8]. 25% of children under 1 year and 6% during the first 6 years have RRIs that can be a sign of an underlying medical condition ranging from congenital to primary immunodeficiency syndromes [6]. There are a lot of causes for RRIs; 50% are healthy, 30% are atopic, 10% suffer from another disorder, and 10% can be immunodeficient. [7]. In the literature review, there was no case report on the association between CMPI and RRIs. Most of the literature cases are in CMPI children with multiple manifestations (gastroenterology, respiratory, skin). In the current study, the child suffered only from RRIs (two episodes every 2 weeks for 3 months). All hematological and respiratory assessment was normal. EGD with a case of histological study confirmed a rare cause of RRIs that was CMPI. Up to 3 in every 10 babies with CMPA experience airway and breathing-related symptoms. CMPI is indicative of further allergies later in life; it developed asthma in 40% of cases, 43% had allergic rhinitis and 21% had atopic eczema 5 years later [9]. Bear in mind that due to the poor situation in Syria, further investigation to assess the immunological basis of intolerance in this patient was not possible. There are no laboratory or radiology tests that diagnose CMPI in children. But the differential diagnosis can be supported by All of the laboratory investigations (microcytic anemia, eosinophilia, mildly elevated serum IgE, decreased albumin, increased platelets, ESR, CRP, and fecal leukocytes are all evidence of inflammation). Until now, the diagnosis of CMPI is clinical as dilation of the cow milk protein elimination from the infant's and mother's diet [2]. The double-blind placebo-controlled food challenge (DBPCFC) is the definitive test for CMPI, which must be done in a provider's office or hospital over several

hours [10]. But it is not used very often because it takes a lot of time, is high cost, and risks the infant for further sensitizing and anaphylaxis. Clinically, the diagnosis is made when symptoms improve after a CMP-free diet and two or more challenging tests for the reappearance of the symptoms [10]. EGD may be normal or it appears as multiple superficial erosions, ulcerations, focal erythema, or lymphoid nodular hyperplasia. Focal infiltrates of eosinophils of more than 15–20 eosinophils/HPF in all mucosal layers, and crypt atrophy were demonstrated in the histological study, or it may be normal [9]. In the current study, our diagnosis was based on the EGD results, and then we suspected CMPI, so we eliminated cow's milk products from the diet of the child, which improved his condition. We did represent CMPI after a month of the diagnosis, which resulted in the reappearance of the symptoms, so we had to re-remove CMP from the diet. EGD showed lower inflammation Grade (A) esophagus with diffuse nodules in the duodenum. Histological study showed an increase of eosinophil infiltration of more than 30/HPF in the duodenum.

The diagnosis of CMPI is by avoiding all food containing cow's milk and given an extensively hydrolyzed formula (EHFs), soy protein formula (∼30% to50% significant risk of cross-reactivity with protein milk), goat's milk (∼30% are similar to cow's milk causing an allergic reaction), or amino acid-based formulas (AAFs) [10].

Despite the rarity of CMPI in children with respiratory symptoms only, it should be kept in mind when the patient has recurrent pulmonary infections that are not improving on appropriate therapy.

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CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

No funding was obtained for this study.

DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This case report did not require review by the Ethics Committee at Tishreen university hospital, Lattakia, Syria.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient's parents for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor.

AUTHORS CONTRIBUTIONS

All authors have read and approved the manuscript.

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