

Heiner's syndrome: Exploring beyond milk

Ritika Chhawchharia¹, Neeraj Gupta¹, Poojan Agarwal², Anil Sachdev¹

¹ Department of Pediatrics, Sir Ganga Ram Hospital, New Delhi, India

² Department of Pathology, Sir Ganga Ram Hospital, New Delhi, India

Abstract

Milk protein allergy, by non-IgE-mediated immune mechanisms, can present with nonspecific alveolar hemorrhage (Heiner's syndrome). We present the case of a 9-month-old infant with hemoptysis and diffuse pulmonary infiltrates who tested positive for milk, rice, and egg-white allergy on skin prick testing. The child responded to specific dietary elimination with reappearance of symptoms on accidental rice exposure. The present case highlights the need for exploring food allergies, other than milk, as a probable culprit in cases of unexplained hemoptysis.

Keywords: Heiner's syndrome, food allergy, milk allergy, unexplained hemoptysis

Introduction

Cow's milk protein allergy (CMPA) commonly presents with atopic dermatitis in infancy. Children with respiratory symptoms warrant nebulized bronchodilators and corticosteroids along with dietary elimination of milk products. Apart from reactive airways, CMPA may be responsible for nonspecific pulmonary manifestations such as diffuse alveolar hemorrhage (Heiner's syndrome) in certain cases. It is often managed by diagnostic and therapeutic milk elimination trial along with other anti-inflammatory agents. Diverse non-IgE-based mechanisms have been postulated for its pathophysiology, but nothing is conclusive. We were able to demonstrate an IgE-mediated food hypersensitivity in an infant with Heiner's syndrome.

Case Report

A 9-month-old, 6 kg, female infant was brought with the complaints of intermittent hemoptysis and posttussive vomiting, with mucus and blood clots for the past 1 month. She had already received blood transfusion 3 days back, in view of severe anemia. There was no history of fever, respiratory distress, diarrhea, trauma, skin rash, or bleeding from any other site. She was born at term gestation with 2.9 kg weight and without any peri/neonatal complications. Her development and immunization were age appropriate. She was exclusively breastfed till 6 months; thereafter milk-based cereal was started and chicken broth was initiated 2 weeks prior to presentation. Physical examination was unremarkable except significant pallor and soft hepatomegaly (3 cm below the costal margin with 9-cm total span). She had microcytic hypochromic anemia (hemoglobin – 8.9 g%), mild eosinophilia (Absolute Eosinophil Count – 631 cells/mm³), and normal coagulation profile, while urine analysis, gastric aspirate, and stool for occult blood were unyielding. There were diffuse infiltrates in chest radiograph, with a bilateral ground-glass appearance on contrast-enhanced computed tomography (CECT) scan. Flexible bronchoscopy revealed an anatomically normal airway without any active bleeding. Bronchoalveolar lavage was positive for hemosiderin-laden macrophages. Investigations for vasculitides (anti-neutrophil cytoplasm antibody, anti-nuclear antibodies, and anti-glomerular basement membrane antibodies) were negative. Two-dimensional transthoracic echocardiography showed partially anomalous pulmonary venous connection, which was not found to be correlated with hemoptysis on literature review. Transthoracic lung biopsy showed old and new hemorrhages with no signs of pulmonary capillaritis. Her total IgE levels were markedly raised (2303 IU/mL), and specific IgE for egg-white, milk, peanut, soybean, and wheat was high (3.61, 7.83, 5.19, 3.81, and 4.73 kU/L, respectively). Upper gastrointestinal endoscopy showed a small duodenal ulcer and biopsy suggested features of chronic duodenitis. Skin prick test (SPT) suggested hypersensitivity to cow's milk (11 mm), rice (6 mm), and egg-white protein (7 mm), with valid histamine (3 mm) and saline (0 mm) controls. With the above evidence, a diagnosis of Heiner's syndrome was considered. Strict dietary restriction of dairy products, rice, and eggs and maternal restriction of dairy products along with oral prednisolone at 2 mg/kg/day for 3 months led to complete cessation of symptoms [Figure 1]. She had an episode of hemoptysis, after accidental ingestion of rice, for which compliance was reassured. Steroids were gradually tapered over the next 3 months. At 1-year follow-up, she had adequate weight gain without any further episodes of hemoptysis. We plan to repeat a SPT and oral food challenge (OFC) on follow-up to attempt reintroduction.

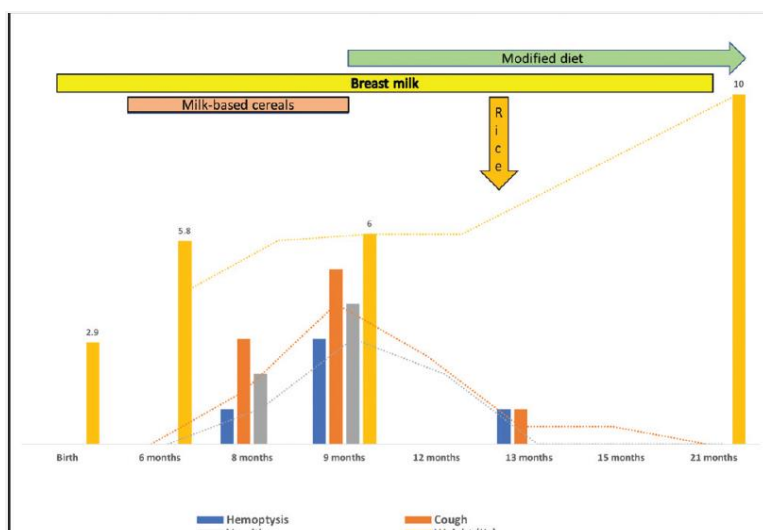


Figure 1: Timeline of clinical features and dietary interventions

[Click here to view](#)

Discussion



Diffuse alveolar hemorrhage or pulmonary hemosiderosis is a chronic disease in children with varied etiologies. While the common immune-mediated cause is vasculitis with pulmonary capillaritis being the salient feature on biopsy, CMPA is another important cause which is largely misdiagnosed and underreported. Pulmonary infiltrates may be identified in 5% of infants with CMPA.^[1]

Heiner in 1962 described seven infants with precipitin antibodies to cow's milk antigens with undefined chronic lung infiltrates, pulmonary hemorrhage, and failure to thrive. Elimination of cow's milk from diet led to symptom resolution.^[2] The exact pathophysiology of this disease is not yet established, though various non-IgE-mediated mechanisms have been postulated.^[3] In 1978, Lee *et al.* demonstrated Type III hypersensitivity and immune complex deposition in two infants.^[4]

Heiner's syndrome is primarily a clinical diagnosis, usually diagnosed in infancy with symptoms of cough, wheeze, hemoptysis, and diffuse or patchy lung infiltrates on chest X-ray or changes of interstitial lung diseases on CECT. Some infants may show raised cow's milk-specific IgG precipitin antibodies. An IgE-based pathogenesis had never been explored in the past. However, the commonality between all cases is complete resolution with elimination of cow's milk from diet.

Moissidis *et al.* reported a case series of eight infants with Heiner's syndrome. They found that all infants who presented within 9 months of exposure to cow's milk, had respiratory symptoms and lung infiltrates and resolution of symptoms with milk avoidance. OFC could be done in only two cases.^[4]

While there is no consensus on the treatment of infantile pulmonary hemosiderosis, oral prednisolone, 2 mg/kg/day, has been suggested for initial 2 weeks followed by tapering over 4–6 weeks. In the case of a recurrence, prednisone may be repeated for another 2 weeks.^[5] Avoidance of milk remains the mainstay of management for Heiner's syndrome.^[6] There is no protocol for reintroduction of milk in diet, however an OFC can be tried after few years of elimination. Heated or baked milk may be tolerated by some children.^[7] Children with IgE-mediated CMPA are more likely to outgrow and can tolerate cow's milk within few years.^{[8],[9]}

In our patient, IgE-mediated cow's milk, rice, and egg allergy was confirmed with an SPT and avoidance led to clinical improvement. One episode of ingestion of rice also led to hemoptysis; this may suggest that IgE-mediated food allergies to other food items, apart from milk, may also cause pulmonary hemosiderosis.

With limited availability of literature about this easily treatable clinical entity, it is necessary that we should suspect and diagnose Heiner's syndrome in children with unexplained hemoptysis or pulmonary infiltrates and avoid chronic consequences. The causative factors should not be limited to milk and dairy products only. An attempt to demonstrate IgE-mediated mechanism may reassure both parents and the clinician about the diagnosis and possible remission.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Lee SK, Kniker WT, Cook CD, Heiner DC. Cow's milk-induced pulmonary disease in children. *Adv Pediatr* 1978;25:39-57. [↑](#)
2. Heiner DC, Sears JW, Kniker WT. Multiple precipitins to cow's milk in chronic respiratory disease. A syndrome including poor growth, gastrointestinal symptoms, evidence of allergy, iron deficiency anemia, and pulmonary hemosiderosis. *Am J Dis Child* 1962;103:634-54. [↑](#)
3. Sicherer SH, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *J Allergy Clin Immunol* 2018;141:41-58. [↑](#)
4. Moissidis I, Chaidaroon D, Vichyanond P, Bahna SL. Milk-induced pulmonary disease in infants (Heiner syndrome). *Pediatr Allergy Immunol* 2005;16:545-52. [↑](#)
5. Saeed MM, Woo MS, MacLaughlin EF, Margetis MF, Keens TG. Prognosis in pediatric idiopathic pulmonary hemosiderosis. *Chest* 1999;116:721-5. [↑](#)
6. Archer JM. Idiopathic pulmonary hemosiderosis treated with a milk-free diet. *Proc R Soc Med* 1971;64:1217-8. [↑](#)
7. Holland NH, Hong R, Davis NC, West CD. Significance of precipitating antibodies to milk proteins in the serum of infants and children. *J Pediatr* 1962;61:181-95. [↑](#)
8. Lee EJ, Heiner DC. Allergy to cow milk-1985. *Pediatr Rev* 1986;7:195-203. [↑](#)
9. Williams S, Craver RD. Cow's milk-induced pulmonary hemosiderosis. *J La State Med Soc* 1989;141:19-22. [↑](#)