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Heiner's Syndrome - A Case Report from Eastern India

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Abstract: ***This is a case report of a female child admitted with complaints of severe pallor along with generalized weakness and lethargy associated with few episodes of hemoptysis. There were no significant clinical findings, either on general survey or systemic examination other than severe to moderate degree pallor, She was thoroughly investigated stepwise for proper diagnosis. Elaborate investigations included complete hemogram along with serum ferritin, TIBC, RDW, which were consistent with iron deficiency anemia, Urine RE/ME, Stool RE/ME, LFT, Blood coagulation profile, USG abdomen, Echocardiography and skeletal Xray in the form of x - ray hand were wnl. Chest imaging were consistent with the findings of pulmonary hemorrhage. Sputum examination showed Pearls stain +ve. On further history, thorough clinical examination and elaborate laboratory investigations patient was diagnosed to be a case of Heiner's syndrome.***

Keywords: Heiner syndrome, cow's milk protein, diffuse alveolar hemorrhage, anaemia, allergy

1. Introduction

A 3yr 1month old female child, born out of non consaguinous marriage, presented with the complaints of Progressive pallor associated with easy fatigability and generalised body weakness for the duration of 6 months. She required repeated blood transfusion (5 times) in the last 6 months and was started on oral iron and folic acid supplements. During that period the child was investigated inadequately due to poor compliance. Finally we were able to admit the patient, take detailed history, do proper examination and investigate methodically. There was history of repeated hospital admissions in the past for the similar complaints, however over the last 6 months it has progressed severely. There was no h/o of recurrent fever, gross weight loss, any significant blood loss in the form of epistaxis, hematuria / hematemesis /malena except for 1 - 2 episodes of mild hemoptysis but without any history of chest trauma and significant respiratory distress. No h/o pain abdomen, vomiting, diarrhea or any GI manifestations. The child was Exclusively Breast - fed only for 15 days, thereafter cow's milk is given along with the breast milk till 6 months of age and is continued till date along with home made diet which is started after 6 months. At present her calorie intake is 1080 - 1230 calories which is slightly defecient of protein. Uneventful birth history. Development in par with normal children of the same age group. Patient was immunized as per age. Weight as 11 kg and height – 90.5 cms On examination, heart rate - 98/min, respiratory rate - 26/min. There were no significant clinical findings, either on general survey or systemic examination other than severe to moderate degree pallor.

Elaborate investigations included Hemoglobin - 4.6gm%, TLC - 8700, Platelet - adequate, DLC - P58, L30, E07, M03, RBC - 1.8 million per mm^3, Microcytic hypochromic, anisocytosis, reticulocytosis, Reticulocyte count – 6%, MCV - 73fl, PCV - 21, MCH - 24.2, MCHC - 30, Serum iron - 5 micromol/dl, Serum ferritin - 5mcg/l, TIBC - 500mcg /dl, RDW: - 15.5%, HbF - 0.6% HB Electrophoresis: Normal pattern, BT: 3.5 mins; CT: 5.8 mins., PT: 11 sec; aPTT: 32sec, Urine RE\ME, Stool RE\ME are found to be normal. Liver and renal function tests are also found to be with in normal limits. Ultrasound abdomen, Chest xray and electrocardiogram showed no significant findings. Mantoux test was Negative. Bone marrow aspiration revealed reactive bone marrow with normoblastic erythroid hyperplasia. Gastric lavage was done and sent for gram and acid fast bacilli staining which was also found to be negative. Finally, Sputum microscopy was done and it showed positive pearls staining and more than 20% hemosiderin laden macrophages. CT Scan chest also revealed "Ground glass appearance", indicating that there is a Diffuse Alveolar Hemorrhage.

Further investigations showed negative work up for antinuclear antibody (ANA) profile, antineutrophil cytoplasmic antibodies (ANCA), anti - citrullinated peptides (anti - CCP), antiglomerular basement membrane (antiGBM), anti phospholipid antibody, rheumatoid factor, antigliadin and anti tissue transglutaminase. But, serum specific IgE to Caesin turned out to be positive establishing an association with cow's milk protein allergy. Thus with the help of detailed history, thorough clinical examination and elaborate laboratory investigations, patient was diagnosed to be a case of Heiner syndrome. In this patient chest xray was found to be normal because in some cases only during the acute episodes of alveolar hemorrhage chest infiltrates can be seen and in between episodes it can be normal. The child had been treated with corticosteroids (prednisolone) and cow's milk had been withdrawn from the diet. Prednisolone helped to prevent further hemorrhagic episodes in the alveoli and helps in resolving the already existing alveolar hemorrhage. The child was followed up every 3 months with report of hemoglobin and RBC indices.

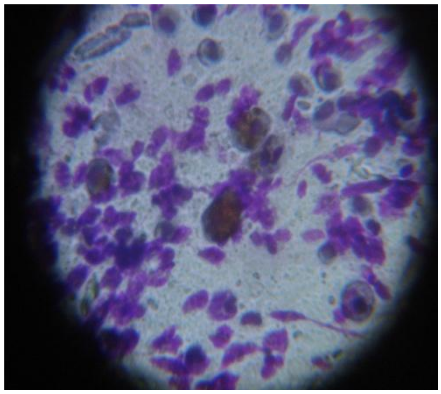

Figure 1: Sputum microscopy showing Positive pearl's staining

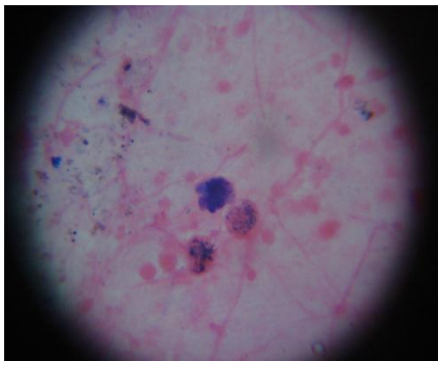

Figure 2: sputum microscopy showing hemosiderin laden macrophages

2. Discussion

HS is a rare hypersensitivity pulmonary disease[2] and the precise mechanism responsible for this syndrome is still poorly understood. However, it is assumed to occur as a result of type 3 hypersensitivity reaction/immune complex depositions. A cell mediated reaction has also been suggested to contribute to the development of the disease[8]. The disease came to the fore when Heiner and his colleagues reported in 1962, the presence of circulating antibodies to cow milk antigens in infants who had presented with cough, infiltrates on chest radiograph, poor weight gain, gastrointestinal symptoms and anaemia[3]. The symptoms of the disease usually commence before the age of one and may occur up to the fifth year of life[4]. Furthermore, Moissidis et al[2] in their case series also reported a range of 1–9 months as the period of onset of symptoms following introduction of cow's milk. An estimated 10% of children with the disease manifest with the severe form of the disease which could culminate in pulmonary haemosiderosis. [4] HS is basically a clinical diagnosis and features of this disorder include recurrent upper or lower respiratory tract symptoms such as cough, dyspnoea, wheeze or rhinitis; gastrointestinal symptoms such as vomiting or diarrhoea; failure to thrive, fever, patchy infiltrates on chest radiograph and iron deficiency anaemia[2]. Hepatomegaly, splenomegaly and peripheral lymphadenopathy may be present in rare occasions[5]. Our highlighted case had virtually all the symptoms above except the wheeze and his gastrointestinal symptom was constipation. Iron - laden macrophages on bronchial or gastric aspirates may be detected in some cases as well as the presence of precipitating IgG antibodies to cow's milk[2]. Strongly positive levels of serum precipitating IgG antibodies to nine cow's milk protein fractions was reported by Sigua et al[1] as well as slightly elevated IgM and negative serum specific IgE to cow's milk. However, serum specific IgE antibodies may also be found in some children[3]. Elevated levels of anti - nuclear antibodies (ANA) has also been reported in a case report[1]. The diagnosis of HS is strongly supported by the resolution of the aforementioned clinical features following strict avoidance of cow milk ingestion[1] which was demonstrated by our patient. Many subjects tend to recover within 5–21 days of removal of cow milk from their diet and reoccurrence of symptoms has been reported with reintroduction[2, 5]. It is however believed that some children may be able to eventually tolerate cow milk within a few years and this can be tested by reintroducing denatured or heated cow milk first whilst strongly watching out for the symptoms[9]. The complications from the disease contribute significantly to morbidity and mortality and occur in settings of delayed diagnosis and treatment. These include alveolar hypoventilation, massive acute pulmonary haemosiderosis, pulmonary hypertension and cor pulmonale[5, 10]. Crescentic glomerulonephritis was also reported as a complication by Yavuz et al[7] in Turkey; further demonstrating the multi - systemic involvement of the disease.

Conflict of Interest: None

Ethical Approval: The study approved by the Institutional Ethics Committee

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Author Profile

Dr S Naresh Kumar finished his MBBS from Tamilnadu DR MGR medical university and is currently doing his post graduate residency in pediatrics in West Bengal university of health sciences. He is actively involved in the research and academic activities.