Early Initiation of Steroid-sparing Drugs in Idiopathic Pulmonary Hemosiderosis

Idiopathic pulmonary hemosiderosis is conventionally treated with steroids, prolonged usage of which maybe deleterious and disease often recurs on tapering. We initiated hydroxychloroquine and azathioprine early in treatment along with steroids in seven children with idiopathic pulmonary hemosiderosis, and observed that early introduction of second line immunosuppressants helped in reducing disease flare and steroid toxicity without serious adverse effects.

Keywords: *Azathioprine, Corticosteroids, Immuno-suppression, Pulmonary hemosiderosis.*

Idiopathic pulmonary hemosiderosis (IPH), a rare and life-threatening condition in children [1], is characterized by a triad of hemoptysis, alveolar infiltrates on chest radiograph and varying degrees of iron deficiency anemia. We describe the clinical presentation and follow-up of seven children with IPH initiated with second-line immunosuppressives at induction.

The retrospective review of case-records involved seven patients (4 boys) with median age of 26 months, diagnosed between January 2011 to September 2014 at Institute of Child Health, Kolkata. The presentations were variable with symptoms like pallor (n=3), poor weight gain (n=4), cough and respiratory distress during acute bleeds (n=3), and unexplained iron deficiency anemia (n=7). Six children had bilateral patchy infiltrates on Chest *X*-ray. Diagnosis was confirmed by detection of hemosiderin-laden macrophages in bronchoalveolar lavage (BAL) in 4 children, and in gastric aspirate in 3 children; secondary causes of hemosiderosis were excluded. Anti-nuclear antibodies, Anti-nuclear cytoplasmic antibodies and Direct Coomb's were negative in all the patients.

All patients were prescribed a milk-free diet, and were treated with oral prednisolone (1–1.5 mg/kg/day) and hydroxychloroquine (HCQ). One child needed pulse methylprednisolone at presentation because of inadequate response to oral steroids. As the first three patients had recurrence of pulmonary bleed on tapering steroids, they were treated with azathioprine, which was subsequently routinely prescribed after 2 to 4 weeks of initiation of treatment when gradual tapering of steroid was started. One child unresponsive to azathioprine was induced by intravenous monthly cyclophosphamide pulses for 6 months followed by azathioprine. On follow-up (average duration 3 years, 10 months), there was no recurrence. After remission for more than two years, azathioprine was gradually tapered off with continuation of hydroxychloroquine.

One of the limitations of current observations is that the diagnosis of IPH was not confirmed by lung biopsy However, in the presence of hemosiderin-laden macrophages in BAL or in gastric aspirate/sputum along with chronic pulmonary symptoms, a diagnosis of IPH can be made [2,3]. Small sample size and lack of a control group were other major limitations.

There are no evidence-based recommendations regarding the treatment of IPH [1,3-7]. In this series of patients, we used prednisolone for induction and maintained remission with early addition of HCQ plus azathioprine/cyclophosphamide. None of them showed any recurrence or any major side effect of immunosuppression.

Prognosis of pulmonary hemosiderosis seems to have improved over time. While two decades ago the mean survival was 3 years from diagnosis, recent data show 5-year survival in 86% of cases [8]. The significant improvement is possibly due to the early initiation and long-term use of immunosuppressive therapy.

Contributors: PP: conceptualized the study. All authors were involved in patient management and data collection. All five authors have contributed to drafting of manuscript.
Funding: None; *Competing interest*: None stated.

PRIYANKAR PAL*, HRIDAY DE, PRABHAS PRASUN GIRI, NUPUR GANGULY AND ALOLIKA MANDAL
Department of Pediatrics,
Institute of Child Health,
Kolkata, West Bengal, India.
**mailme.priyankar@gmail.com*

REFERENCES

1. Taytard J, Nathan N, Blic J, Fayon M, Epaud R, Deschildre A, *et al*. New insights into pediatric idiopathic pulmonary hemosiderosis: The French RespiRare cohort. Orphanet J Rare Dis. 2013;8:161.
2. Nuesslein TG, Teig N, Rieger CH. Pulmonary haemosiderosis in infants and children. Pediatr Respir Rev. 2006;7:45-8.
3. Kabra SK, Bhargava S, Lodha R, Satyavani A, Walia M. Idiopathic pulmonary hemosiderosis: Clinical profile and

follow up of 26 children. Indian Pediatr. 2007;44:333-8.
4. Bulucea C, Sorin D. Idiopathic pulmonary hemosiderosis in children: A Romanian experience. Pediatrics. 2008;121:158-9.
5. Le Clainche L, Le Bourgeois M, Fauroux B, Forenza N, Dommergues JP, Desbois JC, *et al*. Long term outcome of idiopathic pulmonary hemosiderosis in children. Medicine. 2000;79:318-26.
6. Saeed MM, Woo MS, MacLaughlin EF, Margetis MF, Keens TG. Prognosis in pediatric idiopathic pulmonary hemosiderosis. Chest. 1999;116:721-5.
7. Ioachimescu OC, Sieber S, Kotch A. Idiopathic pulmonary haemosiderosis revisited. Eur Respir J. 2004;24:162-70.
8. Kamienska E, Urasinski T, Gawlikowska-Sroka A, Glura B, Pogorzelski B. Idiopathic pulmonary hemosiderosis in a 9-year-old girl. Eur J Med Res. 2009;14:112-5.

Influenza Virus Among Children with Acute Respiratory Infections in Chennai, India

Influenza is a major public health concern. Information on the prevalence of influenza virus in respiratory tract infections in Indian children is very sparse. In the present study, 267 nasal swabs were collected from children with acute respiratory infections in Chennai, India, out of which 22 (8.2%) and 6 (2.3%) samples were positive for influenza A and B virus respectively.

Keywords: *Epidemiology, Etiology, Pneumonia.*

In developing countries, 30% of all childhood deaths are attributed to acute respiratory infections (ARIs) [1]. Due to its ability to cause frequent epidemics and periodic pandemics, influenza virus has a major public health implications. We enrolled 267 children aged 45 days to 16 years visiting the outpatient department of various hospitals and presenting with symptoms of ARI such as cough, fever, sore throat, rhinorrhea, nasal congestion, headache, myalgia, wheezing and dyspnea between April 2016 and March 2018. Children with chronic respiratory infections and other co-morbidities were excluded from the study. The study was approved by the Institutional Human Ethics Committee. Nasal swabs were collected using sterile flocked nylon swabs, which were inserted 2-3 cm deep inside the nostril and rotated 2–3 times. They were transported in a viral transport medium (HiMedia, India) to the laboratory maintaining cold chain. The vials were briefly vortexed, and RNA was extracted from the swabs using the NucleoSpin RNA virus kit (Macherey Nagel, Germany) according to manufacturer's instructions. The extracted RNA was converted to cDNA using RevertAid first strand cDNA synthesis kit (Thermo Fisher Scientific, USA), and stored at –20 ºC.

cDNA was subjected to real time Reverse-transcriptase Polymerase chain reaction (RT-PCR) for the detection of influenza A and Victoria and Yamagata lineages of influenza B virus using hybridization probes according to WHO protocol [2]. Real time RT-PCR was carried out in StepOnePlus real time PCR system (Applied Biosystems, USA). Appropriate positive and negative controls were included in each run. Ct value of ≤40 cycles was considered to be positive. The association between influenza positivity and demographic/epidemiological data was determined using two-tailed chi square test.

The mean (SD) age of the patients was 45.9 (38.5) months. The most common symptoms observed among the patients with ARI were cough (83.1%), rhinorrhea (60.3%) and nasal congestion (57.7%). The influenza A virus was detected in 22 (8.2%) samples, and 6 (2.3%) samples were positive for influenza B virus, of which three samples belonged to Victoria lineage and 3 belonged to Yamagata lineage of influenza B virus. The majority of influenza A virus positive patients had fever as the major symptom (17, 77.2%) followed by cough (16, 72.7%). Seven patients with influenza A virus had myalgia. Among the patients positive for influenza B virus (Victoria lineage), fever was the most common symptom, while cough was the frequent symptom associated with influenza B virus Yamagata lineage positive patients. The mean (SD) age of patients positive for influenza A and B virus was 49.9 (35.4) months and 68.2 (37.4) months, respectively. Influenza A showed highest rates of detection in the months of January and August 2017 (***Fig.* 1**).

In the present study infection with influenza A virus was more common when compared with infection with influenza B virus. Previous studies from the region have shown similar results [3,4]. In an earlier study carried out in Chennai, 30 out of 240 (12.5%) children with ARI were positive for influenza viruses [5]. Fever and cough were the predominant symptoms among positive influenza A and B cases, similar to previous studies from India [4,6]. Studies on seasonal trends of respiratory viruses are very useful in predicting etiological agent during outbreaks. In our study, detection of influenza A virus peaked in the months of January and August. Studies from other parts of India reported detection of influenza A during autumn and winter seasons [7,8].