

Case Reports

Lane-Hamilton Syndrome: Rare Association of Idiopathic Pulmonary Hemosiderosis with Celiac Disease

Idiopathic pulmonary hemosiderosis (IPH) is manifest as a triad of pulmonary symptoms, alveolar opacities on chest radiographs, and iron deficiency anemia. The presence of hemosiderin in macrophages obtained in gastric or bronchoalveolar lavage is considered crucial in the diagnosis of pulmonary hemosiderosis. IPH in association with celiac disease (CD), known as Lane-Hamilton syndrome, could be due to the fact that both entities share a common pathogenic immune pathway. There are limited numbers of case reports of this syndrome in literature.

Case Report

A 14 years old non-smoker adolescent boy presented with complaints of cough associated with intermittent hemoptysis and history of progressive pallor for last 5 months. Cough was present off and on with mild specks of blood. No other significant history was present. Past and family history were unremarkable. On admission, he had severe pallor, tachycardia (pulse rate 140/min) and tachypnea (respiratory rate 42/min) with normal blood pressure and growth parameters. On auscultation, bilateral infrascapular crackles and hyperdynamic

precordium with a hemic murmur was present. There was no hepatosplenomegaly. Investigations revealed severe anemia (Hb of 2 gm/dl), ESR of 10 mm/1st hour; total leukocyte count of 10400/mm³ and platelet count of 3.36 lacs/mm³. He had been investigated for anemia and blood investigations demonstrated iron deficiency anemia (peripheral smear showed microcytic, hypochromic anemia, serum ferritin 5 ng/ml, serum iron 30 µg/dl and TIBC 393 µg/dl). Renal function tests, liver function tests, C-reactive protein, coagulation studies and urine analysis were within normal limits. Chest radiograph demonstrated bilateral lower zone alveolar type opacities (**Figure 1A**). A contrast-enhanced computed tomography scan of the chest revealed scattered ground-glass opacities predominantly in both lower lobe and fibrosis with bronchiectatic changes seen in bilateral upper lobes (**Figure 2A and 2B**). Work-up for pulmonary tuberculosis and HIV ELISA were negative. All laboratory tests for diffuse alveolar hemorrhage (DAH) were negative as mentioned in **Figure 3**. Cardiac evaluation was normal. Pulmonary function tests showed a restrictive pattern with FEV1 63%, FVC 68%, FEV1/FVC 95% and PEFR 78% of predicted. In sputum examination, the smear showed occasional squamous cells, few neutrophils and hemosiderin-laden macrophages (HLM) enmeshed in mucous, suggesting the possibility of intra-alveolar hemorrhage (**Figure 4**). The presence of bilateral ground-glass haziness and iron deficiency anemia along with HLM in sputum examination with an exclusion of other causes confirmed the diagnosis of IPH.

Though there were no gastrointestinal symptoms in our case, the possibility of CD was considered in view of severe iron deficiency anemia (degree of anemia was out of proportion to the chest imaging findings) and previously described association between IPH and CD. Positive serology (Anti-tissue transglutaminase (tTG) IgA titres >100 AU/ml, normal <10 AU/ml), along with the presence of scalloping in second part of duodenum on Esophagogastroduodenoscopy (EGD) and modified Marsh grade 3A histopathology finding on duodenal biopsy (**Figure 5**) were consistent with a diagnosis of CD. Based on this, a final diagnosis of Lane-Hamilton syndrome (CD with IPH) was made. Child was initially managed with blood transfusions and put on a gluten-

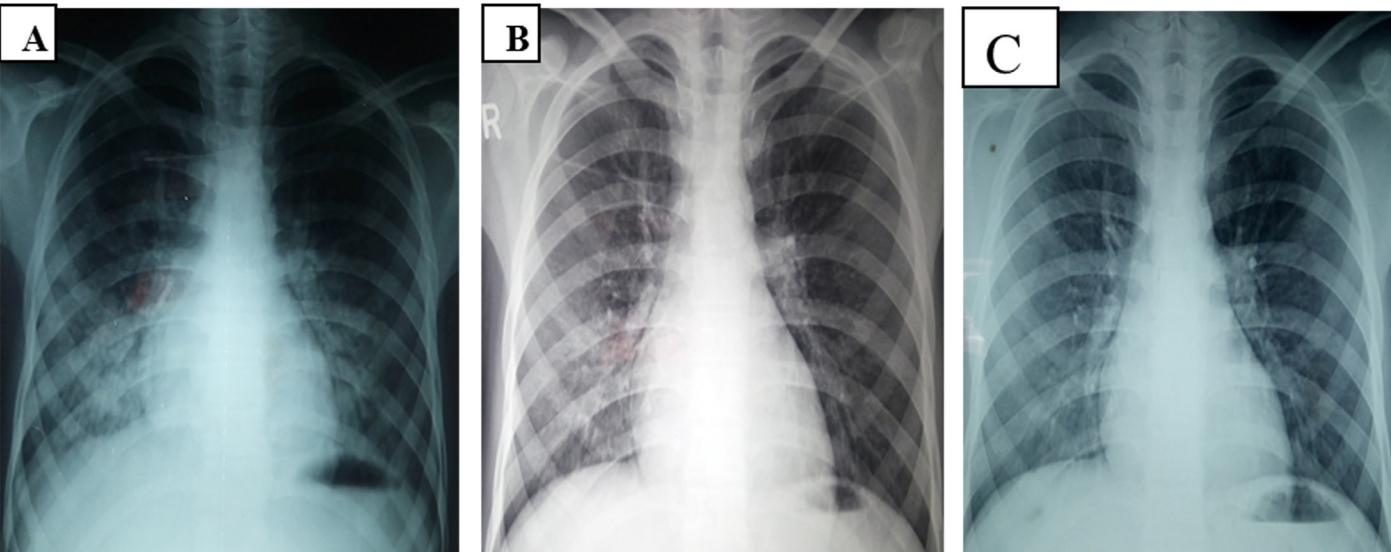


Figure 1: Chest X-ray at various stages (A): Bilateral lower zone alveolar opacities, more in right than left lung, (B): Improvement seen at 7 days after starting GFD, (C): Disappearance of previous findings at 2 months follow up after starting GFD.

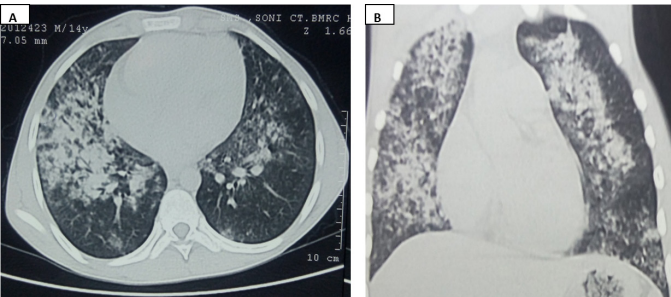


Figure 2: Computed Tomography of the Chest revealed scattered ground-glass opacities predominantly in both lower lobe (more on the right side than left side) and fibrosis with bronchiectatic changes seen in bilateral upper lobes (A: Axial view, B: Coronal view).

free diet (GFD). Pulmonary symptoms completely resolved after few days. Hemoglobin at 2 months follow up was normal with complete disappearance of previous radiological findings in chest X-Ray (**Figure 1B, 1C**). Long-term follow up was advised to check the compliance of GFD and recurrence of sign or symptoms.

Discussion

IPH is a rare disease of unknown etiology, predominantly affects children and adolescent and incidence varies from 0.24 to 1.23 patients per million children.¹ Cough,

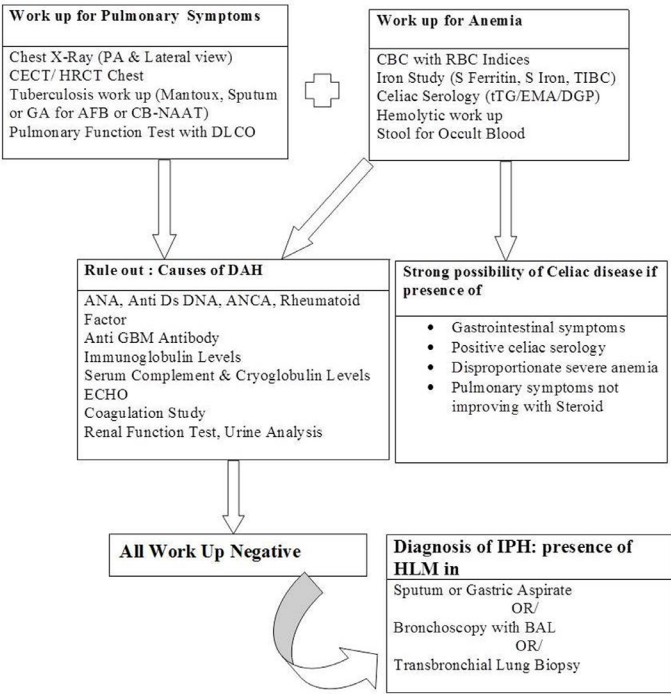


Figure 3: Schematic representation of the work-up for Diffuse Alveolar Hemorrhage (DAH), CBC: Complete blood count, GA: Gastric Aspirate, DLCO: Diffusion Lung Capacity for Carbon Monoxide, AFB: Acid Fast Bacilli, CB-NAAT: Cartridge Based Nucleic Acid Amplification Test, BAL: Bronchoalveolar Lavage.

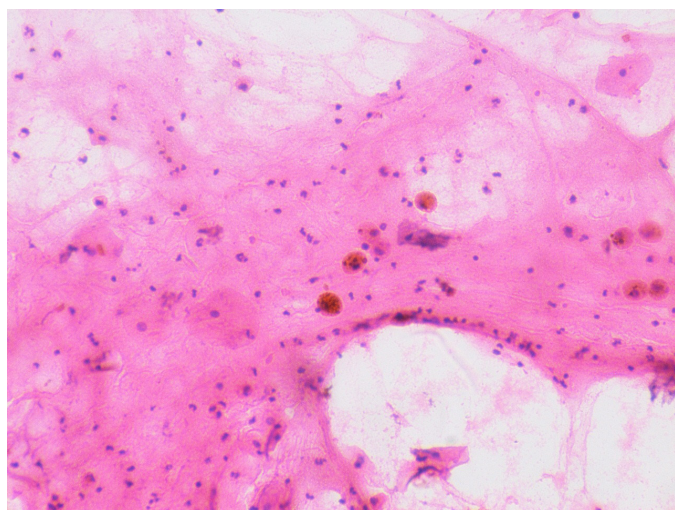


Figure 4: Smear of sputum showing occasional squamous cells, few neutrophils and hemosiderin-laden macrophages enmeshed in mucous [H and E, × 400].

anemia and failure to thrive with or without hemoptysis is the usual presentation in children. Diagnosis of IPH requires evidence of DAH and exclusion of other causes of DAH.² Diagnostic work-up for the evaluation of IPH/DAH is shown schematically in **Figure 3**. A diagnosis by lung biopsy is considered gold standard. But many authors have accepted the presence of HLM in sputum, gastric or broncho-alveolar lavage (BAL) fluid as diagnostic if typical clinical features are present and are not accompanied by evidence of extrapulmonary disease. In 1971, Lane and Hamilton described the association of IPH with CD in a young man for the first time.³ While immunological mechanisms are believed to be effective in the formation of IPH and CD, a pathogenic link between them cannot be precisely understood. Routine screening of CD is recommended in all cases of IPH, even in the absence of gastrointestinal symptoms by many authors.^{4,5}

In Lane-Hamilton syndrome, a gluten-free diet for CD, with or without steroids for IPH, is the mainstay of therapy. The clinical importance of this association is that a significant improvement can be obtained with gluten-free diet not only in intestinal but also in pulmonary symptoms. Use of gluten-free diet (GFD) results in partial or complete cessation of lung hemorrhage and reduced the need for blood transfusions and steroid therapy in Lane-Hamilton syndrome.^{4,5} In a report of 20 patients

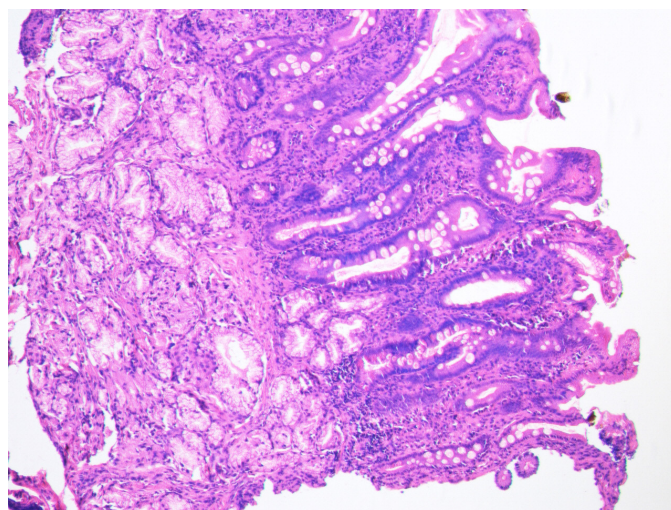


Figure 5: D2 biopsy showed greater than 30 intraepithelial Lymphocytes per every 100 enterocytes, Crypt hyperplasia and partial villous atrophy (H and E, x 40).

with IPH associated with CD, GFD alone had been prescribed for 16 of them and pulmonary symptoms were improved in 12 patients.⁴ In Lane-Hamilton syndrome, gastrointestinal symptoms are reported to occur in about 50% of cases only.³ Emphasising this, our patient had no prior history of diarrhea, steatorrhea, flatulence or weight loss. Pulmonary symptoms improved on a gluten-free diet alone within 7 days of admission with complete resolution of chest X-ray findings 2 months after starting GFD.

In conclusion, a high index of suspicion for celiac disease should be kept in patients with pulmonary hemosiderosis, especially with disproportionately severe anemia inspite of absence of gastrointestinal symptoms and vice-versa. Non-invasive investigations such as sputum examination for hemosiderin-laden macrophages can be considered diagnostic. This entity is important to recognize as treatment with a gluten-free diet alone can lead to remission of the pulmonary symptoms.

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Duodenal Intramural Gallstone Mimicking Malignancy

Gallstones have been known to migrate and get impacted in the proximal duodenum or pylorus producing gastric outlet obstruction (GOO). Leon Bouveret, in 1896, was first to report two cases of gastric outlet obstruction due to impacted gallstones.¹ Since then, about 300 such cases had been reported in the world literature.² While the presentation is usually non-specific, the diagnosis can be established by endoscopic and imaging studies in most of the cases.³ We report a case of gallstone impaction in the duodenal wall that posed a unique diagnostic challenge and therapeutic dilemma. The etiopathogenesis and clinical presentations were similar to that of classical

Bouveret syndrome but the submucosal location of stone produced deceptive endoscopic and imaging findings. The condition mimicked duodenal neoplasm and resulted in major surgical resection. To the best of our knowledge, this is the first report describing a case of intramural impaction of gallstone causing GOO.

Case Report

A 60-year old lady presented with complaints of recurrent mild upper abdominal pain for the last one year along with multiple episodes of postprandial nausea, non-bilious vomiting since last 2 months with anorexia and significant weight loss. There was neither history of fever, jaundice, gastro-intestinal bleed or dyspeptic symptoms nor any past abdominal surgery. On examination, she was dehydrated, undernourished, afebrile and anicteric. Per-abdominal examination revealed distended stomach with succussion splash and mild tenderness over right hypochondrium. Her laboratory reports including liver function tests were normal. A contrast-enhanced computed tomography (CECT) scan of abdomen showed a contracted, thick-walled gallbladder with a large stone impacted at its neck, compressing the common bile duct. Gallbladder was abutting the antro-pyloric region, though there was no evidence of cholecysto-duodenal fistula or pneumobilia. Stomach was distended and there was an irregular thickening in the proximal duodenal wall causing luminal narrowing (**Figure 1A, 1B**). An upper gastrointestinal endoscopy revealed distended stomach and a bulge at the junction of 1st and 2nd part of duodenum (D1-D2 junction) (**Figure 1C**). The scope couldn't be passed beyond the lesion. Multiple biopsies were taken from the site of bulge and sent for histopathology. The patient was explored with suspicion of duodenal malignancy. Operative findings revealed distended stomach with thick-walled gallbladder densely adhered to the duodenum. A large solitary stone was found impacted at the gallbladder neck. However, there was no evidence of any fistulous connection between gallbladder and duodenum. A hard mass of 3 X 3 cm size could be palpated in the duodenum, close to the head of pancreas. In view of strong suspicion for duodenal neoplasm, classical Whipple's pancreatoduodenectomy was