# A RARE CAUSE OF HEMOPTISYS: IDIOPATHIC PULMONARY HEMOSIDEROSYS (IPH)

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***Keywords:*** *idiopathic alveoli hemorrage, idiopathic pulmonary haemosiderosis*

***Abstract:*** *We present the case of a 19 years old male with a rare cause of haemoptysis: idiopathic alveoli hemorrage. Classic triade made the diagnosis possible: intermittent haemoptysis, secondary iron deficiency anemia, diffuse alveoli opacity. The thoracothomy with pulmonary biopsy substantiated the diagnosis. Negative immune balance sheet among other performed tests preclude other pathology. The course of the disease was favourable under oral corticotherapy (clinical, hematological and radiological improvement). Also the favourable evolution maintained after the end of the treatment, follow-up period was of 2 ½ years.*

***Cuvinte cheie:*** *hemosideroză pulmonară idiopatică, hemoragie pulmonară alveolară*

***Rezumat:*** *Prezentăm cazul unui tânar de 19 ani având o cauză rară de hemoptizie: hemoragia alveolară idiopatică. Diagnosticul a fost fundamentat pe triada clasică: hemoptizii intermitente, anemie feriprivă secundară, opacităţi alveolare difuze. Toracotomia cu biopsie pulmonară fundamentează diagnosticul. Bilanţul imunologic negativ precum şi alte teste efectuate exclud altă patologie. Pacientul a evoluat favorabil sub corticoterapie orală (ameliorare clinică, hematologică şi radiologică). De asemenea, evoluţia favorabilă s-a menţinut dupa încheierea tratamentului, perioada de urmărire a cazului fiind de 2 ½ ani.*

## INTRODUCTION

IPH (idiopathic pulmonary haemosiderosis) is a rare of unknown etiology condition which is characterized through increased pulmonary hemosiderosis due to chronic or recurrent hemorrhage (1). The incidence and prevalence is unknown, about 500 cases were described until nowadays (2). IPH is described more frequently among children and teenagers, very rare among old people (3). IPH is a potential severe and with a high mortality condition.

Clinically the condition is characterized by the classic triad: intermittent haemoptysis, secondary iron deficiency anemia, diffuse alveoli opacity. Secondary iron deficiency anemia can precede respiratory symptoms by months (4).

The histopathology exam cannot be spared and reveals iron overload macrophages due to increased fagocitation of haematids (this appearance is also met among other alveoli hemorrhage syndromes) without signs of vasculitis, granuloma or Ig deposits.

## CASE PRESENTATION

18 years old, B.I. without personal antecedents of cardiac conditions, arterial hypertension, reflux disease, no drug intake history (cocaine or alcohol) and without particular familiar antecedents, working in a farm, incidental 2-3 cigarettes smoker presents himself in our ward to complete the balance sheet for a repetitive small haemoptysis started a few months before and small efforts progressive dyspnoea. He was admitted two weeks ago into another ward due to a loss of consciousness; here was identified a clinical and radiological pulmonary alveoli syndrome associated with a microcitary anemia (Hb = 6 g/l) which was corrected through a blood transfusion. The unique loss of consciousness was due to anemia and was considered to be lipothymia. The patient was not under any previous treatment and he did not suffer any environmental exposure.

Physical findings: good general appearance, no fever, normal height and weight, BP 120/80 mmHg, HR 60 bpm, small conjunctive congestion, bilaterally laterocervical and submandibulary angle microadenopathy, productive cough with mucopurulent sputum and rare haemoptysis, rapid walking progressive dyspnoea, bilateral basal dullness to percussion, diffuse bilateral fine crackles, especially right base, a few isolated sibilant and sonorous rhonchus, without any cardiovascular and gastrointestinal findings; without obvious clinical neurogical findings.

At PA plain chest radiograph multiple alveoli opacities not well outlined, homogenous, especially at the right basis probably due to the presence of blood in the alveoli.

Biologically two weeks before initial presentation the patient had a 6 g/dl hemoglobin; in our department he had an anemia of 8.5 g/dl hemoglobin and a MCV=76.9 fl, Fe=6 µg/dl, normal leukocite formula, normal platelets, ESR=12/34, normal renal function, normal hepatic enzimes, normal bleeding and clotting tests. The urine examination was normal as well as Addis – Hamburger test. Bacteriological examination of specimens of sputum revealed Moraxella Catharalis. The direct RAAB and the cultures were as well normal.

Bronchoscopy: normal pharynx, larynx and vocal cords; trachea: adherent, viscos opalescence secretions, congestioned, edemationed mucosa. The bilateral bronchial arborisation is entirely permeable, a few sanguinolent sacretions which does not abate after aspiration, bronchial mucosa intense congestioned. Left bronchial arborisation has abundant secretions (contradictorily aspect with the one revealed by the radiology), without revealing the exact source of the

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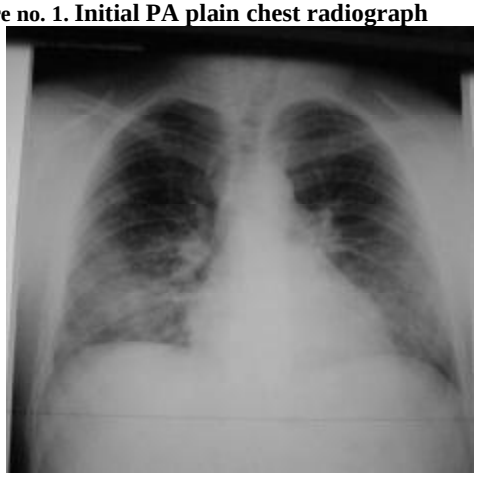
hemorrhage.

Bronchial aspiration: inflammatory infiltration, 95% PMN, 2% macrophages, 1% eosinofiles, fibrin and epithelial cells, some Gram + germs; the culture shows oropharinx contamination germs, no fungi developed.

**Figure no. 1. Initial PA plain chest radiograph**



Abdominal and Thoracic CT with and without contrast: a large number of miliar interstitial micro nodular images, bilateral medium and inferior lobes, no adenopathies and tumor masses. There are no hepatic or suprarenal changes. The examination was performed after two months apart from the moment of symptom appearance.

The spirometry was normal also the ABG. Cardiac ultrasound: interatrial communication near foramen ovale, without hemodynamic significance, normal valvules, normal right and left cardiac cavities, normal pulmonary artery without signs of pulmonary arterial hypertension.

Bone marrow biopsy: normal erythrocyte lineage, there are normo and microblasts, and also frequent macroblasts, Pappenheimer corpuscule. Granulocyte lineage: a few Pelger – Huet elements with partial or total degranulation. Megakaryocytic lineage is hyperplasitic. Haemosiderin Perls reaction negative, 20% sideroblasts, and 1% ring like sideroblasts, absent siderocytes.

Immune balance sheet: RF negative, normal IgG, IgA, IgM, $C_3$, $C_4$, the presence of cryoglobulins, negative ANA, ANCA, SMA, AMA. The patient wasn't investigated for caeliac disease, being completely asymptomatic. There was no evidence of hidden digestive hemorrhage or other sources of hemorrhages.

These results were interpreted initial as an infectious pneumopathy; it wasn't excluded a hypersensitivity pneumopathy such as farmer's lung disease which was treated with inhaled corticosteroids (beclometasone propionate 250 µg x 3/day), antibiotic (oxacillinum 500 mg x4/day, 10 days then ciprofloxacinum 250 mg x 2/day, 10 days) according to the antibiogram, theophyllinum 100 mg/day, acetylcysteinum, treatment which induceses a slight clinical improvement.

Due to the recurrence of the hemoptysis and the persistence of bilateral alveoli images after 3 months from the symptom inception one has decided to perform an exploratory right thoracotomy. During thoracotomy, one may observe on the rib side of RIL (right inferior lobe) and on the mediastinum side of RML (right medium lobe), pleural adherences. Pulmonary parenchyma has a increased consistence, slightly yellowish nuance and multiple, micronodular disseminated lesions among RIL and RML. It was performed the lisis of the adherences and pulmonary biopsy through atypical resection of RIL and RML. Postoperatory evolution is without complications.

Anatomopathology examination: pulmonary parenchyma fragments with hemorrhagic infiltrates and hemosiderin piled up macrophages; thickened septum through fibrosys, isolated aspects of leiomiomatosys; polimorfonuclear infiltrate. Some bronchi have a hemorrhagic and leucocyte lumen infiltrate; the blood vessels have a thickened wall due to wall media hypertrophy, fibrosys and images of intima mixoid degenerescence. The cappilaries of the pleura are slacked, filled with hematides and moderate lymphocyte infiltrate. RML has a fibros nodule with $Ca^{2+}$ deposits. Conclusion: pulmonary hemorrhage, interstitial pneumopathy possible association. One has tried to highlight the presence of antibasal membranae antibodies without succeeding (unappropiate sample fasten).

**Figure no 2. Pulmonary biopsy with hematide infiltrate.**

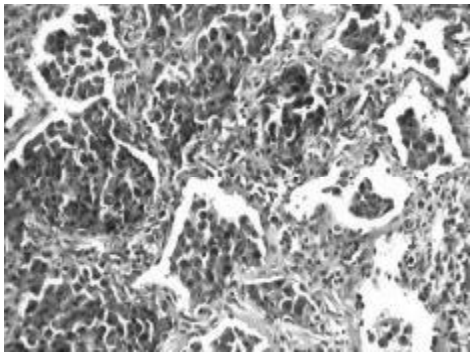
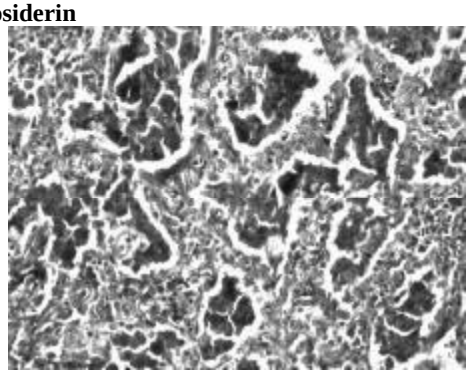


**Figure no. 3. Pulmonary biopsy staining for hemosiderin**



## DISCUSSION

Based upon clinical (hemoptisys, dyspnoea), laboratory (iron deficiency anemia), radiological (both CT and PA plain chest radiography: interstitial and alveoli infiltrate) and the absence of other organs involvement alongside of initial and follow up arguments, the diagnosis established was idiopathic pulmonary haemosiderosis.

It was initiated corticotherapy with prednisone 1mg/kg, for weeks followed ba reduction of the dosage with 5 mg/week, monthly follow-up checks. Treatment tolerance was good; the martial therapy continued paralelly. At the end of the corticotherpy radiological aspect shows a radical improvement, normal ABG, normal CBC, normal serum iron. One has decided to discontinue treatment and to keep the patient under the family practioner observation and follow-up checks as needed. 2 ½ years later the favorable evolution is maintained beyond any treatment, the patient presenting no symptom or a general function limitation.

IPH is a rare condition with an incidence raging between 0.24/1.000.000 children/year, by a Swedish study and 1,23/1.000.000 children/year by a japanesse study (11). 80% of the cases appear under 10 years old children, 20% among teenagers and adults most frequently under 30 years old (1, 11). First description of the disease was made by Virchow in 1864 as ″lung's brown induratio″, Ceelen reported in 1931 the first two cases. Waldernström made the first antemortem diagnosis of idiopathic pulmonary haemosiderosis in 1944 (10). Idiopathic pulmonary haemosiderosis is characterized by the classic triad: intermittent haemoptysis, secondary iron deficiency anemia, diffuse alveoli opacity (accompanied or not by mediastinum or hilum adenopathy shown on the CT and PA plain chest radiography). One may observe a male predominance. Sometimes it can be described a family aggregation. Many theories tried to explain the appereance of idiopathic pulmonary haemosiderosis as a result of genetic transmission or an exposure to an environmental factor (11). Other studies sustain the role of autoimmune theory through circulant immune complexes. ¼ of those who pass the 10 years survival rate can develop different types of autoimmune diseases.

For the allergic theory pleades the detection of specific IgE for cow milk as well as the remission after the lack of gluten diet among those patients who have had caeliac disease associated. Environmental exposure theory wasn't demonstrated although it has been quoted in some studies (insecticides, fungi toxins – Alternaria, Aspergillus, Penicillum, Trichoderma).

Metabolic theory implies an iron metabolism defect (11). The diagnosis of idiopathic pulmonary haemosiderosis implies two stages. First stage is to highlight the alveoli hemorrhage. Second stage is to rule out other secondary alveoli hemorrhage due to autoimmune diseases associated or not with glomerulopathies (11).

**Table no 1. The most frequent causes of teenage pulmonary hemorrhage are**

| **Causing focal pulmonary hemorrhage:** | **Causing diffuse pulmonary hemorrhage:** |
|---|---|
| Bronchogenic cysts | Pulmonary arterial hypertension |
| Cystic fibrosis with bronchiectasis | Pulmonary embolism |
| Pulmonary abceses | Congestive heart failure |
| Tuberculosis | Alveoli proteinosis |
| Hemangioma | Wegener's disease |
| Foreign bodies | Idiopathic pulmonary haemosiderosis |

Other causes of rare hemorrhage:

- Behcet disease
- Lupus
- Reumathoid arthritis
- Churg – Strauss disease
- Essential cryoglobulinemia
- Hypersensitivity vasculitis
- Retinoic acid syndrome
- Bone marrow transplant
- Pulmonary transplant rejection
- Ulcerative colitis (11, 12)
- Cocaine infusion
- Propiltiouracil treatments
- Amiodarone
- Nitrofurantoine
- Environmental exposure to: hidrocarbures, infections (12)

Clinical examination can include two stages: an acute phase of respiratory distress, cough, hemoptisys and signs of anemia and a second phase a chonic one including: pallor, emaciation, delay of child development, hepatosplenomegaly, pulmonary fibrosis and hipocratic fingers. The laboratory reveals different grades of anemia, microcytosis, sideropenia, without affecting the platelets, coagulation or inflammatory syndrome.

Bone marrow biopsy reveals erythtocyte hiperplasis and low marrow iron deposits. Bronchoscopy highlights hemoptisys. Bronchioalveolar lavage shows hemosiderine presence in typical macrophages only 48 h to 5 days after hemorrhage (alveloli macrophages transform the iron from hemoglobin into hemosiderine between 36 and 72 hours and abides in th lung betweeb 4 and 8 weeks) (10).

Pulmonary biopsy acknowledges the alveolar hemorrhage and the presence of hemosiderine filled macrophages in the alveoli and interstitial space and also the thickening of the intraalveolar septa through fibrosis (1, 2). The plain chest radiography may show diffuse alveolar infiltrate especially in the inferior pulmonary field, blind glass CT aspect. After remission one may observe microopacities with variable grade of fibrosis. Tc-99m or Cr usage to highlight intraalveolar hemorrhage is very rare. ANA, ANCA, ds-DNA, basal membrane antibodies, antiphoslipidic antibodies, IgG, RF, could be helpful in establishing the diagnosis (1, 11). Until specific IPH tests are developed the diagnosis is one of exclusion (1).

Treatment consists in corticosteroids and imunosupresors having good results and having an impact over mortality rate only in the acute phase and an uncertain role in the second phase which has a poor prognosis. The most common cause of death is acute respiratory distress due to massive alveolar hemorrhage or chronic recpiratory distress and cor pulmonale due to severe pulmonary fibrosis. Among one study the average survival rate was of 2 ½ years (only 41% were treated with corticosteroids), Chryssanthopolos reported in a 30 years study a mortality rate of 60% (87% were treated with corticosteroids) (11).

## CONCLUSIONS

IPH (idiopathic pulmonary haemosiderosis) is a rare of unknown etiology condition. Sometimes it can precede the appereance of autoimmune disease (11). Glucocorticoids treatment and imunosupresors treatment has its efficacy, improving the patient's survival. The diagnosis of IPH is one of exclusion.

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