CASE REPORT

Idiopathic pulmonary hemosiderosis: case report

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Abstract

Objective: to alert pediatricians to the possibility of childhood idiopathic pulmonary hemosiderosis in cases of anemia associated with chronic lung disease.

Methods: this is a case report of idiopathic pulmonary hemosiderosis in a 6-year old child, histopathologically documented; the case is also reviewed in comparison to literature.

Results: a 6-year old child with history of anemia and lung disease characterized by wheezing, recurrent pneumonia, and clubbing was admitted to the hospital for investigation. The patient suffered sudden respiratory failure and hemoptysis, and was then submitted to lung biopsy, which showed histopathologic diagnosis compatible with pulmonary hemosiderosis. Therapy with high doses of corticosteroids was initiated with a good early response. After 2 1/2 months of therapy, the patient had another bleeding episode, which culminated in death.

Conclusion: idiopathic pulmonary hemosiderosis should be included as a possible diagnosis of children with anemia and chronic lung disease. This case should be taken as an example.


Introduction

Idiopathic pulmonary hemosiderosis (IPH) is a rare disease that affects pediatric patients in approximately 80% of the cases.¹ The uncommon characteristic of the disease may be related to the fact that it is usually underdiagnosed.² It is often diagnosed as normochromic or normocytic anemia, and its treatment is difficult. Late diagnosis of IPH may allow complications, such as the identification of the disease at a stage when pulmonary fibrosis has already developed, consequently yielding poorer prognosis.³

This paper is a case report of IPH and it discusses characteristics related to this disease.

Case report

A 6-year old male patient from the city of Itapeva, São Paulo, with history of wheezing from 7 months to 3 years of age. At 3 years of age, the patient presented with anemia and required blood transfusion. The patient’s clinical status stabilized from 3 to 5 years of age, at which point the patient presented recurrence of wheezing with episodes of limb and labial cyanosis, and of epistaxis. One month prior to recurrence, the patient was submitted to treatment for pneumonia at another hospital. Patient was dismissed from that hospital with terbutaline and dexamethasone prescriptions, which he was still using upon admission to our hospital.

Physical examination

The patient presented with good overall condition, normal pigmentation, weight of 15.780 kg (2.5 percentile; Marques, 1982), height of 108 cm (10th percentile; Marques, 1982), cardiac frequency of 90 beats per minute, and respiratory frequency of 26 bpm, with arterial saturation of 95% at pulse oximetry. The patient’s cardiorespiratory symptomatology indicated apex beat at left, fifth intercostal space of the midclavicular line; bigeminal heart rate with systolic murmur of +++/6+ at left edge of the sternum; increase in anteroposterior diameter of the thorax with convexity to the right; no adventitial noise at pulmonary
auscultation. The patient presented with distention of the abdomen, indicating palpable liver at 3 cm from the right costal margin; liver was rigidified and presented nodulous surface. The patient’s spleen was not palpable. He presented without neurological alterations and with clubbing of hands and feet (Figure 1).

Additional exams

Conventional chest X-ray upon hospital admission (Figure 2). Hemogram indicating 12,700 leukocytes/mm³, with 1% rod-shaped, 67% segmented, 1% eosinophilic, 1% basophilic, 23% lymphocytes, and 7% monocytes; hemoglobin at 12.1 g%; hematocrit at 36.4%; 270,000 platelets/mm³; 49-mm hemosedimentation rate (1 hour); negative for solubility test (Itano). Immunoglobin content according to nephelometry indicated IgE at 159 UI/ml, IgG at 1,798 mg%, and IgM at 241.2 mg%. The patient presented with normal coagulogram, negative fecal fat using Sudam III, urine I with traces of protein; normal hepatic and renal function tests, electrocardiogram indicating nodal escapes, echocardiogram indicating slight right chamber enlargement, and symptoms of pulmonary artery hypertension and slight tricuspid insufficiency.

On the 2nd day of hospitalization, our patient presented sudden paleness, cyanosis, dry cough, and tachypnea (respiratory frequency of 72 bpm), cardiac frequency of 120 beats per minute, pulse oximetry indicating 63% saturation (in normal hospital environment), diffuse wheezing with acutation of respiratory failure. Arterial gasometry, with FiO₂ at 60%, indicated PAO₂ of 66.6 mmHg and PACO₂ of 31.9 mmHg. Subsequently, our patient was admitted to the Pediatric Intensive Care Unit presenting the mentioned clinical status and respiratory failure. Chest X-ray indicated mixed interstitial and alveolar infiltration (Figure 3). The patient required tracheal intubation and mechanical ventilation; bleeding was observed in the cannula, and the patient was suspected with IPH.

Figure 2 - Chest X-ray upon hospital admission indicating interstitial reticular infiltration, involving mainly the lower and mid thirds of both left and right lungs; left lung was more severely compromised; X-ray also indicates thickening of horizontal scissure

On the 1st day of admission to the Pediatric Intensive Care Unit, the patient was submitted to open-lung biopsy, which indicated, macroscopically, areas of hemorrhage. Microscopic investigation indicated alveolar spaces filled with red blood cells and macrophages containing hemosiderin, interstitial chronic pneumonitis with diffuse fibrosis, muscling of septa, hemosiderosis of elastic laminae of arteries, and indication of recent alveolar hemorrhage (Figure 4).

At the Pediatric Intensive Care Unit, the patient was administered vancomycin, ceftriaxone, sulfamethoxazole-trimethoprim, and methylprednisolone at doses of 1 mg/kg every 6 hours. All dairy products were excluded from the patient’s meals. Antibiotics were administered up to the 5th day of admission to the Pediatric Intensive Care Unit, with the exception of chloramphenicol. The above histological examinations were concluded on the 5th day. The patient presented a progressive ventilatory improvement, allowing ventilator weaning and subsequent extubation on the 7th day at the Pediatric Intensive Care Unit. On the 18th day of intensive care, methylprednisolone was replaced with prednisone at one daily dose of 2 mg/kg.

The patient was dismissed form the Pediatric Intensive Care Unit on the 23rd day, not presenting any respiratory symptoms. The patient was seronegative for cytomegalovirus and HIV tests, and normal for eyeground and intraocular pressure examination.

Three weeks after dismissal from the hospital, prednisone doses were reduced from 2 to 1 mg/kg per day. Reduction of daily doses of prednisone was carried out in three steps, first reducing them to 1.5 mg/kg for one week, second, to 1.2 mg/kg for another week, and third, to 1 mg/kg. At the third-week appointment, the patient presented with Cushingoid features and hair loss; moreover, the patient had not been observing the recommendation of following a dairy-free diet.
One month after the first follow-up appointment, prednisone doses were reduced to 1 mg/kg every other day. The patient had to be readmitted after 1 week presenting reacutization of respiratory condition and fever; methylprednisolone was reinstated at 1 mg/kg every 6 hours. Subsequently, the patient presented a progressive improvement, and was dismissed after 9 days with prednisone doses of 2 mg/kg/day. The patient was instructed to reduce dosage to 1 mg/kg/day, and to return in 3 weeks. After 3 weeks, the patient missed the follow-up appointment. He did not attempt any contact with the hospital for 1 month and a half, and at this point, a contact was attempted with the patient’s city of origin. We were informed that the patient had died after acute aggravation of respiratory failure, and that the patient was dead-on-arrival at the local emergency hospital. The patient was not submitted to necropsy.

Discussion

IPH is a rare disease characterized by the triad hemoptysis, iron deficiency anemia, and parenchymal infiltrate at chest X-ray. Other studies, however, have included different respiratory symptoms, such as recurrent cough, wheezing, and tachypnea.\(^3\) IPH clinical status also includes hyperthermia and hepatosplenomegaly in 20% of cases.\(^1\) Average IPH survival is of 3 years.\(^7\) We verified all of these findings in the case studied, with the exception of splenomegaly.

The pathogenesis of IPH is still not well-defined, and there are numerous theories about it. Most theories are related to autoimmune factors.\(^8\) Correlation with autoimmune factors is suggested because alveolar hemorrhage in IPH is similar to that in other autoimmune diseases, such as systemic lupus erythematosus; because autoimmune diseases, such as celiac disease, present an increased incidence in IPH-carriers;\(^9\) and because immunosuppressants are effective in improving IPH clinical status.

In the literature, there are references to association of IPH with hypersensitivity to cow milk, which was first described by Heiner and Seas.\(^10\) Immune responses type I (anaphylactic) and IV (cell-mediated) have been related to hypersensitivity to cow milk. This was observed in laboratory assays that demonstrated an increase in histamine and in peripheral eosinophilia in IPH patients who were given cow milk.\(^11\) In this sense, our patient was instructed to follow a dairy-free diet; the patient, however, did not follow this recommendation.

The diagnosis of IPH can be confirmed only after excluding other causes of pulmonary hemorrhage, such as mitral stenosis, chronic venous hypertension, periarteritis nodosa, Wegener’s granulomatosis, Goodpasture’s syndrome, and others. The diagnosis of IPH may also be indicated by clinical status, but it requires anatomicopathological confirmation by open-lung or transbronchial lung biopsy, or by bronchoalveolar lavage fluid with siderophages. Findings of siderophages in gastric lavage fluid are also suggestive of IPH diagnosis.

Currently, the use of bronchoalveolar lavage fluid is indicated for investigating etiology in cases of pulmonary hemorrhage, since it is a simple and mildly aggressive procedure, and yields significant sensitivity and specificity.\(^12\) In our case, however, the patient was submitted to open-lung biopsy due to his unstable oxygenation and ventilation rates, and to his mechanical ventilation requiring high respiratory parameters.

Figure 3 - Chest X-ray after acute aggravation indicating mixed infiltrate (interstitial with alveolar areas spread in both left and right lungs, especially in the lower thirds, and more significant at left lung) and thickening of the horizontal scissure.

Figure 4 - Histopathological findings at lung biopsy. Staining with Perl’s method was employed (200 x). Image allows visualization of siderotic pigmentation in alveolar macrophages at both alveolar wall interstice and elastic laminae of arteries, which appeared fractured.
Histopathological findings in IPH patients include presence of macrophages carrying hemosiderin (siderophages) in the pulmonary parenchyma, of lymphoid hyperplasia, and of iron impregnation of the basement membrane and elastic fibers. None of the referred findings is, however, pathognomonic of IPH; the referred findings are in agreement with those observed in our patient.

It is possible that X-ray may present normal at the beginning of the disease, but the development of the disease will indicate reticular and nodular opacification in perihilar and base regions, sparing apices and costophrenic angles. Images may migrate or disappear. Later on, alterations may become permanent, with acute perihilar infiltrate and cardiomegaly.

The majority of cases will respond to corticoids, especially in cases of controlling acute hemorrhage; cases of corticoid dependence and also corticoid resistance may also respond to corticoids. For acute crises, the use of methylprednisolone at doses of 1 to 2 mg/kg every 6 hours is indicated; and for the prevention of recidivism, the use of prednisone is indicated. The literature indicates advantages in the use of liposteroids (dexamethasone-palmitate in liposome) in the control of acute crises, which cause less adverse effects and greater concentration at the site of action.13 Our patient could be defined corticoid-dependent, since he presented aggravation of clinical status at both attempts of reducing corticoid dosage and improvement of clinical status at increase in dosage.

Corticoid-resistant patients who present recurrent life-threatening episodes or progressive deterioration of pulmonary function may be submitted to therapy with immunosuppressants. In this sense, azathioprine has been frequently indicated. In case of unsuccessful therapeutic response to azathioprine, it is also possible to indicate cyclophosphamide. The use of cyclophosphamide has been reported with improvement in the clinical status without adverse effects.14 It is also possible to find in the literature reports of the use of chloroquine therapy, which is effective and causes less adverse effects than immunosuppressants. Chloroquine does require, however, periodic eye examinations by an ophthalmologist due to its toxicity, which affects the retina.5,15

Conclusion

We have concluded that this is a case of idiopathic pulmonary hemosiderosis, since other underlying diseases were ruled out.

The diagnosis was carried out immediately, and despite the indicated therapy, it was not possible to avoid massive pulmonary hemorrhage, which culminated in death.

We understand that prognosis of IPH is variable, that it depends on the frequency and gravity of episodes of hemorrhage. Also, regardless of corticoid prevention, massive and deadly pulmonary hemorrhage may still occur.

References