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Case Report

Occupational Asthma in Non Previously Patient Diagnosed HIV-Infection

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Abstract

Respiratory symptoms are varying in HIV-infected patients and among them; airway hyperactivity from bronchial asthma is relatively frequent. We present a case of a severe bronchial asthma attack caused by occupational asthma, in a patient that was not previously identified as HIV-positive.

The occupational asthma was diagnosed considering the patient's history, bronchial response to bronchodilatation and serial peak flowmetry. Occupational asthma can benefit by recommending employment redeployment. This reduces the symptoms, the need for medication that might interfere with the long term medication prescribed for controlling the HIV infection and the overall prognosis of lung function. For these reasons, investigating occupational aspects in all patients HIV-infected with asthma need to be considered.

Keywords: Occupational Bronchial Asthma; HIV-Infected Patient

Background

Pulmonary manifestations in patients with HIV are very diverse [1], the most common respiratory symptoms, in decreasing order of frequency, are coughing, sputum production, dyspnea, and wheezing. All these symptoms are significantly more frequent in subjects that are HIV-positive as opposed to those that are seronegative [1,2]. Also, bronchial asthma is relatively frequent, but it rarely is the cause of the initial healthcare contact.

We will present an occupational asthma case in a patient that had not been previously diagnosed as HIV-positive and whose first doctor's visit was for a severe bronchial asthma attack.

Case Presentation

A 42-year woman presented to the emergency room for the following symptoms: wheezing, dyspnea at rest, symptoms that occurred during the working hours, at her workplace, from where she was taken by an ambulance.

Approximately 2 weeks before the hospital admission, the patient had dry cough bouts and in the previous 24 hours, the cough became almost constant.

The clinical examination showed an febrile patient, had the petechial rash on the upper limbs, warm cyanosis of extremities, the respiratory frequency of 34 /minute, blood pressure of 96/60 mmHg, heart rate of 110 beats/minute, a hyper-inflated thorax, a global reduction of the vesicular murmur, no rales. All pointed out to acute respiratory insufficiency.

Peripheral capillary oxygen saturation (SaO_2) was 82%, partial pressure of O_2 (PaO_2) was 66 mmHg, the partial pressure of CO_2 ($PaCO_2$) was 42 mmHg. These values supported the diagnosis of pulmonary insufficiency.

The chest x-ray showed signs of hyperinflation with no other signs present.

The most probable causes of hyperinflation were discussed for this patient:

- Pulmonary embolism but the clinical examination of the limbs didn't show signs of deep vein thrombosis and the heart examination excluded atrial fibrillation.
- Parenchymal diseases: the X-ray excluded pneumonia
- Bronchiolitis obliterans was also excluded due to the lack of high body temperature and the age of the patient at the time.
- Exacerbation of COPD: the patient was a non-smoker, and there was no expectoration.

An asthma attack could not be excluded, although there was no typical anamnesis of a previous presentation

The patient received oxygen at 3L/min, hydrocortisone hemisuccinate 400 mg, aminophylline 240 mg, acetylcysteine 300 mg by the intravenous route (glucose 5% - 500ml).

After 45 minutes of treatment, the skin color returned to normal; respiratory frequency was 40 respirations/min, pulse rate was 82, and SaO_2 = 96%. Bronchial rales and prolonged expiratory phase

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were perceived at lung auscultation. The patient continued to receive treatment with systemic corticosteroids (hydrocortisone hemisuccinate 200 mg every 6 hours), β-agonist (Ventolin 4 puffs every 6 hours) and O_2 with continued monitoring.

Spirometry was performed 72 hours after admission and about 12 hours after the last use of the respiratory medication and it showed an obstructive disjunction (FEV1 reduction of 23% and MEF 50 reduction of 55%). The bronchodilator test was positive.

The Working Diagnostic was Asthma, Probably Occupational-Related

Due to the severe abnormalities of the lab tests (Table 1), a hematology consult was conducted.

Table 1: The blood cell count

	Patient	Normal range
WBC	3.32 x 1000/µl	4.8 - 10.8 x 1000/µl
Neutrophils	1.2 x 1000/ µl	2.2 - 4.8 x 1000/µl
Lymphocytes	1.1 x 1000/µl	1.3 - 2.9 x 1000/µl
Monocytes	0.1 x 1000/ µl	0.3 - 0.8 x 1000/µl
Eosinophils	0.920 x 1000/ µl	0.0 - 0.2 x 1000/µl
Basophils	0 x 1000/ µl	0.0 - 0.1 x 1000/µl
Thrombocytes	92000/µl	150000-300000/µl
RBC	3.82 x 10^6/ µl	4.7 - 6.1 x 10^6/ µl
Hb	8.5 g/dl	13.5-16 g/dl
Hct	26.5 %	42-45%

WBC = white blood cells, RBC = red blood cells Hb = hemoglobin Hct = hematocrit

The hematologist raised the suspicion of an HIV-infection based on the normocytic normochromic anemia, leucopenia, and lymphopenia, no lymph nodes larger than 1cm, no splenomegaly, and no history of frequent infections. The hematologist asked for a CD4 cells count. The CD4 cells were 249 cells/ mm^3 and the infectious disease consult confirmed HIV-infection and initiated the specific antiretroviral therapy.

After one week of inpatient care in our clinic, the patient was discharged in an improved state, both clinically and functionally: the FEV1 and MEF50 were 82% and, 66% of predicted, respectively. She was prescribed treatment with inhaled corticosteroid (beclomethasone) and short-acting β-agonist as rescue medication. The patient has been asked to return periodically for further reevaluation.

After 2 weeks, the patient was reevaluated. The anamnesis showed that she had frequent airway infections in the previous 2 years, followed by long periods of time, even months, of dry cough bouts. Two weeks before the admission, she had an episode of fever (2 consecutive days, a maximum of 38°C) followed by the persistent dry cough.

The patient didn't smoke and neither experienced passive smoking inhalation. The home is sanitary. She gave birth naturally. She is divorced. No family history of allergic diseases. She has been working at the same place for the last 20 years, as a knitter in a textile workshop, with occupational exposure to cotton, wool, polyester, flax and colorants. She continues to work in 2 shifts, 8 hours each, with other 9 colleagues per shift.

Given the occupational exposure of the patient and the age of onset, in the context in which the patient is HIV-positive, we suspected a sensitization to textile dust, so we initiated the monitoring of peak expiratory flow (PEF) values both at home, during the free time, and at work. The results of this monitoring are presented in Fig 1. The variability of PEF values was important during the days spent at work and this supports the diagnosis we formulated. A final diagnosis of occupational asthma has been concluded, according to current standards [3].

We recommended the subject to consider changing her occupation if possible, because HIV-patients have a higher occurrence of airway hyper reactivity and because the trigger for asthma attacks (the textile dust) lower the efficiency of the treatment.

The asthma evolution was good: there was no major attack in the next 6 months of follow-up. However, mild asthma symptoms (cough and dyspnea) reversible to short acting betamimetics, less than 3 times/week persisted during this follow-up period.

Discussion

The anamnesis did not provide sufficient information to establish the moment of infection with HIV. The only objective measurement for evaluation was the low count for CD4 cells at the moment of diagnosis, which shows that the disease has been evolving for more than a year [4]. That is why it is difficult to tell if the asthma attacks were influenced by the presence of the HIV.

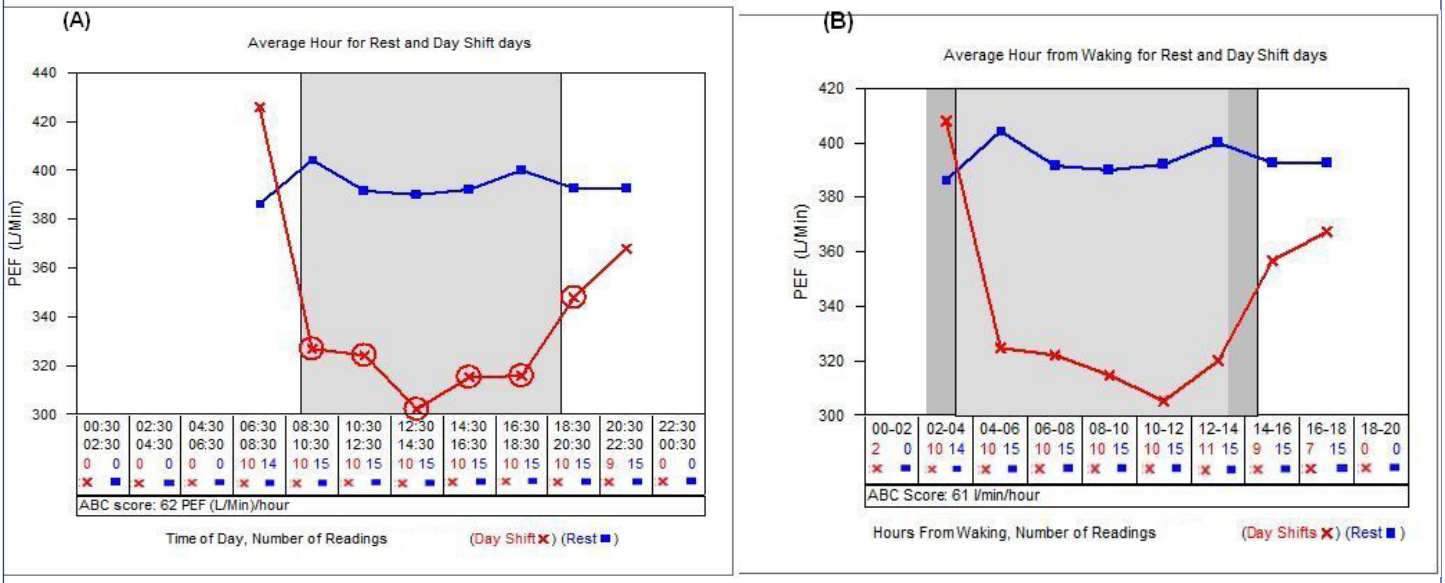
It is known that before the antiretroviral therapy era the bronchial hyper reactivity was very frequently encountered in seropositive patients. Therefore we had to take it into account for our subject.

Mechanism

The hyper reactivity is closely linked with the evolution of the HIV-infection. The HIV activates the lymphocyte in order to multiply. The increase in activity for CD4+ lymphocytes is accompanied by an increase in IL4 production, promoting IgE synthesis [5,6]. The switch to the TH2 type of the lymphocytes and IgE production occurs at the moment of contact with the antigen. The presence of lymphocytes is needed during the first contact with the allergen, but not so during subsequent exposures. That is why it is considered that the sensitization takes place during the early stages of the viral infection and that the reduction in the number of CD4 cells does not exclude the possibility of asthma to manifest [7]. The hyper reactivity can also be attributed to the direct aggression of the HIV through its own viral proteins. These proteins have a destructive action in the airways.

Another clinicopathological mechanism could be due to global immune disorder [8] which can be associated with inflammatory cells infiltrate in the bronchial mucosa, as well as the presence of a large number of eosinophils.

Fig 1: Evolution of peak expiratory flows during rest and shift days



(A): Shows the average PEF value for the same time of the day, for rest days (■) and day shift days (x).

The table includes the time intervals, in 2 hour quanta, starting with the 00:30 AM to 02.30 AM interval, and the number of readings used for the average (to the left, the number of readings for the day shift days, marked x underneath, and to the right the rest days, marked ■ underneath.

(B): Shows the average PEF value for the same time since waking, for rest days (■) and day shift days (x).

The table includes the time intervals, in 2 hourly, starting with the first 2 hours after waking, and the number of readings used for the average (to the left, the number of readings for the day shift days, marked x underneath, and to the right the rest days, marked ■ underneath.

Both graphs show a clear decrease of the average PEF values on day shift days compared with the rest days.

The occupational exposure to respirable textile dust is actually a very complex exposure, because it contains cotton, flax, wool, polyester, dyes or contaminants (bacteria, fungi). The primary effect is allergic. The toxic effect is fairly rare [9]. In the weaving shop, working on the knitting machine implies exposure to greater quantities of inhalable textile fibers compared to other stations [10].

Given the presence of the HIV-virus in the described patient, we can hypothesize a synergic effect of its action with that of the textile fibers on the bronchial mucosa. The main argument is the clinical one: the presentation of a severe asthma attack in a patient that previously tolerated various respiratory symptoms, preferred auto medication and used medical services sparingly.

Another mechanism involved in the development of the bronchial hyper reactivity could be the repeated airway infections [11,12]. Our patient had several episodes of airway infections.

The patient described multiple dry cough bouts, in the last 2 years. For an HIV infected patient, the dry cough can be a consequence of pulmonary infections secondary to immunosuppression or could be a sign of an ignored diagnosis of asthma. Persistent dry cough is frequent, between 23-37.1% of HIV-infected patients will develop it [13].

Curiously, in this case, are the hematologic findings on admission: leukopenia with neutropenia and a low CD4+ count.

Existing data confirm that low CD4+ T-lymphocyte counts and high level of viral RNA are directly related to the incidence of respiratory infections [11,14] and that eosinophilia is associated with allergic manifestations [6]. We don't have previous data about the blood cell count, but it is reasonable to assume that these are chronic hematological modifications that have contributed to the recurent infections.

Occupational asthma in an HIV-positive patient raises numerous therapeutic issues, due to the reciprocal influences of the drugs prescribed for each of the two diseases.

The presence of HIV-infection is an aggravating factor for asthma by remodeling the immune response. Therefore, reduction of the viral load is an essential element of the HIV infected patient. This is achieved by antiretroviral therapy (ART). ART raises the circulating CD4+ cell number which might have a paradoxical effect of TH2 reaction amplification in the lungs, with increased bronchial hyper reactivity. In this respect, fungal infections, more frequent in HIV patients, have the same effect [15]. The paradoxical effect of ART on asthma incidence can also be explained by the effect on peroxisome-proliferator activated receptor g (PPARg)) increased expression in bronchial epithelium and smooth muscle of the airways. PPARg activation is associated with the cell growth that translates to thickening of the respiratory mucosa and the smooth muscle bronchial fibers, characteristically found in individuals with bronchial hyperreactivity and explaining the negative correlation cu FEV1 [16].

It is not just the ART that impacts asthma, the corticoid treatment influences HIV evolution also. Inhaled corticoids are administered to asthma patients for long periods of time for crises prophylaxis. This therapy diminishes the local immune defence mechanisms, increasing the risk of infections, including tuberculosis, a side effect that has been reported in HIV patients treated with inhaled corticoids [7,18]. Inhaled corticoids also raise the risk for oral candidiasis [19] that might quickly spread to a systemic infection. Because this medication also has a direct effect on CD4+ cells reduction, caution should be taken and also carefully adjustment of the treatment scheme.

The current HIV-infection therapy involving protease inhibitors could interfere with inhaled corticosteroids and salmeterol with deleterious consequences. Protease inhibitors inhibit cytochrome p450. The inhibition is more or less expressed according to the different pharmacological compounds. For the ones with potent inhibition, such as ritonavir, the systemic corticoid level can be high enough to cause a Cushing-like syndrome. For this reason, the actual guidelines [20] don't recommend the association between fluticasone or budesonide and ART. The therapeutic alternative accepted for inhaled corticoids is the only beclomethasone. Because the plasmatic activity of salmeterol is also raised by protease inhibitors, increasing the risk of cardiac side effects, this long-acting beta-agonist should also be avoided [20].

A confirmation of the diagnosis of occupational asthma implies a recommendation of changing the workplace. Continuation of exposure would maintain the inflammatory response and would diminish the chances of asthma control. This recommendation is reinforced in an HIV-infected patient as both the course of this infection itself and the influence of the ART have negative effects on the natural history of bronchial asthma.

Conclusions

Bronchial asthma might be the first manifestation in patients infected with the HIV-virus, particularly in persistent, long term exposure to occupational allergens or irritants.

Occupational exposure and HIV-infection are risk factors with additive effects on bronchial inflammation. HIV-positive patients with occupational asthma should be provided, under the specific health and safety regulations applicable, all necessary measures to reduce exposure in order to avoid a severe lung function decline.

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