Case report

Chronic eosinophilic pneumonia: Adjunctive therapy with inhaled steroids

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ABSTRACT

Idiopathic chronic eosinophilic pneumonia (ICEP) is a rare form of diffuse parenchymal lung disease first identified by Carrington et al. in 1969. It is characterized by the presence of constitutional and respiratory symptoms with associated peripheral opacities on imaging and elevated serum and/or bronchoalveolar eosinophilia. Although data is limited regarding etiology or prevalence, it is known that ICEP has a 2:1 female: male predominance and typically affects non-smokers. Diagnosis rests on the clinical constellation of respiratory symptoms of at least 2–4 weeks duration, the presence of diffuse pulmonary alveolar consolidation, classically described as the “photographic negative of pulmonary edema”, the presence of eosinophils ≥40% on bronchoalveolar lavage or ≥1000/mm3 eosinophils on peripheral blood and the exclusion of other known causes of eosinophilic lung diseases such as drugs, toxins, fungi, parasites, and collagen-vascular disorders. A dramatic response is achieved with systemic corticosteroids, which is typically dosed over 6 months to 1 year. Despite this response, approximately 30–50% of patients will relapse upon cessation of steroids or during the taper. Although these patients respond well to another trial of steroids, the side effects of long term steroids are well known, including osteoporosis, diabetes, hypertension and cataracts. Inhaled corticosteroids as monotherapy has been trialed in the past without success. However, we report a case of a patient who underwent treatment with systemic corticosteroids followed by inhaled steroids who has remained in remission for 2 years.

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1. Introduction

Idiopathic chronic eosinophilic pneumonia (ICEP) is a rare form of diffuse parenchymal lung disease of unknown etiology first described by Carrington et al. in 1969 [1]. It is characterized by progressive dyspnea, cough, fevers, malaise and weight loss over a period of several weeks [1–3]. Non-dependent pulmonary opacities are typically seen on thoracic imaging [1–4]. Alveolar and/or blood eosinophil levels tend to be elevated (Alveolar eosinophilia ≥40% on BAL; blood eosinophilia ≥1000/mm3) [2]. In some cases, lung biopsy demonstrating eosinophils infiltrating the interstitium and alveoli is needed [5]. Exclusion of parasitic or drug exposures as well as systemic and infectious etiologies, such as eosinophilic granulomatosis with polyangiitis or allergic bronchopulmonary aspergillosis, is key to making the diagnosis [1–4]. Due to the dramatic resolution in symptoms, oral corticosteroids are the mainstay of treatment [1–4, 6,7]. However, relapse is frequently seen following cessation, with reports varying from 37 to 58% risk of relapse within one year [2, 5, 8, 9]. There is increased risk of relapse during tapering as well [5, 8, 9]. Prolonged oral steroid treatment is not without its own risks, however. Despite a generally good prognosis, patients may contend with the long-term complications of steroid-related adverse effects [5, 8, 9]. We report a case of a patient who has remained in remission following treatment with systemic corticosteroids followed by maintenance with inhaled corticosteroids.

2. Case

A 60-year old female undergoing pre-operative evaluation for sinus surgery underwent a chest x-ray (Fig. 1). New left upper lobe infiltrates were seen on plain film, prompting referral to Pulmonary clinic. Her history was significant for a chronic sinusitis, cough and remote tobacco use disorder. She endorsed a history of intermittent fevers, dyspnea and cough over two years. No skin
lesions, renal involvement or neuropathies were noted at that time.

CT Thorax with contrast revealed bilateral confluent areas of pulmonary consolidation with air bronchograms, involving the bilateral upper lobes and superior segments of the lower lobes. Mild mediastinal and bilateral hilar adenopathy were also noted. Pulmonary function testing demonstrated an isolated reduced residual volume, 65% of predicted, but was otherwise unremarkable. Due to concerns of malignancy, a PET scan was obtained, showing heterogenous uptake of mild to significant intensity involving the parenchyma. Bronchoscopy was performed. Transbronchial needle aspirates from precarinal and right hilar nodes demonstrated admixed large atypical cells and the transbronchial lung biopsy was nonrevealing. Flow cytometry performed on the lymph node needle aspirate was unremarkable. Cultures were sterile.

Laboratory work up was notable for elevated inflammatory markers, ESR 113 mm/hr and CRP 65 mg/L. LDH was elevated at 147 IU/L. ACE level was 32 U/L. Serum creatinine was 0.5 mg/dL and sodium was 133 mEq/L. A complete blood count demonstrated a normal white count of $6.4 \times 10^9$/mm$^3$ with 17.7% eosinophils. Hemoglobin was 10 g/dL and platelet count was $330 \times 10^9$/mm$^3$. C3 and C4 were within normal limits. ANA, c-ANCA and p-ANCA were negative. Rheumatoid factor was negative. HIV antibody was negative and cryoglobulins were negative. Fraction of exhaled nitric oxide (FeNO) was 170 ppb. Her IgE level was elevated at 310 IU/mL (upper limit of normal 158 IU/mL). Fungal serologies were negative. Stool ova and parasites were negative. A video-assisted thoracoscopic for surgical lung biopsy was performed, which demonstrated diffuse eosinophils with evidence of interstitial fibrosis and emphysematous changes, consistent with ICEP (see Figs. 1, 2 and 3).

A prednisone taper starting at 40 mg daily was initiated for fourteen days, followed by 20 mg daily for 3–4 months with pneumocystis prophylaxis and then gradually decreased to discontinuation at 12 months. During this period, the patient’s symptomatic, laboratory and radiologic abnormalities rapidly improved and stabilized (Fig. 1). A follow up Chest CT after 8 months of treatment revealed resolution of the opacities. Given the concerns for relapse, the patient was transitioned to mometasone 440 mcg MDI q12h inhaler, tapered over 24 months to one puff daily for maintenance. Currently, the patient feels well and has had minimal recurrence of symptoms. Her most recent FeNO was mildly elevated at 35 ppb, serum IgE was 68 IU/mL and inflammatory biomarkers remain low. The patient has not developed extra-sinopulmonary symptoms in follow up. However, a recent endoscopic nasal biopsy demonstrated eosinophilic infiltration of nasal polyps.

### 3. Discussion

The diagnosis of ICEP involves the exclusion of other forms of eosinophilic disease, including eosinophilic granulomatosis with polyangiitis (eGPA), formerly known as Churg-Strauss Syndrome. In 1990, the American College of Rheumatology released formal guideline recommendations for the diagnosis of eGPA based on meeting at least four of 6 criteria [10]. Our patient met three (eosinophilia, pulmonary infiltrates and paranasal sinus findings) without extra-sinopulmonary involvement. However, some studies suggest that ICEP may present with sinopulmonary features including allergic rhinitis, nasal polyps and patients may progress to developing asthma [5,8,9]. The clinical course of eGPA and ICEP
in ICEP with asthma despite the lack of efficacy of ICS as monotherapy [6,11]. The role for inhaled corticosteroids is well described in airway diseases such as asthma, cystic fibrosis and bronchiectasis [6,16]. Some reports do suggest that both mucosal and submucosal endobronchial lesions may be a feature of ICEP [5,17]. However, it is uncertain to what degree inhaled steroids may penetrate alveolar lesions in ICEP. Penetration into peripheral lung lesions may depend on the presence and degree of airflow obstruction. We suspect that the use of oral steroids may resolve the initial lesions and that transitioning the patient to inhaled corticosteroids may continue to suppress the eosinophilic migration into the alveoli. To our knowledge, there have been no documented reports of the effect of ICS in ICEP with bronchial involvement.

Our case report highlights an alternative strategy in which oral corticosteroids are utilized to abate eosinophilic inflammation which are then followed by ICS maintenance to maintain remission. To date, our patient has done well, not requiring additional doses of oral corticosteroids to control pulmonary symptoms. She has since developed nasal polyps with eosinophilic infiltration, but is otherwise asymptomatic. She remains on a simple once daily ICS therapy at this time.

Limitations to this report include a small sample size of 1 as well as open label therapy. ICS can resolve spontaneously as well, which may confound results [2,5,6]. A larger study would be needed to verify response to treatment.

4. Conclusion

Inhaled corticosteroids should be considered as an adjunct following oral corticosteroid therapy as a means of reducing risk of relapse in ICEP. Further investigation into this regimen is warranted.

Conflicts of interest

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