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Eosinophilic pneumonia: experience at two tertiary care referral hospitals in Saudi Arabia

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BACKGROUND AND OBJECTIVE: Eosinophilic lung diseases are a diverse group of disorders characterized by pulmonary opacities associated with tissue or peripheral eosinophilia.

DESIGN AND SETTING: A retrospective study conducted at two tertiary care hospitals from January 1999 to December 2009.

METHODS: All cases with the diagnosis of pulmonary eosinophilia were reviewed over a period of 10 years. Data on demographic, clinical, and radiologic characteristics were collected.

RESULTS: Thirty-five patients with a mean age of 33.9 (16.2) years, of which 20 (57.1%) were male and meeting the criteria of eosinophilic lung disease were identified. Cough and dyspnea were the most frequent symptoms at presentation in 29 (82.9%) and 27 (77.1%) patients, respectively. Reticulonodular and airspace patterns were the most common radiographic findings in 17 (48.6%) and 15 (42.9%) patients, respectively. Peripheral eosinophilia was present in 33 (94.3%) patients. Twenty-four patients (68.6%) were labeled as having idiopathic pulmonary infiltrate with eosinophilia. Complete remission was achieved in 13 (54.2%) of 24 patients, while 10 (41.7%) patients relapsed within a few months of discontinuation of therapy. Specific therapy for a specific disease was administered in 8 patients: 2 patients for pulmonary tuberculosis, 2 for Churg–Strauss syndrome, 1 for lymphoma, 1 for schistosomiasis, 1 for acute eosinophilic pneumonia, and 1 for Wegener granuloma; 3 patients were treated as allergic bronchopulmonary aspergillosis.

CONCLUSIONS: Pulmonary eosinophilia remains rare but challenging, and it can have the same diverse clinical and radiographic presentations seen with other common pulmonary conditions. Clinicians should be alert to these syndromes and must think of them in any lung disease differential diagnoses.

Eosinophilic lung diseases are a heterogeneous group of disorders characterized by abnormal accumulation of eosinophils in the distal airways, air spaces, and the interstitial compartment of the lung, with or without peripheral blood eosinophilia.[1-3] The first detailed description of chronic eosinophilic pneumonia (CEP) was provided by Carrington et al, in 1969.[4] The specrtum of this respiratory syndrome includes eosinophilic lung disease of known causes, which include allergic bronchopulmonary aspergillosis (ABPA), bronchocentric granulomatosis, parasitic infections, drug reactions, and eosinophilic vasculitis (allergic angiitis, Churg–Strauss syndrome), and eosinophilic lung disease of unknown causes, which include simple pulmonary eosinophilia, also known as Loeffler syndrome, acute eosinophilic pneumonia (AEP), CEP, and idiopathic hypereosinophilic syndrome.[1,3,5-10] Infectious causes of pulmonary eosinophilia include parasitic infections, particularly ascariasis and *Mycobacterium tuberculosis*.[11-13]

Diagnosing eosinophilic lung disease is challenging because of the overlap of the clinical and radiological presentation with those of other forms of diffuse lung diseases. The clinical presentation can range from chronic to a subacute form to even acute respiratory failure. Radiological presentations range from pulmonary infil-

trates, which might be minimal, to migratory ones, or diffuse and bilateral presentations.[14-16]

Accurate identification of the underlying cause, when possible, is important because it can influence treatment. Corticosteroids remain the cornerstone in treating eosinophilic lung diseases.[14] Despite the high response rate, there is a chance of relapse and recurrence of the disease. The incidence and prevalence of eosinophilic pneumonia in Saudi Arabia is not known. Medical knowledge regarding eosinophilic lung diseases has been acquired mostly from case series and case reports. In this study, we have performed a retrospective evaluation of our experience with eosinophilic lung diseases in the last 10 years.

METHODS

We used medical records with the coding system of the diseases and the pathology database to retrospectively review all cases with a diagnosis of pulmonary esoinophilia over a period of 10 years, from January 1999 to December 2009, at the King Abdualziz Medical City (KAMC) and King Faisal Specialist Hospital and Research Center, both in Riyadh, Saudi Arabia. This study was approved by the KAMC ethics committee. We included all cases with a diagnosis of eosinophilic lung disease that were based on two or more of the following criteria: an increased number of eosinophils in peripheral blood, eosinophilic infiltration of the lung biopsy, or more than 10% eosinophilia in bronchoalveolar lavage (BAL) fluid. We excluded all cases in which the secondary etiology was known, such as secondary to drug reaction or parasitic infection, or diagnosed clinically without tissue confirmation. Data were collected on the demographic characteristics, symptoms, physical findings at presentation, treatment administered and response to therapy, and cause of disease after therapy. All pathology reports were reviewed; chest x-ray and computed tomography (CT) reports were also reviewed, and if the reports were not avaliable, then films were reviewed by a radiologist. All laboratory data pertinent to the diagnosis of pulmonary eosinophila were also collected.

RESULTS

We identified 35 patients from 1999 to 2009 fulfilling the criteria of eosinophilic lung disease, comprising 20 (57.1%) males and 15 (42.9%) females, with a mean age of 33.9 (16.2) years. Bronchial asthma was the most common comorbidity diagnosed in 18 patients (51.4%). Cough and dyspnea were the most frequent symptoms at presentation in 29 (82.9%) and 27 (77.1%) patients, respectively. Other symptoms included fever in 11 patients (31.4%), weight loss in 11 patients (31.4%), and arthralgia in 7 patients (20%) (**Table 1**).

Chest examination was normal in 12 (34.3%) patients, while crackles and wheezing were present in 23 (65.7%) patients. Physical findings were bilateral in 21 (60%) patients and unilateral in only 2 (5.7%) patients.

Radiological findings at presentation are summarized in **Table 2**. A reticulonodular pattern was the most frequent pattern encountered in plain chest x-ray, with 17 (48.6%) patients. This was closely followed by airspace pattern, with 15 (42.9%) patients. Pleural involvement was present in 11 (31.4%) patients. Chest CT was carried out for all patients. Mediastinal lymphadenopathy was seen in 9 (25.7%) patients, even though reported as nonsignificant. Reticulonodular and airspace disease patterns were the most commonly encountered abnormalities, with 17 (48.6%) and 16 (45.7%) cases, respectively. Almost all radiologic abnormalities were bilateral in CT of the chest, with 30 (85.7%) patients.

Peripheral eosinophilia (more than 10% in the peripheral smear) was present in 33 (94.3%) patients; the mean (SD) eosinophilic count was 26.8 (12.3). Fiberoptic bronchoscopy was performed on 32 (91.4%)

Table 1. Patient characteristics and presenting symptoms.

Characteristics	No. (35)	%
Gender		
Male	20	57.1
Female	15	42.9
Symptoms		
Cough	29	82.9
Dyspnea	27	77.1
Fever	11	31.4
Weight loss	11	31.4
Wheezing	10	28.6
Arthritis/ arthlalgia	7	20.0
Night sweat	5	14.3
Chest pain	5	14.3
Sinusitis	4	11.4
Hemoptysis	4	11.4
Skin rash	3	08.6
Others	10	28.6

Table 2. Radiologic features.

Characteristics	Number	%
Radiology chest x-ray		
Reticulonodular	17	48.6
Airspace	15	42.9
Cavity/mass	4	11.4
Pleural	11	31.4
Effusion	9	25.7
Thickening	2	5.7
Chest CT scan findings		
Lymphadenopathy	9	25.7
Mediastinal	5	14.3
Hilar	8	22.9
Parenchyma radiological pattern		
Airspace	16	45.7
Interstitial (reticulonodular)	17	48.6
Ground-glass appearance	9	25.7
Other (mass/cavity)	2	5.7
Pleural	6	17.1
Effusion	10	28.6
Thickening	2	5.7
Location of abnormalities		
Bilateral	30	85.7
Unilateral	5	14.3

Table 3. Diagnostic procedures.

Characteristics	Number	%
Procedure		
Bronchoscopy	32	91.4
Transbronchial biopsy (TBBx)	25	71.4
Bronchioalveolar lavage (BAL)	18	51.4
Transthoracic biopsy	4	11.4
Thoracoscopic biopsy	6	17.1
Others	8	22.9
Pathology result (for 31 patients)		
Eosinophilia tissue infiltration	29	93.5
Inflammation and granuloma	2	6.5
BAL differential result (for 18 patients)		
Eosinophilia (>10%)	16	88.9
Macrophages	1	5.5
Reactive bronchial cell	1	5.5
Reactive bronchial cell and macrophages	2	8.7
Reactive bronchial cell and eosinophilia	1	5.5
Normal	2	8.7

patients, and transbronchial biopsy was performed on 25 (71.4%) of them. Transthoracic biopsy and thoracoscopic biopsy were performed on 4 (11.4%) and 6 (17.1%) patients, respectively (**Table 3**).

BAL was performed on 18 patients, and the sputum cell count and differential count were obtained from all of them; eosinophilia (>10%) was present in 16 of 18 (88.9%) patients. Twenty-four (68.6%) patients were labeled as idiopathic pulmonary infiltrate with eosinophilia. One case was diagnosed as schistosomiasis based on the biopsy finding showing schistosomiasis ova in the lung biopsy and subsequent high-serum titer of schistosomiasis; the patient improved after treatment with antischistosomiasis therapy. Other diagnoses are shown in **Table 4**. Complete remission with no further relapse was achieved in 13 (54.2%) of 24 patients labeled as idiopathic eosinophilic pneumonia after treatment for 6 months to 1 year, and no relapse up to 1 year from stopping corticosteroids, while 10 (41.7%) patients relapsed within a few months of discontinuation of therapy and required reinstitution of steroid and 1 patient was lost to follow-up. Specific therapy for a specific disease was administered in 8 patients: in 2 patients for pulmonary tuberculosis, 2 for Churg–Strauss syndrome, 1 for lymphoma, 1 for schistosomiasis, 1 forAEP, and 1 for Wegener granuloma. Three patients were treated for ABPA with variable doses of corticosteroids for a short period ranging from 2 to 4 weeks.

DISCUSSION

Pulmonary eosinophilic syndromes are rare and are generally placed under two broad categories: (1) extrinsic eosiniphilic sydromes [such as parasitic or fungal causes, AEP, Loeffler, or DRESS (drug rash with eosinophilia and systemic symptoms) syndromes] and (2) intrinsic eosinophilic syndromes with mostly unknown pathogenesis as in CEP, eosinophilic granuloma, or Churg–Strauss syndrome.[17]

In our series, less than one-third of patients had an

Table 4. Final diagnosis.

Characteristics	Number	%
Idiopathic pulmonary eosinophilia[a]	24	68.6
ABPA	3	8.6
Churg–Strauss syndrome	2	5.7
Schistomiasis	1	2.9
Acute eosinophilic pneumonia	1	2.9
Hodgkin lymphoma	1	2.9
Pulmonary TB	2	5.7
Wegner granuloma	1	2.9

[a]Pulmonary infiltrate with eosinophilia with no specific underlying etiology.

identifiable extrinsic etiology while the remainder were idiopathic in nature. We are presuming that the latter had intrinsic causes, but definitive diagnoses were not established. We also tended to classify most as idiopathic chronic eosinophilic pneumonia (ICEP) or Carrington disease for two main reasons known with this condition: its close relationship with asthma and its exceptional response to corticosteroid therpy.[17,18] In addition, no other etiologies were identified during the follow-up period. Bronchial asthma has been reported in 30% to 50% of patients with chronic eosinophilic pneumonia.[10] In Saudi Arabia, the prevalence of asthma has been on the rise recently.[19] Not all patients with asthma have clinically significant symptoms and are diagnosed or treated in a timely fashion. In our series, asthma was diagnosed in more than half of them. Furthermore, the positive response to glucocorticoid treatment was achieved in more than 95% of our patients with idiopathic pulmonary eosinophilia. Therefore, these findings strengthen the likelihood of ICEP as the main diagnosis in our patients, as postulated earlier.

These findings are also interesting from another angle. The rate of identifiable extrinsic etiologies in our series was relatively low. We diagnosed only two patients (5.7%) with tuberculosis causing pulmonary eosinophilia. This has been reported previously.[20] This is surprinsingly low in a country where tuberculosis is prevalent, and probaly even underdiagnosed.[21] Furthermore, one single case (2.7%) of AEP was identified. Again, this finding is extremely low, knowing that the prevalence of cigarette smoking is high in the Saudi population,[22] and any change in the smoking habit is associated with the development of AEP.[23] It is possible that such less-severe and transient cases were presented to primary care centers and general hospitals, and that only the more severe and symptomatic cases came to our study hospitals (which are tertiary care hospitals). One case of peripheral eosinophilia Wegener granulomatosis was reported in our series; however, this has also been reported previously.[24,25]

Pulmonary eosinophilia was reported to have a gender predilection. Some studies report a female preponderance, while in our series the opposite was observed (57%). Symptoms reported by patients in our series were diverse and well known for their association with pulmonary eosinophilic syndromes. Cough, dyspnea, fever, followed by other presentations such as wheezing are documented and recognized.[26] Bronchoscopy with BAL demonstrated a high eosinophil level in the eosinophilic lung. This finding, associated with the clinical presentation, peipheral eosinophilia, and the radiographic evaluation is helpful in the diagnosis. Extremely rare cases of ICEP without eosinophils in the bronchial lavage can occur occasionally.[27]

In keeping with previous studies, radiographic presentations in our series were varied. In the eosinophilic lung, all forms of parenchymal opacities can be observed in both standard radiography and CT, the latter being better in demonstrating the ground-glass appearance.[28,29] Mediastinal adenopathies and pleural effusions are also common findings.[30]

Most of our patients responded well to the classic therapy with corticosteroids. This treatment can be administered in its intravenous, oral, or inhaled forms, with a variable treatment duration.[18,31] Our patients also did very well with glucocorticoid treatment. This treatment reversed not only the respiratory symptoms of this disease but also possibly the extrapulmonary eosinophilic manifestations. Padi and colleagues reported a reversal of left bundle branch block in a young female with severe eosinophilia, fever, wheezing, and abnormal CT chest findings after treatment with steroids.[32]

In conclusion, pulmonary eosinophilic syndromes remain rare, but challenging. They can have diverse clinical symptomatology and a wealth of radiographic presentations seen with other much-common pulmonary conditions. Clinicians should be alert to these syndromes and must think of them in the differential diagnoses of any lung disease. Eosinophilia can provide an important clue toward clinching the diagnosis. Bronchoscopy with BAL and, occasionally, lung biopsy remain the gold standard for establishing the diagnosis. Certainly more prospective studies are needed to better elucidate the scope of these syndromes in areas where trigger factors (such as asthma, cigarette abuse, medication use) are on the rise.

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