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Review Article

Chronic Eosinophilic Pneumonia

Idiopathic Chronic Eosinophilic Pneumonia: A Rare Condition

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Abstract: Respirational and universal indications that be chronic or acute, blood and alveolar eosinophilia, and distal respiratory infiltrates on chest imaging describe idiopathic-chronic-eosinophilic-pneumonia (ICEPn). Most individuals have eosinophilia, which is generally more than 1000/mm^3. The lack of substantial blood eosinophilia syndrome reinforces an identification of ICEPn. Eosinophilia in the Bronchoa-Alveolar-Lavage(BrAL) is usually linked with elevated eosinophil levels. ICEPn is an uncommon condition with an unknown origin. Its precise prevalence needs to be clarified. ICEPn can affect anybody at any age, although it is more common in children. It affects women twice as much as males. Asthma affects one-third to one-half of all ICEPn patients. Systemic corticosteroids are the source of ICEPn therapy. Outlying blood eosinophilia may be evident during the initial case presentation, but it might be missing or delayed, particularly in smoking-related AEPn. Our review is focused on ICEPn, Lung Diseases, Chest Imaging, Pathogenesis, and Pathology. The basis of treating AEPn of non-infectious etiology is the termination of exposure to the inciting substance (e.g., smoking) and glucocorticoids. If AEPn is identified and treated promptly, the prognosis is typically favorable, with early and full clinical recovery.

Keywords: Idiopathic-Chronic-Eosinophilic-Pneumonia-(ICEPn), Respiratory Distress, Lung Diseases, Chest Imaging, Pathogenesis and Pathology

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1. INTRODUCTION

Chronic-Eosinophilic-Pneumonia can be identified by peripheral blood eosinophilia (defined as an eosinophilic count > 500X10^9 cells/L), raised eosinophils in BrAL fluid (defined as > 5% eosinophils in the differential cell count) or eosinophilic infiltration of lung parenchyma displayed on lung biopsy specimens[1]. Some researchers divide eosinophilic lung illnesses into primary and secondary disorders based on the lack or presence of an identified root cause. The main eosinophilic illnesses are further classified as regional and lung-limited disorders, with the latter group encompassing Idiopathic-Acute-Eosinophilic-Pneumonia (AEPn), ICEPn, and simple pulmonary eosinophilia, commonly known as Loeffler syndrome[2]. In certain disorders, eosinophils are increased in the blood but not in the lung tissue; in others, eosinophilia is elevated in the lung tissue and not in the peripheral blood. Others may have lung eosinophilia despite radiographic signs of illness. Given that eosinophilia exists in a diversity of diseases, the initial phase in identifying pulmonary eosinophilic syndromes is to distinguish among cases where eosinophilia is high and cases where eosinophilia is supplementary to an individual event, for illustration, a carcinoma, an infection, a drug reaction or another pulmonary scenario such as asthma[3]. Eosinophilia is a symptom of a variety of lung illnesses. In certain disorders, eosinophils are raised in the circulatory system nevertheless, not at all lung tissue; in others, there is an increase in both; there may be substantial eosinophilia in the lung tissue but not in the peripheral blood[4]. Rapid and chronic eosinophilic pneumonia are the two primary parenchymal eosinophilic disorders. Even though these entities are widely regarded, it is critical to detect idiopathic diseases, and both illnesses can be linked to a diverse range of issues that must be addressed and recognized for best management. In this review, we concentrate on recent improvements in our comprehension of AEPn[5]. Eosinophils are elevated in the blood yet not in lung tissue; in other words, there might be substantial eosinophilia in the tissue of the lungs but not in the blood. The blood in the extremities, others may have pulmonary eosinophilia without any additional symptoms[6]. The presence of illness can be seen on radiographs. Eosinophilia is a symptom of a variety of lung disorders. Others might have lung eosinophilia without any radiographic signs of illness[7]. Since eosinophilia is a critical feature of such numerous illnesses, the initial phase in categorizing pulmonary eosinophilic syndromes is to differentiate between primary pulmonary eosinophilic lung disorders and those where the eosinophilia is secondary to a particular trigger. Eosinophilic pneumonia is distinguished by the presence of eosinophilia in lung tissue on histology or by increased eosinophils in BrAL fluid. It might also be inferred from increased peripheral blood eosinophils and penetrates on chest radiographs.

2. DEFINITION

Chronic-Eosinophilic-Pneumonia (CEPn) is a category of heterogeneous parenchymal lung diseases, defined by polymorphonuclear eosinophilization of the lung interstitium and alveolar regions with preservation of lung morphology[8]. It is categorized by a widespread range of clinical and radiological findings, ranging from mild, self-limiting disease to unadorned, life-threatening illness[9]. Treatment focuses on controlling the underlying cause, such as asthma or allergies, and improving symptoms. Corticosteroids are commonly used to reduce inflammation[10]. Bronchiolitis is a lower airway infection of the lungs caused by viruses or bacteria. It is most common in infants and young children. Symptoms include wheezing, coughing, difficulty breathing, and a bluish tint to the skin due to lack of oxygen. In severe cases, it can be a source of respiratory failure. Treatment includes supportive care such as oxygen therapy, hydration, and rest. In a few cases, corticosteroids can reduce inflammation and improve symptoms. Blood-eosinophilia is defined as having an eosinophil blood-cell count more than 0.5 X *10^9/L, and hypereosinophilia as having an eosinophil blood cell count higher than 1.5 X* 10^9/L on at least two examinations separated by a minimum of a month 3-5[11-13]. Alveolar eosinophilia is determined by a difference in cell count of no less than 25 percent eosinophils at BrAL, usually exceeding forty percent. It is a sign of a primary illness or sickness, such as an allergic reaction, asthma, parasitic infection, or cancer. It is used as a marker for diagnosing and monitoring these conditions.

3. CLASSIFICATION

CEPn can manifest as chronic or acute pneumonia or the temporary Loffler syndrome, frequently initiated by parasites. An increase of eosinophils, a type of white blood cell, in the pulmonary alveoli and the surrounding bronchioles[14] characterizes it. Symptoms include squatness of breath, chest pain, cough, and fever. Treatment involves corticosteroids, antibiotics, and anti-parasitic drugs. In a few cases, the source of the CEPn can be unknown, and potency can result from an allergic response to an environmental allergen or a drug[15]. In other cases, the cause can be identified as a parasite, fungus, or virus. The sternness of the condition will depend on the cause and the degree of inflammation in the lungs. The most common causes are drug or toxin exposure and fungal infection; nevertheless, chronic eosinophilic pneumonia is sometimes idiopathic, whereas AEPn is frequently associated with medicines or cigarette smoking. In a few cases, the basis of CEPn might be identified as a parasite, fungus, or virus[7]. However, in other cases, the cause may be unknown, making it hard to determine the sternness of the condition and the best course of treatment. In these cases, it is important to consider any possible drug or toxin exposure and fungal infection, as these could be the fundamental source of the condition.

4. EOSINOPHILS AND IMMUNITY

Eosinophils have a substantial function in natural immunity. Through cell membrane signaling compounds and receptors such as Toll-like receptors and receptors for cytokines, complement, and immunoglobulins, they collaborate with mast cells, macrophages, endothelial cells, fibroblasts, platelets, and basophils[16]. Metalloproteases, chemoattractants, enzymes, arachidonic acid-derived mediators, complement proteins, chemokines, reactive oxygen species, Pro-inflammatory cytokines, and cationic proteins are released by activated eosinophils[17]. The degranulation of activated eosinophils produces the latter and has a range of functions, including direct cytotoxicity, chemoattraction upregulation, adhesion molecule expression, vascular permeability modulation, and smooth muscle cell contraction[18]. Individuals with eosinophilic pneumonia have activated, degranulated ("hypodense") eosinophils in their BrAL and lung tissue. The cardiac damages noticed in hypereosinophilic syndrome or tropical eosinophilia are manifestations of tissue destruction controlled by eosinophil cationic proteins[19]. Through interactions with T-lymphocytes, eosinophils play a vital role in developing immunity towards bacteria, viruses, and malignancies. In the

major histocompatibility complex class II framework, they deliver antigens to T-helper-2 cells in tissues and drain lymph nodes, stimulating T-cell growth, stimulation, and emigration to areas of illness.

5. IDIOPATHIC-CHRONIC-EOSINOPHILIC-PNEUMONIA-(ICEPN)

ICEPn, first described by Carrington and peers, is well-defined by the progress of weight loss, dyspnea, malaise, and cough during a couple of weeks, with widespread lung infiltrates. An eosinophilic infiltrate is seen on chest radiography and confirmed by transbronchial or open lung biopsy[20]. Treatment usually involves systemic steroid therapy, and the prognosis is usually satisfactory with appropriate treatment [21]. However, cases of ICEPn can be complicated by the presence of underlying conditions, such as asthma or COPD, which can make diagnosis and treatment more difficult. Additionally, the presence of ICEPn can increase the possibility of developing more serious respiratory situations, such as pulmonary fibrosis. CEPn is a sneaky illness with symptoms lasting 7-8 months before a clinical diagnosis. It is because the symptoms of ICEPn can be similar to those of other illnesses, making diagnosis problematic[22]. Additionally, the long-term effects of ICEPn can be serious, as the disease can cause permanent lung destruction and increase the possibility of developing other respiratory conditions. CEPn should be measured in individuals suffering from growing breath difficulty for several months and have radiographic evidence of bilateral peripherally localized opacities. Furthermore, it is linked to peripheral blood eosinophilia. It is vital to note that the analysis of ICEPn must be confirmed with a BrAL or a transbronchial biopsy. Treatment includes corticosteroid therapy and specific anti-inflammatory medications. Fig-01

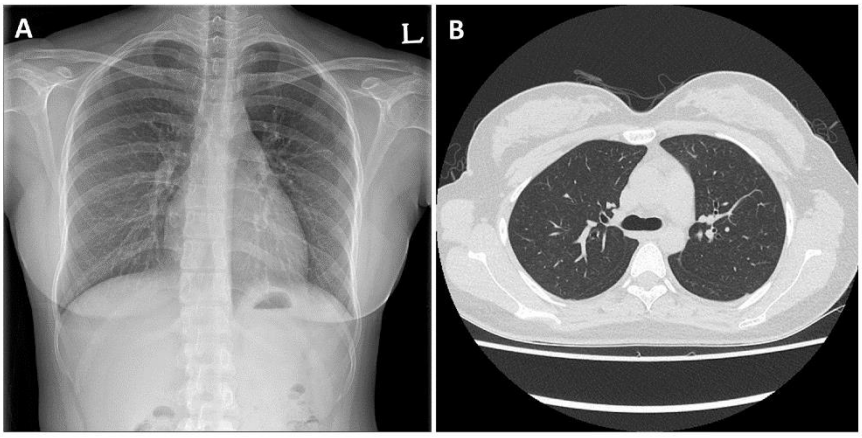

Fig 1- A Chest X-ray (A) and CT scan (B) of a patient with persistent eosinophilic pneumonia[23]

6. EPIDEMIOLOGY AND RISK FACTORS

ICEPn is a rare lung disease characterized by inflammation of the lungs, the reason for an accumulation of white blood cells called eosinophils[24]. Eosinophils are typically involved in allergic reactions, but their role in ICEPn is not fully understood. ICEPn is more common in women than men, with a female-to-male ratio 2:1[25]. It may happen at any stage of life, but the average age of diagnosis is 45 years old. There is no established genetic predisposition for ICEPn. People with ICEPn often have a history of allergies or asthma. About two-thirds of ICEPn individuals have a history of allergies, and about half have a history of atopy, a group of allergic conditions including hay fever, asthma, eczema, and food allergies. ICEPn is a rare disease but is the most collective eosinophilic pneumonia in non-tropical areas where parasitic infections are uncommon[26]. Eosinophils are typically elaborate in the body's immune response to parasites. The symptoms of ICEPn can vary from person to person, but they often include cough, shortness of breath, fatigue, fever, and weight loss. In some cases, ICEPn can also cause chest pain, wheezing, and skin rashes. The analysis of ICEPn is by an amalgamation of medical history, physical examination, chest X-ray, and lung biopsy[27]. The chest X-ray may show diffuse infiltrates, which are areas of inflammation in the lungs. The lung biopsy will show an increased number of eosinophils in the lungs. There is no cure for ICEPn, but it can be treated with medications that reduce inflammation, such as steroids and immune-suppressants. Treatment usually results in a good outcome, with most individuals fully recovering.

7. CLINICAL DESCRIPTION

The manifestation of ICEPn is gradual or subacute, with indications appearing weeks or months before the diagnosis. A shortness of breathing is the supreme shared clinical sign, occurring in between sixty percent and ninety percent of individuals. Cough (90%), rhinitis or sinusitis (20%), and, in occasional circumstances, chest discomfort or hemoptysis (10% or fewer) are also possible[25]. At examination, one-third of individuals have wheezes or crackles. Respiratory failure demanding mechanical ventilation is infrequent in ICEPn, as opposed to the common respiratory failure seen in IAEPn[26]. Fatigue, malaise, fever, anorexia, night sweats, and weight loss (sometimes severe) are common systemic symptoms. There were a few reports of extrathoracic indications, such as pericardial effusion, arthralgias, nonspecific cutaneous signs, and abnormal liver function tests; nonetheless, any major extrathoracic manifestation ought to indicate the possibility of EGPA[28]. Breathlessness and cough are common respiratory symptoms. The intensity of dyspnea varies greatly. In opposition to ICEPn, respiratory letdown demanding mechanical ventilation is quite rare. In almost half of the instances, wheezing develops. The results of chest auscultation are non-specific, with probable inspiratory crackles or expiratory wheezes. ICEPn lacks extrathoracic characteristics. When extra-pulmonary symptoms and indications are current, a diagnosis of Churg-Strauss-Syndrome (CSS) or Idiopathic-Hypereosinophilic-Syndrome (IHS) needs to be explored[29]. When extra-pulmonary symptoms and indications appear, the possibility of CSS or IHS should be explored[30]. Nevertheless,

a few individuals with a preliminary diagnosis of ICEPn can get mild extra thoracic symptoms without meeting the diagnostic conditions for CSS or IHS. The condition has a slow start, with an average of seven to eight months between the arrival of indications and diagnosis [31]. A persistent cough, fever, dyspnea, loss of weight, and night sweats are all possible symptoms. Hemoptysis, chest discomfort, and myalgias are uncommon symptoms. In the utmost circumstances, a physical examination will detect wheezing and crackles but will be unremarkable. Individuals often need to be better appearing. While a lung biopsy is not required for diagnosis, pathology may reveal extensive alveolar destruction and eosinophilic infiltration. Fig-02

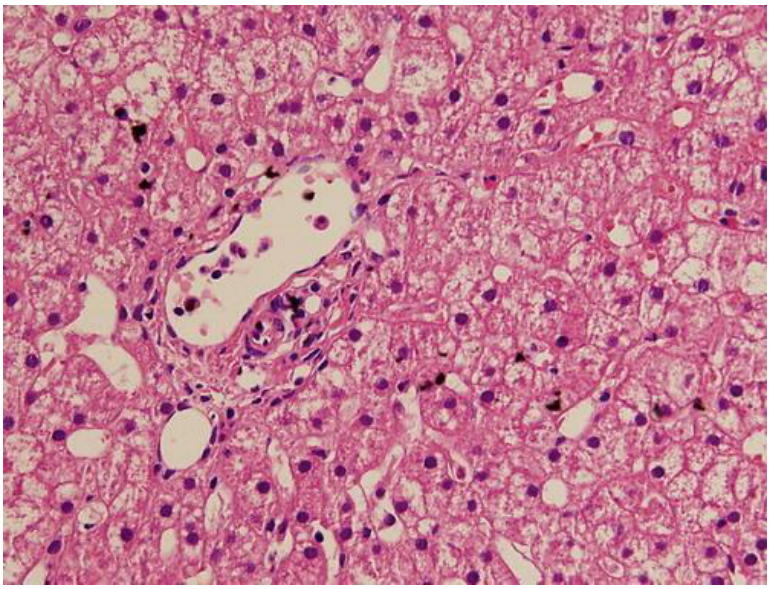

Fig 2 - A transbronchial lung biopsy revealed persistent eosinophilic pneumonia.[32]

8. CHEST IMAGING

The imaging signs of ICEPn are frequently recognizable but vague and may be recognized on a chest radiograph in nearly all instances before therapy. Roughly 25% of patients comprise bilateral alveolar infiltrates with ill-defined boundaries, with a characteristic peripheral predominance[33-35]. The uncontrolled transfer of opaqueness reported in a quarter of the individuals supports ICEPn or cryptogenic organizing pneumonia. Confluent reorganizations and ground-glass opacities, nearly usually bilateral and prevailing in the upper lobes and peripheral sub-pleural regions, are characteristic findings on excellent quality computed tomography (HRCT). Corticosteroid treatment causes imaging abnormalities to resolve rapidly. In roughly 75 percent of instances in the right environment, this pattern is sufficiently common to indicate the cataloging of ICEPn. On chest imaging, ICEPn is distinguished by peripheral parenchymal infiltrates[25]. These infiltrates might be unilateral or, most commonly, bilateral. Some of the most striking chest X-ray pictures seem like a snapshot of acute pulmonary edema. This normal outline is missing in the popular ICEPn instances and is not unique to the condition. Alveolar parenchymal infiltrates range from ground-glass opaqueness to alliance with air bronchogram[36]. They are occasionally migratory. Pleural effusion is unusual. CT imaging may reveal distinct ground glass opaqueness not seen on X-rays. CT is frequently used to detect bilateral parenchymal abnormalities. Enlargement of the mediastinal lymph nodes has been documented[37]. Clinical and radiological characteristics individuals arrive with a subacute disease that lasts weeks to months, categorized by a cough, low-grade fevers, increasing dyspnea, weight loss, wheezing, malaise, night sweats, and a chest radiograph showing migrating bilateral, peripheral, or pleural-based opacities. Despite this "photographic-negative pulmonary edema" on chest radiographs and chest CT is pathognomonic of persistent eosinophilic pneumonia," it occurs in less than 25% of individuals[25]. Bilateral, diffuse, mixed ground glass and reticular opacities are seen on chest radiographs. Bilateral pleural effusions are also possible. While not required for AEP diagnosis, a chest CT scan aids in better pinpointing both the spatial distribution of airspace opaque areas and the optimal place to capture BAL fluid for diagnosis. CT results are well-known by dispersed, bilateral, patchy ground glass opaqueness dispersed randomly. A chest radiograph or CT scan of the chest could show symmetrical peripheral opacities, sometimes referred to as the "photographic negative" of lung edema and "classic" for CEPn. CEPn on HRCT often reveals airspace consolidation and ground glass attenuations. Airspace amalgamation with a mostly peripheral spread is typically used (Fig 03). Suppose sequential imaging is acquired; radiographic opaqueness in the upper lobe predominates fifty percent of the time and is frequently migratory. Pleural effusions, nodules, tooth decay, and reticulations are uncommon observations. Because several eosinophilic lung illnesses have similar radiographic characteristics to CEP, CEP cannot be diagnosed solely on chest imaging.

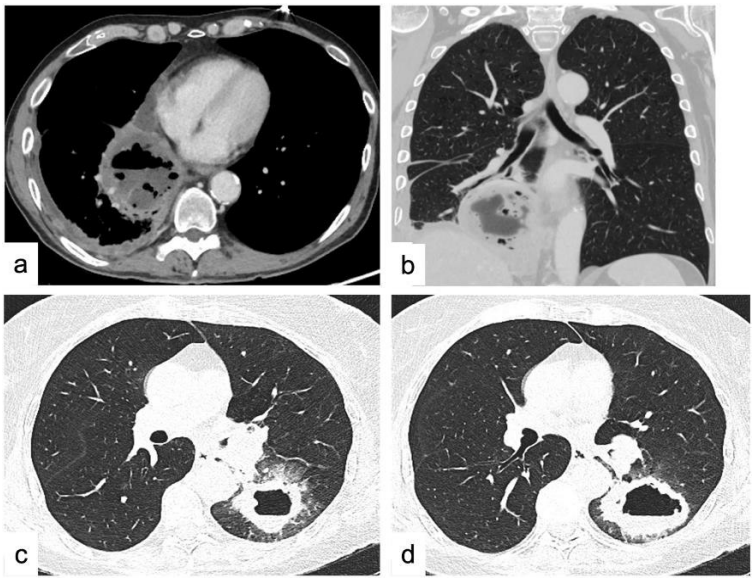

Fig 3 -Chest CT image of an individual with CEPn- (a) Coronal view (lung window) (b) in a 72-year-old individual who had been suffering from fever, cough, and chest discomfort for a few weeks, had laboratory testing that revealed infection, and was refractory to first-line antibiotic therapy. Inner air-fluid level, rim contrast enhancement, and clinical findings all point to a lung abscess. CT axial scans (lung window) (c,d) in a 68-year-old male individual: the existence of an air-fluid inner stage might indicate a lung abscess, but a shortage of clinical proof of infection, thick walls, ground-glass opacities in the adjacent pulmonary parenchyma, and tiny satellite pulmonary nodules indicate squad-monocellular lung cancer.[38]

9. LABORATORY FINDINGS

The main clue to the identification of ICEPn is high-level blood vessel eosinophilia. It means that there are a high number of eosinophils in the blood vessels. Eosinophils are a type of white blood cell involved in allergic reactions. In ICEPn, the eosinophils are thought to respond to an unknown trigger, which causes them to accumulate in the lungs and damage the tissue. The average number of eosinophils in the blood of people with ICEPn is between 5 and 6000/mm^3. [25] This represents between 20 and 30% of the blood leukocytes. The eosinophil count in the BrAL fluid is often higher than 40%. BrAL fluid is a fluid model collected from the lungs using a thin tube[26]. It is a good way to measure the quantity of eosinophils in the lungs. Sputum eosinophilia is possible in people with ICEPn, but it is less useful for diagnosis. Sputum is a mixture of mucus and cells coughed up from the lungs. Eosinophils in the sputum can be a sign of ICEPn, but other circumstances, such as asthma or allergic bronchitis, can also cause it. The Erythrocyte-Sedimentation-Rate (ESR) and C-reactive-protein (CRP) are two blood tests that could be cast to measure inflammation[39]. The ESR is a measure of how quickly red blood cells settle in a tube of blood. The CRP is a protein produced by the liver in reaction to inflammation. Both the ESR and CRP are often elevated in people with ICEPn. Total immunoglobulin E (IgE) is an antibody involved in allergic reactions [40]. The levels of IgE are often enlarged in people with ICEPn, but this is not specific to the disease. IgE levels can also be increased in people with other allergic conditions, such as asthma and allergic rhinitis. In summary, the main clue to identifying ICEPn is high-level blood vessel eosinophilia[41]. Other findings that can be helpful in diagnosis include increased ESR, CRP, and IgE levels. However, these findings are not specific to ICEPn and can be realized in other conditions.

10. PATHOGENESIS

The pathophysiology of ICEPn is thought to be a direct result of eosinophil lung colonization. These resources show that eosinophils are thought to be the main cause of the disease[42]. Eosinophils are a type of white blood cell involved in allergic reactions. They release chemicals that can damage lung tissue. Studies have shown that eosinophils from ICEPn patients release more pro-inflammatory chemicals and have higher levels of activation markers than eosinophils from healthy people[43]. It suggests that the eosinophils in ICEPn individuals are more activated, causing more lung damage. Pulmonary function tests are accustomed to measuring the lungs' capability to function [44]. In ICEPn, pulmonary function tests can show either a restrictive or a convoluted pattern. A restrictive pattern means that the lungs cannot expand and a convoluted pattern confirms the lungs are filled with fluid or other material [45]. The latter pattern is more common in people with a history of asthma. It is because asthma is also a condition that can cause lung inflammation. Spirometry is a test that measures the amount of air that can be breathed in and out. In equal to one-third of circumstances of ICEPn, spirometry remains within normal ranges. It implies that the lungs can still function normally, even though inflammation is present. Displacement tests measure the diffusion of Carbon Monoxide (CO) across the alveolar-capillary membrane[46]. The alveolar-capillary membrane is the thin layer of tissue that separates the air in the lungs from the blood in the capillaries. A decreased CO transfer factor (DLCO) means that the CO is not diffusing across the alveolar-capillary membrane as well as it should. It is a sign of lung damage [47]. The CO transfer coefficient-(KCO) measures the CO transfer factor adjusted for the patient's lung volume. Up to one-quarter of ICEPn individuals have a decreased KCO. When certain parasites or fungi bind to airway or alveolar epithelial cells, they can trigger inflammatory signals that release IL-33 and thymic stromal lymphopoietin (TSLP) [48]. These cytokines are powerful initiators of type 2 immunity, often characterized by the recruitment of eosinophils and T cells that secrete canonical T-helper (Th)-2 cytokines such as IL-5. (See Fig 04.) Arterial blood gases measure the oxygen and carbon dioxide levels in the blood. In ICEPn, arterial blood gases typically show a slight to moderate hypoxemia. It means that the blood is not getting

enough oxygen[49]. In summary, the pathophysiology of ICEPn is believed to be a direct result of eosinophil lung colonization. It causes lung inflammation, leading to an obstructive or convoluted outline on pulmonary function tests. Spirometry may be normal in up to one-third of cases. Displacement tests frequently show a decreased DLCO, and up to one-quarter of individuals have a decreased KCO. Arterial blood gases typically show a slight to modest hypoxemia.

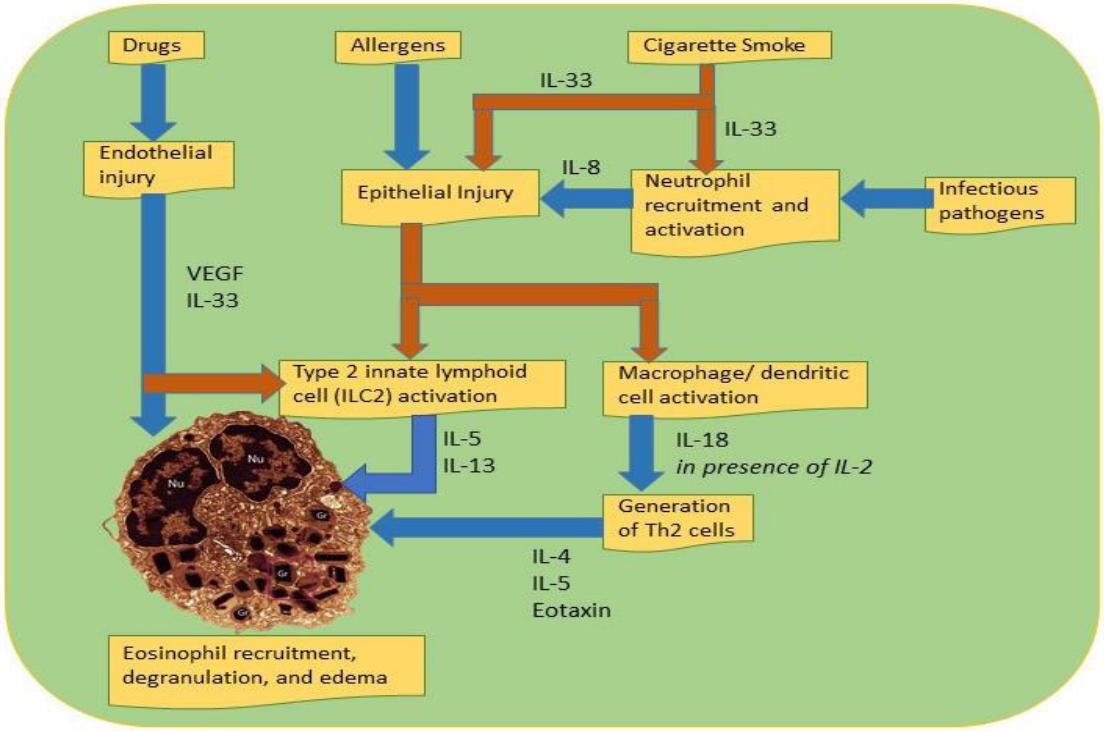

Fig-04-A model for the pathophysiology of CEPn is presented. Impaired epithelium cells may produce IL-33 in response to unpleasant stimuli such as allergens, pathogenic microorganisms, and additional inhalational toxins, including cigarette smoke. Endothelial cells may also produce IL-33 and vascular endothelial growth factor (VEGF) upon drug-induced damage. Along with IL-33, acute cigarette smoking causes epithelial cell production of IL-8, promoting neutrophil recruitment and activation. The activation of innate type 2 lymphoid cells, which can create IL-33 in response to specific stimuli quickly, might be another source of IL-33 in the lung.[50]

11. LUNG FUNCTION

The lung function in ICEPn individuals can vary from individual to individual. Roughly half of ICEPn individuals have airflow obstruction, while the other half have a restrictive ventilatory defect caused by pulmonary infiltration[51]. Airflow obstruction means that the airways in the lungs are narrowed, making breathing difficult. It can be indicated by inflammation, mucus production, and narrowing of the airways due to scar tissue[52]. Restrictive ventilatory defect means the lungs cannot expand as much as they should. Several things can indicate it, including inflammation, scarring, and fluid buildup in the lungs. In ICEPn, the restrictive ventilatory defect is indicated by pulmonary infiltration. Pulmonary infiltration is the gathering of fluid or other material in the lungs. In ICEPn, the pulmonary infiltration is caused by the accumulation of eosinophils, which are a type of white blood cell[53]. The imaging findings in ICEPn can also vary. In the circumstance of airflow obstruction, the imaging may show hyperinflation of the lungs. Hyperinflation is an abnormal increase in the size of the lungs. In the circumstance of restrictive ventilatory defect, the imaging may show ground-glass opacities. Ground-glass opacities are areas of hazy opacity in the lungs. Lung function testing can assess the severity of ICEP and monitor the response to treatment. In the case of airflow obstruction, lung function testing may show a decreased forced expiratory volume in one second (FEV-1) [54]. The FEV-1 measures how much air can be forcefully exhaled in one second. In the case of a restrictive ventilatory defect, lung function testing may show a decreased total lung capacity (TLC) [55]. The TLC measures the total volume of air in the lungs. The carbon monoxide transfers factor (DLCO) measures how well oxygen can move from the lungs to the blood. The DLCO is often decreased in ICEP individuals, even in those who do not have airflow obstruction. The carbon monoxide transfers coefficient (KCO) measures the DLCO adjusted for the patient's lung volume [56]. The KCO is also often decreased in ICEPn individuals. In summary, the lung function in ICEPn individuals can vary from person to person[57]. Roughly half of ICEPn individuals have airflow obstruction, while the significant other have an obstructive ventilatory defect caused by pulmonary infiltration. The imaging findings in ICEPn can also vary. Lung function testing can evaluate the severity of ICEPn and monitor the response to treatment.

12. PATHOLOGY

Pathology is distinguished by eosinophil infiltration of the lung interstitium and alveolar spaces, complemented by a fibrinous effusion and the maintenance of lung structure. There are also eosinophilic microabscesses, a non-necrotizing non-granulomatous vasculitis, and a few multinucleated large cells (but no granuloma), which reveals interstitial and alveolar inflammation with a significant eosinophil predominance. Although eosinophils may infiltrate pulmonary arteries, ICEPn does not have necrotizing or granulomatous vasculitis[58]. Lung biopsy is seldom carried out on AEPn individuals. Pathology is unnecessary for diagnosis, and individuals are frequently too ill to endure an open lung biopsy[59]. Histopathological results, if

tissue is recovered, often demonstrate acute and organized diffuse alveolar destruction with tissue and alveolar eosinophils[60]. Because the alterations are found heterogeneously across the sampling lung, the extent of illness is also severe. On histological inspection, EPn is distinguished by eosinophil infiltration of the lung parenchyma, but other inflammatory cells, including lymphocytes, plasma cells, and polymorphonuclear neutrophils, may be present[61]. The pathogenic abnormalities reported in ICEPn may be regarded as the mutual denominator of EPn. In some situations, they might be coupled with traits specific to the origin of EPn. Eosinophils (which might be degranulated) and a fibrinous discharge also fill alveolar gaps, preserving the lung's overall architecture. In ICEPn, particularly in IAEPn, eosinophilic microabscesses and non-necrotizing vasculitis are prevalent. The infiltration might comprise macrophages, dispersed multinucleated enormous cells, and eosinophilic particles or Charcot-Leyden crystals[62].

13. DIAGNOSIS

Table 2 contains the current ICEPn diagnostic criteria. Before the illness is ruled idiopathic, a comprehensive evaluation for probable reasons of eosinophilia, such as drug consumption, infections with parasites or fungus, and exposure to poisons or illegal substances, is critical. Although a BrAL can usually benefit individuals with suspected eosinophilic pneumonia and those with dispersed alveolar opaqueness on imaging, markedly elevated peripheral blood-eosinophilia combined with typical clinical, radiologic characteristics suggest ICEPn[63]. Type III and I immune responses against *Aspergillus fumigatus* or other fungi describe Allergic-Broncho-Pulmonary Aspergillosis (ABPA) alongside other allergic broncho-pulmonary mycoses[64]. High total IgE levels, central bronchiectasis, migratory pulmonary infiltrates associated with blood and alveolar eosinophilia, Asthma, positive right away and late skin tests when exposed to the causative agent, and positive specific IgE and precipitins are all symptoms of ABPA. Certain transitory parasite infections are linked with eosinophilia and pulmonary infiltrates. The pathogenic organisms Toxocara canis, Taenia saginata, Trichinella spiralis, and Fasciola hepatica are the causative agents[65]. Additional organisms must be searched in individuals who live in tropical locations or have a history of travel to tropical places: Schistosoma-haematobium, Brugia malayi, Wuchereria bancrofti, Schistosoma-mansoni, and Strongyloides stercoralis. Serologic tests and stool examinations are used to make the diagnosis[66]. One must rule out any of the numerous drugs or poisons that have been linked to eosinophilic pneumonia. It is necessary to rule out Aspergillus colonization, which could be linked with allergic bronchopulmonary aspergillosis[67]. Contamination with other microorganisms is also possible. In the end, one must consider a thorough history and examination to rule out malignancies, various systemic disorders, including sarcoidosis, and lung diseases, such as pulmonary fibrosis and bronchiolitis obliterans, both of which can occur. Eosinophilia is a kind of allergy. Since all pulmonary eosinophilic disorders are distinct, they can be detected by blood, BrAL eosinophilia and lung infiltrates. It's critical to classify them. Indeed, it is frequently thought that all of these scenarios are linked and exist on a continuum, with some being unknown mechanisms in charge of directing eosinophils and their poisons to certain site organs, such as the lung. Yet a diagnosis may typically be made using clinical, laboratory, pathologic, and radiographic criteria (Table 1) [68]. For example, based on the rigorousness of symptoms, isolated pulmonary involvement with peripheral eosinophilia is linked to both acute and chronic eosinophilic pneumonia. In the utmost circumstances, the incidence of ANCA, vasculitis, and eosinophilia in a person with airway obstruction is sufficient to diagnose CSS. HES individuals have eosinophilia with multi-organ participation and may appear similar to CSS; nevertheless, these illnesses are not linked with vasculitis and frequently have no asthma as a predominant clinical characteristic. Yet a diagnosis may typically be made using various clinical, laboratory, pathologic, and radiographic criteria (Table 1).

Table 1-Characteristics of different eosinophilic pneumonia

Feature	Chronic eosinophilic pneumonia
Onset	Indolent (weeks/months)
Imaging	Peripheral
Fulminant respiratory failure	*
Asthma/allergy history	^
Smoking history	-
Vasculitis	-
Anti-neutrophil cytoplasmic antibody	-
Cardiac involvement	#
Neurologic	#
Requirement for therapies other than corticosteroids	-

- rarely occurs, ^ - commonly occurs, # - occasionally occurs

For example, founded on the relentlessness of symptoms, discrete pulmonary involvement with peripheral eosinophilia is linked to both acute or CEPn[69]. In most cases, the occurrence of ANCA, vasculitis, and eosinophilia in a person with airway obstruction is sufficient to diagnose CSS. HES individuals have eosinophilia with multi-organ involvement and may appear in similar ways to CSS; nevertheless, these illnesses are not linked with inflammation and frequently have no asthma as a predominant clinical characteristic. A variation of laboratory studies should be performed on the patient with eosinophilia and lung disease: complete blood cell count with differential, ESR, C-reactive protein, ANCA, vitamin B12, immunoglobulins including IgE, electrolytes and liver enzymes, tryptase, urinalysis, stool assessment for ova and parasites, and thoughtful deliberation of bone marrow analysis[70]. CEP is clinically and radiographically similar to other eosinophilic and

non-eosinophilic lung disorders. AEP is distinguished from CEP by its abrupt onset, lack of peripheral blood eosinophilia, and diffuse radiographic opacities. Comparable to CEP, ABPA has a history of asthma, peripheral blood eosinophilia, and upper lobe radiographic opacities[12,13].

Table 2- Diagnostic criteria ICEPn

Criteria	Description
1. Diffuse pulmonary alveolar consolidation	Accumulation of fluid in the air sacs of the lungs, with air bronchograms (airways filled with air that appear as dark streaks on imaging) and ground-glass opacities (areas of hazy opacity in the lungs)
2. Eosinophilia at bronchoalveolar lavage differential cell count >40%	Eosinophils make up more than 40% of the cells in the fluid that is collected from the lungs using a thin tube
3. Respiratory symptoms present for at least 2 to 4 weeks	Symptoms such as cough, shortness of breath, and fatigue have been present for at least 2 to 4 weeks
4. Other recognized manifestations of eosinophilic lung disease are not present.	There are no additional documented reasons for the lung illness, such as medication consumption that might result in pulmonary eosinophilia.

14. TREATMENT AND OUTCOMES

Therapy aims to elicit the depth of illness and lower the pathology of the disease while balancing the strength of treatment with the essential to limit corticosteroid side effects. A common protocol may include an initial dose of 0.5 mg/kg^{-1} day^{-1} of oral prednisone for two weeks, followed by 0.25 mg/kg^{-1} day^{-1} for two weeks[71] before corticosteroids are gradually lowered over six months and discontinued. Corticosteroids usually have a significant effect, with clinical improvement within 2 days and clearance of chest opacities within 1 week[72]. Relapses happen to more than half of these individuals when corticosteroids are reduced or stopped; nevertheless, they react extremely healthy to corticosteroid therapy when it is restored. Relapses are usually treated with 20 mg of prednisone each day. Individuals should be advised of the likelihood of recurrence as corticosteroids are gradually lowered and eventually discontinued[73]. This method decreases the individual's total exposure to long-term corticosteroids. Substantial comorbidity is connected with adverse events associated with oral corticosteroids and the possibility of chronic airflow blockage that may occur despite bronchodilators, inhaled corticosteroids, and, in many cases, oral low-dose corticosteroids. Oral corticosteroids are accustomed to manage ICEPn. After starting the therapy, symptoms and blood eosinophilia disappear within a few hours, and chest imaging findings return to normal within a few days. Because of this significant reaction to medication, corticosteroid challenge is considered a diagnostic test for ICEPn. Whereas corticosteroid therapy produces significant results and invariably results in a complete cure, relapses of ICEPn are found in as many as fifty percent of individuals[8]. Such relapses occur during the tapering of corticosteroid doses or after weaning. Relapses continue to be as sensitive to corticosteroids as the initial episode. To avoid relapses, inhaled corticosteroids were originally advocated. Many artificial intelligence (AI) technologies have sped up the clinical use of AI-enabled devices in the healthcare industry. Clinical applications of medical devices utilizing AI technology are underway in cancer and ICEPn[74].

15. CONCLUSION

ICEPn can be initiated by a diversity of conditions. Some eosinophilic pneumonias possess well-defined etiologies, such as parasite contaminations and drugs that cause pulmonary eosinophilia, but some, such as ICEPn, are idiopathic. Using the rare case of AEPn, which requires quick detection and therapy with corticosteroids for the probable intensity of the breathing disorder, most ICEPn are not immediately life-threatening. A full medical history and physical checkup, medication and travel history, laboratory evaluation to include assessment for peripheral blood eosinophilia, pulmonary function testing, chest imaging, and bronchoscopy are all required to diagnose eosinophilic lung disease.

16. AUTHORS CONTRIBUTION STATEMENT

Huma Firdaus developed the theoretical formalism. Both the authors Shadam sadaf and Maqsumi Reza contributed to the final version of the manuscript. All authors approved this study draft.

17. CONFLICT OF INTEREST

Conflict of interest declared none.

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