

***CHRONIC EOSINOPHILIC
PNEUMONIAS
CHURG-STRAUSS SYNDROME
IDIOPATHIC
HYPEREOSINOPHILIC
PNEUMONIAS***



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Idiopathic chronic eosinophilic pneumonia (ICEP)



Disease name and synonyms

- Idiopathic chronic eosinophilic pneumonia (ICEP);
- Chronic eosinophilic pneumonia (CEP);
- Carrington's disease

DEFINITION



- Idiopathic chronic eosinophilic pneumonia (ICEP) is a rare disorder of unknown cause characterized by subacute or chronic respiratory and general symptoms, alveolar and/or blood eosinophilia, and peripheral pulmonary infiltrates on chest imaging.

Diagnosis criteria



- There are no strict diagnostic criteria for ICEP. Diagnosis is usually based on the association of:
 - 1) respiratory symptoms of usually more than 2 weeks duration;
 - 2) alveolar and/or blood eosinophilia (alveolar eosinophilia $\geq 40\%$ at bronchoalveolar lavage (BAL) differential cell count; blood eosinophilia $\geq 1000/\text{mm}^3$);
 - 3) pulmonary infiltrates with usually a peripheral predominance on chest imaging;
 - 4) exclusion of any known cause of eosinophilic lung disease.

Epidemiology



- ICEP is a rare disorder. Its exact prevalence remains unknown.
- ICEP has been reported to contribute to 0-2.5% of total cases of interstitial lung diseases
- Most cases occur in Caucasians
- Twice as frequent in women as in men
- The peak incidence occurs in persons 30 to 40 years of age.
- One third to one half of the ICEP patients have a history of asthma
- Less than 10% are active smokers
- It has recently been reported that ICEP may be primed by radiation therapy for breast cancer

Clinical Features



- Symptoms are non-specific and usually include respiratory and general symptoms, which are either subacute or chronic.
- The symptoms are most often present for about a month before diagnosis is made.
- ***General manifestations***
- Asthenia, weight loss (sometimes marked), and nocturnal sweats or low grade fever
- ***Respiratory signs***
- Cough, often dry initially and later productive
- Progressive dyspnoea, which may be associated with wheezing
- Some patients with ICEP may also have severe acute respiratory failure or ARDS, with severe hypoxemia requiring mechanical ventilation

Extrathoracic manifestations



- Extrathoracic features are rare in ICEP
- When the symptoms and signs of extra-pulmonary involvement are present, a diagnosis of Churg-Strauss syndrome (CSS) or idiopathic hypereosinophilic syndrome (IHS) should be considered.
- A few patients with an initial diagnosis of ICEP, however, may develop minor extrathoracic manifestations without further fulfilling the diagnostic criteria for either CSS or IHS
- Rarely, arthralgias, skin rash, pericarditis or unexplained heart failure may be present suggesting a continuum between ICEP and CSS.

Laboratory findings



- Moderate leukocytosis
- Majority (66 to 95 percent) have peripheral blood eosinophilia ($>1000/\text{mm}^3$), with eosinophils constituting more than 6 percent of their leukocyte differential
- ESR is typically elevated (greater than 20mm per hour)
- IgE levels are elevated in up to one-half of cases.
- A moderate normochromic, normocytic anemia and thrombocytosis may be present

Chest imaging



- Three radiographic features that are characteristic for CEP
- (1) peripherally based, progressive dense infiltrates
- (2) rapid resolution of infiltrates following corticosteroid treatment, with recurrences in identical locations
- (3) the appearance of infiltrates as the “photographic negative of pulmonary edema.”

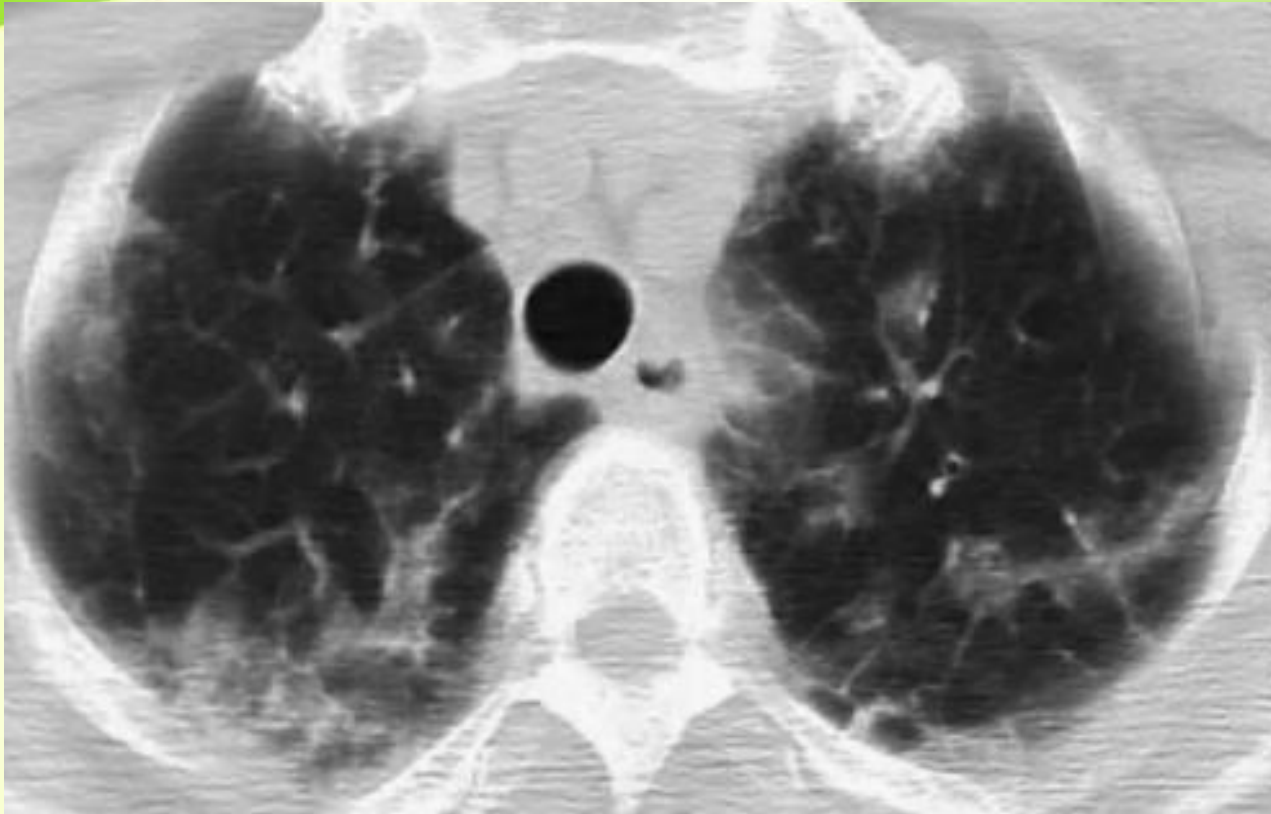
CT FINDINGS



- Ground-glass opacities
- Mediastinal adenopathy
- Nodular infiltrates
- Linear oblique or vertical densities
- Fibrosis



- Typical areas of dense, peripherally located airspace consolidation are found in most cases within the first several weeks of disease onset
- Streaky band like opacities may appear when symptoms have been present for more than 2 months



HRCT showing peripheral upper-lobe predominant infiltrates with ground-glass appearance



HRCT showing regions of dense consolidation or nodular opacity

Bronchoalveolar lavage



- Bronchoalveolar lavage in ICEP always reveals abnormally high levels of eosinophils, representing 12% to 95% (mean: 58%) of the total cell count
- Transbronchial biopsy, usually performed to rule out other diagnostic entities, may reveal eosinophil and mononuclear cell infiltrates.

Pulmonary function tests



- ICEP can be associated with either a restrictive or an obstructive pattern on pulmonary function tests.
- Spirometry remains within normal limits in up to one third of the cases
- Diffusion tests often show a reduced carbon monoxide (CO) transfer factor (DLCO) in up to one quarter of the patients with ICEP

Pathological findings



- Leukocytic infiltration of the alveolar airspaces and interstitium which are predominantly eosinophilic
- Distruption of the alveolar wall architecture, usually without causing wall necrosis.
- Focal edema of the capillary endothelium, focal type II epithelial cell hyperplasia, proteinaceous alveolar exudates, and multinucleated histiocytes within alveolar spaces can also be appreciated.
- A small percentage of lesions (less than 20 percent) may have frank intra-alveolar necrosis, eosinophilic microabscesses, or noncaseating granulomas.
- Biopsy specimens of lymph nodes from patients with intrathoracic lymphadenopathy reveal lymphoid hyperplasia and eosinophil infiltration

TREATMENT



- Corticosteroids are the mainstay of therapy for CEP
- Recommended regimen is prednisone (40 to 60 mg a day) continued until 2 weeks after resolution of symptoms and radiographic abnormalities.
- The dose of prednisone can then be tapered slowly.
- Treatment is usually maintained for at least 3 months and optimally for 6 to 9 months



- In most cases, treatment with steroids leads to
- Defervescence within 6 hours,
- Cough, and blood eosinophilia within 24 to 48 hours,
- Resolution of hypoxia in 2 to 3 days,
- Radiographic improvement within 1 to 2 weeks,
- Complete resolution of symptoms within 2 to 3 weeks,
- Normalization of the chest radiograph within 2 months.

PROGNOSIS



- The prognosis of CEP is generally favourable.
- Spontaneous remissions seldom occur in untreated patients.
- Patients may require 1 to 3 years of initial steroid treatment to control the disease, and up to 25 percent may require long-term maintenance treatment (2.5 to 10 mg prednisone a day) to remain disease-free.
- The lowest possible dose of steroid that suppresses disease activity should be used.



- Clinical, hematological, or radiographic evidence of relapse occurs in approximately one-third to one-half of patients when steroids are tapered or discontinued.
- Relapses may involve radiographic infiltrates in the same or different anatomic distribution compared to the original disease.
- Relapsing CEP must be distinguished from the development of new or worsening asthma

CHURG-STRAUSS SYNDROME



Disease name and synonyms

Allergic Angiitis and Granulomatosis

Allergic Granulomatosis and Angiitis

Eosinophilic Granulomatous Vasculitis

Churg-Strauss Vasculitis




- Churg-Strauss syndrome (CSS) is a systemic disorder characterized by asthma, transient pulmonary infiltrates, hypereosinophilia, and systemic vasculitis.
- Eosinophilic vasculitis may involve multiple organ systems, including the lungs, heart, skin, gastrointestinal tract and nervous system.
- The three main histological features found on the pathological examination of CSS cases are extravascular granulomas, tissue eosinophilia, and necrotizing vasculitis.
- Thus allergy and angiitis are the two hallmarks of CSS.

History and Diagnostic Criteria



- Churg and Strauss first described this syndrome in 1951 when they reviewed a number of autopsy cases that were previously classified as polyarteritis nodosa.
- These cases were atypical: they were associated with asthma and extravascular granulomas as well as systemic vasculitis.
- This disease is now known as “Allergic granulomatosis and angiitis” or “Churg-Strauss syndrome”.

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- In 1984, Lanham et al noted that not all patients have the extravascular granulomas, necrotizing vasculitis, or eosinophilic tissue infiltration and they emphasized a more clinical approach to this disease.
 - According to the Lanham criteria, CSS is defined by asthma, peripheral eosinophilia, and systemic vasculitis involving two or more organ systems.
 - According to the Chapel Hill criteria, CSS was defined as asthma and eosinophilia in association with eosinophil-rich and granulomatous inflammation involving the respiratory tract, with necrotizing vasculitis affecting small to medium-sized vessels.

- The most commonly used criteria are those developed by the American College of Rheumatology (ACR).
- The ACR criteria include both clinical and pathological features and classify CSS as the presence of four of the following six features



**Table 1.—American College of Rheumatology 1990
Classification Criteria for Churg-Strauss Syndrome**

Asthma

Eosinophilia > 10%

Paranasal sinus abnormality

Pulmonary infiltrates

Mono- or polyneuropathy

Extravascular eosinophils on biopsy


A patient has CSS if at least 4 of these 6 criteria are met. If 4 of 6 criteria are met, the sensitivity is 85% and the specificity is 99.7%

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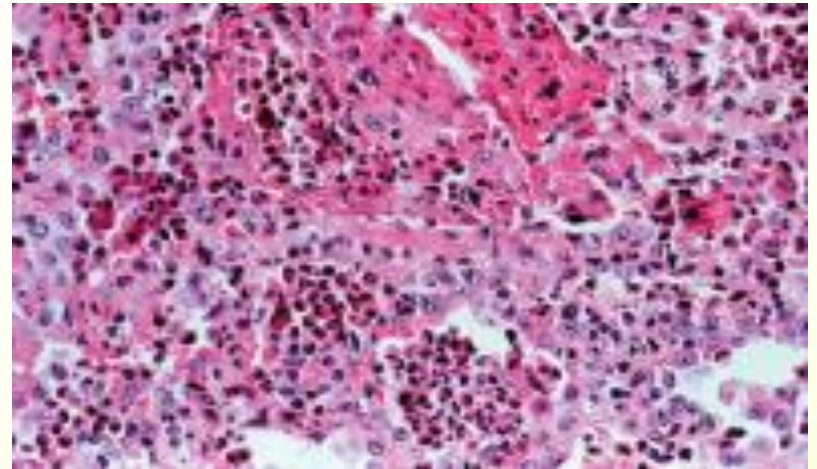
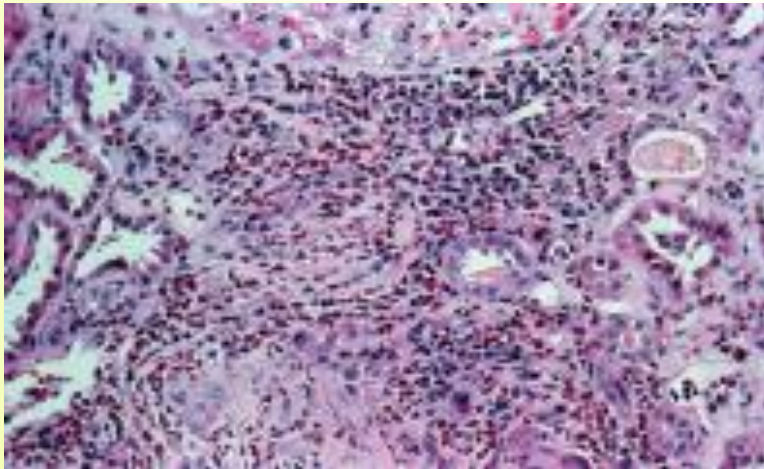
Etiology and Pathologic Features



- The exact etiology of CSS is unknown, it is believed that this syndrome likely represents an autoimmune process because of the prominence of
- allergic features and the presence of immune complexes,
- heightened T-cell immunity,
- altered humoral immunity,
- elevated immunoglobulin (Ig) E and rheumatoid factor.
- antineutrophil cytoplasmic antibodies (ANCA) are present in most patients with CSS.

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- The binding of ANCA to vascular walls contributes to vascular inflammation and injury as well as to chemotaxis of inflammatory cells, such as eosinophils, which can cause tissue damage with release of eosinophil cationic protein and other toxic granules.
 - CSS has been associated with various asthma therapies, including leukotriene modifiers, such as zafirlukast and montelukast, and inhaled corticosteroids, such as fluticasone and budesonide, but no causal link has been established.
 - It appears that the syndrome occurs coincidental to the use of these medications or that these medications facilitate systemic steroid withdrawal that unmasks the syndrome

- Pathologically, CSS is characterized by tissue infiltration by eosinophils, extravascular granulomas, and necrotizing vasculitis commonly involving the lungs, heart, skin, muscle, liver, spleen, and kidneys.
- Eosinophilic vasculitis predominantly affects small and medium-sized arteries and veins and may include fibrinoid necrosis and thrombosis.



Two tissue biopsy specimens from patients with Churg-Strauss syndrome, demonstrating extensive infiltration of the organs by eosinophils. The image on the left is a kidney biopsy specimen showing eosinophil infiltration, and the one on the right shows a lung biopsy specimen with eosinophil infiltration.



- CSS may occur in patients of any age, but it develops most commonly in patients **between the ages of 38 to 50.**
- Typically occurs in three phases
 1. Prodromal Phase
 2. Eosinophilic Phase
 3. Vasculitic Phase

Table 3: Clinical phases of Churg-Strauss Syndrome

Prodromal phase

“Late-onset” allergic disease, early twenties

See evidence of asthma (cough, wheezing, dyspnea)

Allergic rhinitis, (nasal obstruction, chronic rhinitis, nasal polyposis)

Eosinophilic phase

Marked peripheral eosinophilia, eosinophilic tissue inflammation

Typical organs involved include lungs, GI tract, and skin

Vasculitic phase

Constitutional symptoms (fever, myalgias, weight loss)

Cardiac symptoms: principle cause of death (coronary vasculitis, congestive heart failure, endocarditis, pericarditis)

Neurological symptoms (mononeuritis multiplex)

Skin symptoms (subcutaneous skin nodules)

Kidney disease

Respiratory symptoms



- The most common presenting manifestation of CSS is asthma, although as many as 2% of patients may develop airway symptoms after the onset of systemic vasculitis.
- Asthma often develops later in life, with a mean age of onset of 35 years, and it often occurs in individuals who have no family history of atopy
- Asthma is often severe, requiring treatment with oral corticosteroids to control symptoms, which may lead to suppression of vasculitic symptoms



- In some instances, asthma symptoms may abate as the vasculitis becomes manifest.
- Common symptoms of cough, dyspnea, sinusitis, and allergic rhinitis, alveolar hemorrhage and hemoptysis may also occur

Neurological symptoms



- Neurological involvement is the second most common manifestation and occurs in approximately 78% of patients.
- Mononeuritis multiplex most commonly involves the peroneal nerve but may involve the ulnar, radial, internal popliteal and occasionally, cranial nerve.
- Foot drop, is a common manifestation.
- Cerebral hemorrhage and infarction may also occur and are important causes of death.

Cardiovascular and GI symptoms



- Cardiomyopathy and heart failure may be seen in up to half of all patients
- Granulomas, vasculitis and widespread myocardial damage may be found on biopsy or at autopsy
- Gastrointestinal symptoms consist of an eosinophilic gastroenteritis characterized by abdominal pain, diarrhoea, gastrointestinal bleeding, and colitis.
- Ischemic bowel, pancreatitis, and cholecystitis also have been reported in association with CSS

Dermatologic symptoms



- Half of CSS patients develop dermatological manifestations.
- These include palpable purpura, skin nodules, urticarial rashes, and livedo reticularis. They usually present on the limb surfaces but can affect any part of the body.



Skin involvement in Churg-Strauss syndrome (CSS). Biopsy showed vasculitis of the skin and abundant eosinophils, which are characteristic in CSS.

Renal and Constitutional Symptoms



- Constitutional symptoms are very common in CSS and include weight loss, fever (commonly higher than 38°C for 2 weeks), and diffuse myalgias and migratory polyarthralgias.
- 25% of patients experiencing some degree of renal involvement.
- Renal involvement may include proteinuria, glomerulonephritis, interstitial nephritis, and renal failure.
- Renal biopsy may show focal segmental glomerulonephritis, crescents or other necrotizing features.
- Systemic hypertension is also common.

Diagnostic methods



- Systemic eosinophilia is the hallmark laboratory finding in patients with CSS
- **Eosinophilia greater than 10%** is one of the defining features of this illness and may be as high as 75% of the peripheral white blood cell count.
- It is present at the time of diagnosis in more than 80% of patients but may respond quickly (often within 24 hours) to initiation of systemic corticosteroid therapy
- **ANCA are present in up to two thirds of patients**, mostly with a **perinuclear staining pattern**
- Other nonspecific laboratory abnormalities that may be present in patients with CSS include a marked elevation in ESR, normochromic normocytic anemia, elevated IgE levels, hypergammaglobulinemia, and positive rheumatoid factor and antinuclear antibody.



- Bronchoalveolar lavage often reveals significant eosinophilia, which may be seen in other eosinophilic lung diseases
- Pulmonary function tests in Churg-Strauss syndrome may reveal a mixed pattern of obstructive and restrictive processes.
- This is a primary difference between asthma and Churg-Strauss syndrome. Asthma generally presents as a normal or obstructive process with reversibility.

Radiographic Features



- Chest X-ray Findings include
- Bilateral nonsegmental, patchy infiltrates that often migrate and that may be interstitial or alveolar in appearance
- Reticulonodular and nodular disease without cavitation
- Pleural effusions and hilar adenopathy



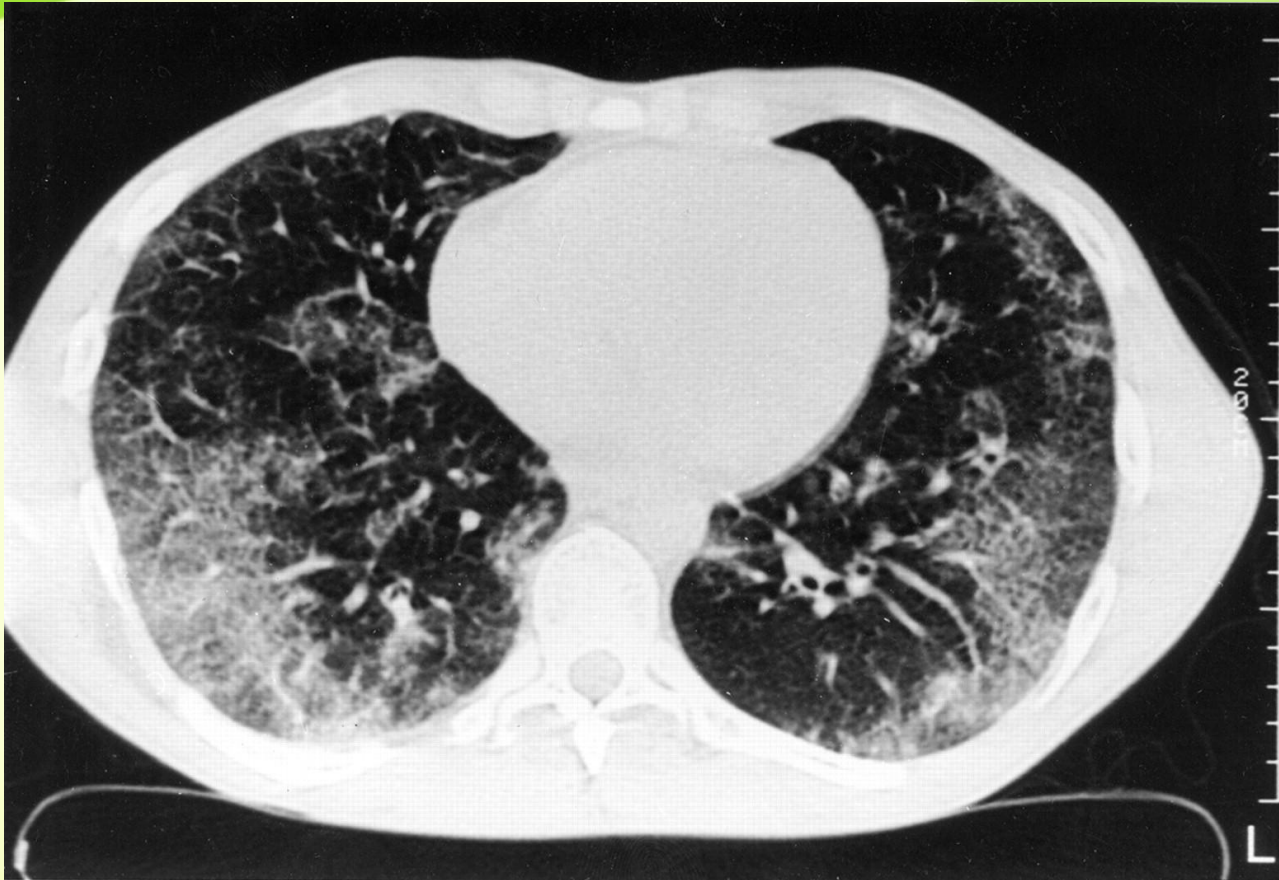
Chest radiograph showing progressive lung hemorrhage in a 73-year-old woman. Fluffy infiltrates in both lungs represent bleeding from damaged capillaries.



- The most common thin-section computed tomographic (CT) findings include bilateral ground-glass opacity and airspace consolidation that is predominantly subpleural and surrounded by the ground-glass opacity.
- Other CT findings include bronchial wall thickening, hyperinflation, interlobular septal thickening, lymph node enlargement, and pericardial and pleural effusions.



CSS in a 72-year-old asthmatic man who presented with chronic cough and dyspnea. He had a history of persistent eosinophilia and sinus polyposis. CT images (lung window) show small centrilobular nodules (arrows in a) and diffuse bronchial wall thickening (arrows in b), with some areas of tree-in-bud pattern.



Computed tomographic (CT) scan of a patient with Churg-Strauss syndrome showing a peripherally distributed parenchymal infiltrate that is also characteristic of eosinophilic pneumonia

HISTOPATHOLOGY



- A biopsy specimen with eosinophilic vasculitis is the best diagnostic test
- The most commonly biopsied sites include the skin, nerve, and muscle, although pathologic specimens may be obtained from biopsy of any affected organ system, including the
 - a. lung (by open-lung or thoracoscopic biopsy; transbronchial
 - b. biopsy is generally not helpful),
 - c. heart (by endomyocardial biopsy),
 - d. gastrointestinal tract (endoscopically),
 - e. liver, or kidney.

Differential Diagnosis



Table 3.—Diseases Associated With Pulmonary Infiltrates and Eosinophilia in the Differential Diagnosis of Churg-Strauss Syndrome

Churg-Strauss syndrome
Acute eosinophilic pneumonia
Allergic bronchopulmonary aspergillosis (ABPA)
Asthma
Bronchocentric granulomatosis
Chronic eosinophilic pneumonia
Drug reactions
Eosinophilic granuloma/histiocytosis X
Infections: bacterial, fungal, mycobacterial, and parasitic
Malignancy
Wegener's granulomatosis



Contrasting Features of Churg-Strauss Syndrome and Major Conditions in the Histologic Differential Diagnosis

	CSS	CEP	HES	BCG	WG
Blood eosinophilia	Yes, high	Occasionally present	Yes, high	Yes	Rare
Asthma	Yes	Occasionally present	No	Frequently present	No
Extrapulmonary involvement	Yes	No	Yes	No	Yes
ANCA	Yes (P-ANCA in 70%)	No	No	No	Yes (60%-90%), usually C-ANCA
Eosinophilic pneumonia	Yes	Yes	No	Yes	No
Necrotizing vasculitis	Yes	No	No	No	Yes
Necrotizing granuloma	Yes	No	No	Yes	Yes

ANCA, antineutrophil cytoplasmic autoantibody; BCG, bronchocentric granulomatosis; CEP, chronic eosinophilic pneumonia; CSS, Churg-Strauss syndrome; HES, hypereosinophilic syndrome; WG, Wegener granulomatosis.

Treatment and Prognosis



- Treatment with corticosteroids (starting at 1 mg/kg and tapering over 3 to 6 months) dramatically alters the course of CSS
- Pulses of methylprednisolone (15 mg/kg) may also be used for 1 to 3 days to obtain rapid control of life-threatening general symptoms
- Most patients diagnosed with CSS have previously been diagnosed with asthma, rhinitis, and sinusitis and have received treatment with inhaled or systemic corticosteroids.
- Because these agents are also the initial treatment of choice for CSS, institution of these therapies in patients with CSS may delay the diagnosis of CSS because signs of vasculitis may be masked



- 50% of those who are untreated die within 3 months of diagnosis, whereas treated patients have a 6-year survival of over 70%
- Common causes of death include heart failure, cerebral hemorrhage, renal failure, and gastrointestinal bleeding
- Clinical remission may be obtained in over 90% of treated patients; approximately 25% of those patients may relapse, often due to corticosteroid tapering
- Myocardial, gastrointestinal, or renal involvement most often portends a poor prognosis
- In such cases treatment with higher doses (1-1.5 mg/kg) of corticosteroids for longer time periods or the addition of cytotoxic agents such as cyclophosphamide may be done

Other Therapies



- Induction therapy with pulse cyclophosphamide (0.6 to 0.7 g/m²) is the most common alternative
- Azathioprine
- Intravenous gamma globulin
- Interferon alfa
- Plasma exchange
- Mepolizumab, an anti-IL-5 antibody, is under investigation with promising results
- *Pneumocystis jiroveci* prophylaxis with co-trimoxazole (400 mg/day or 800 mg thrice weekly) should be prescribed to patients receiving cyclophosphamide
- Physiotherapy in treating peripheral neuropathy motor deficiencies and sequelae.

Five-Factor Score (FFS)



- Prognostic FFS was obtained by univariate and multivariate analyses of 342 vasculitis patients
- The five factors (each accorded 1 point) conferring a higher risk of mortality rate were
 - (1) proteinuria > 1 g/24 hours;
 - (2) serum creatinine level > 140 (150 in the revised version of FFS) $\mu\text{mol/L}$;
 - (3) myocardial involvement;
 - (4) severe gastrointestinal involvement;
 - (5) central nervous system involvement.

Adding the assigned points gives clinicians a strong prognostic indicator of mortality because patients with FFS of 0, 1, or 2 had increasing 5-year mortality rates of 12%, 26%, or 46%, respectively

Idiopathic Hypereosinophilic Syndrome



- Disease name/Synonyms
 - Idiopathic hypereosinophilic syndromes (IHES)
 - Hypereosinophilic syndrome
 - Eosinophilic leukemia,
 - Loeffler's fibroplastic endocarditis
 - Disseminated eosinophilic cardiovascular disease

Definition/Diagnostic criteria



- The definition of “idiopathic” HES currently in use was proposed by Chusid in 1975:
- Defined as sustained peripheral blood eosinophilia of unknown origin, exceeding 1500/ μ l for more than 6 consecutive months, and responsible for the development of organ dysfunction and/or damage

Epidemiology and Etiology



- IHES is a rare disorder, and a diagnosis of exclusion
- It is a predominantly male disorder, with an estimated male to female ratio of 9:1.
- Disease tends to occur in patients aged from 20 to 50, but all age groups may be affected



- Three major pathogenetic and clinical variants of IHS have been reported

- (1) Patients with clonal abnormalities in eosinophils;
- (2) Patients with features of myeloproliferative disorder and chromosomal aberrations leading to abnormal constitutive production of tyrosine kinases;
- (3) Patients with dysregulation of T lymphocytes with overproduction of IL-5, a cytokine important for eosinophil growth, differentiation, and chemotaxis.

Clinical Features



- Symptoms vary according to the organ system(s) affected
- Involvement of virtually every organ system can occur
- Presenting complaints are often nonspecific and include weakness, fatigue, low-grade fevers, myalgias, cough, angioedema, rash, retinal lesions, and dyspnea

RESPIRATORY MANIFESTATIONS



- The respiratory system is affected in an estimated 40 percent of patients with HIS
- Nocturnal cough, which is either nonproductive or productive
- Wheezing and dyspnea are also common, without evidence of airflow obstruction on spirometric examination
- Pulmonary hypertension, ARDS, and pleural effusions may be seen

Cardiac and Neurological Manifestations



- Progressive CHF due to eosinophilic myocarditis and endocarditis, intracardiac thrombi, and endocardial fibrosis
- Restrictive cardiomyopathy or valvular dysfunction such as mitral regurgitation
- **Neurological manifestations of IHS include**
 - a. Encephalopathy with neuropsychiatric dysfunction,
 - b. Memory loss,
 - c. Gait disturbances with or without signs of upper motor neuron injury,
 - d. Visual changes
 - e. Hemiparesis

Other Manifestations



- Venous and arterial thromboembolism, anemia, thrombocytopenia, elevated vitamin B12 levels, hepatosplenomegaly, and lymphadenopathy (in 12 to 20 percent)
- GI (20 to 30 percent of patients), cutaneous (25 to 56 percent), renal (10 to 20 percent), musculoskeletal, ocular, and endocrine manifestations are all also well described

Diagnostic methods



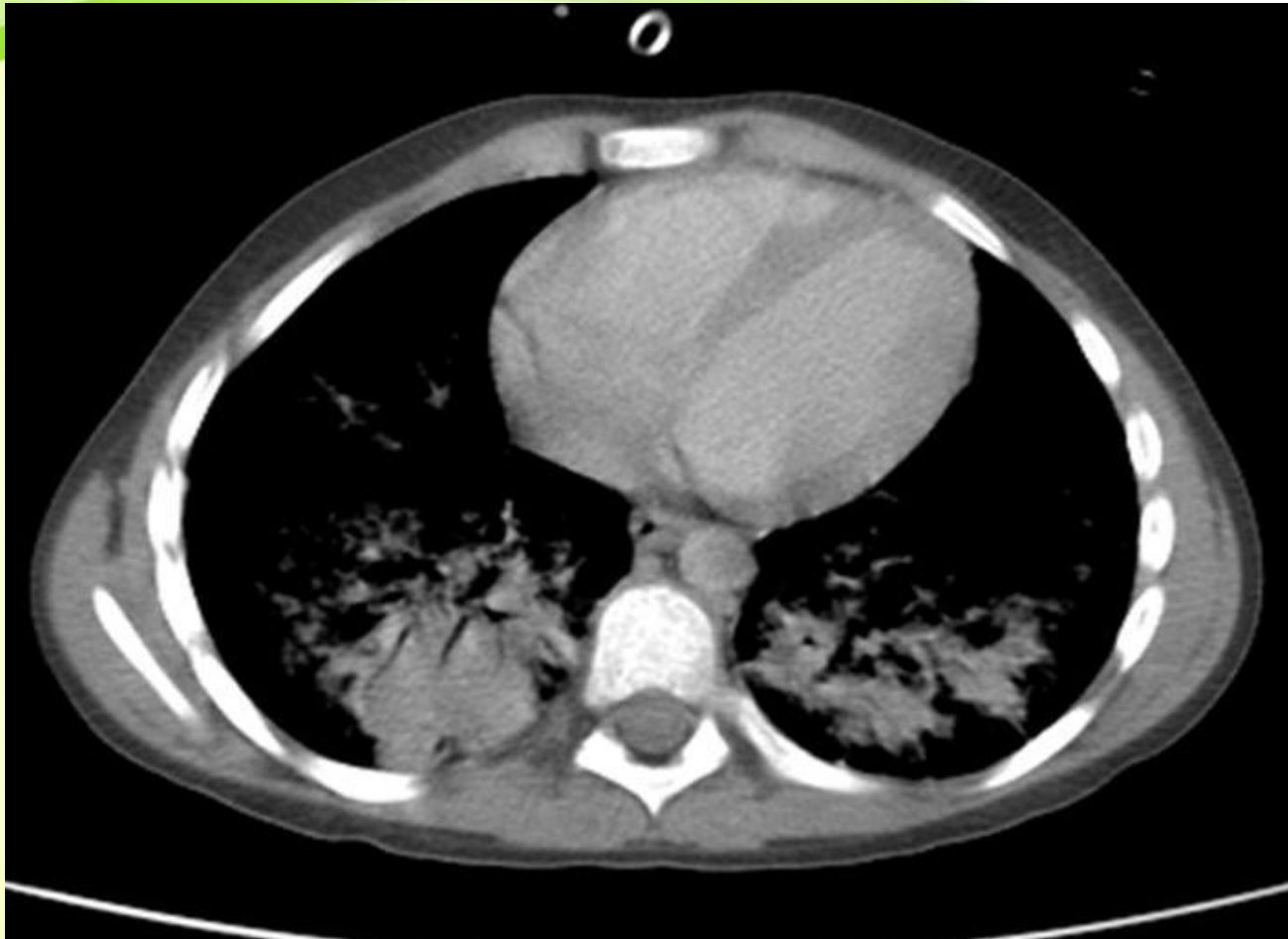
- When confronted with a new hypereosinophilic patient, the physician must first exclude all diseases known to be associated with hypereosinophilia before considering diagnosis of “idiopathic” hypereosinophilia
- Laboratory findings associated with IHS include an elevated
- Total serum IgE (25 to 38 percent),
- Hypergammaglobulinemia,
- Circulating immune complexes (32 to 50 percent),
- ESR above 15 mm/h (68 percent).
- Elevated serum B₁₂ and leukocyte alkaline phosphatase levels
- Blood and BAL eosinophilia are both prominent in persons with pulmonary involvement
- The diagnosis of IHS is established by demonstrating multi-organ dysfunction, severe peripheral blood eosinophilia (greater than 1500/ μ L) *for at least 6 months (or with death before then)*, and an absence of any other known causes of peripheral blood eosinophilia



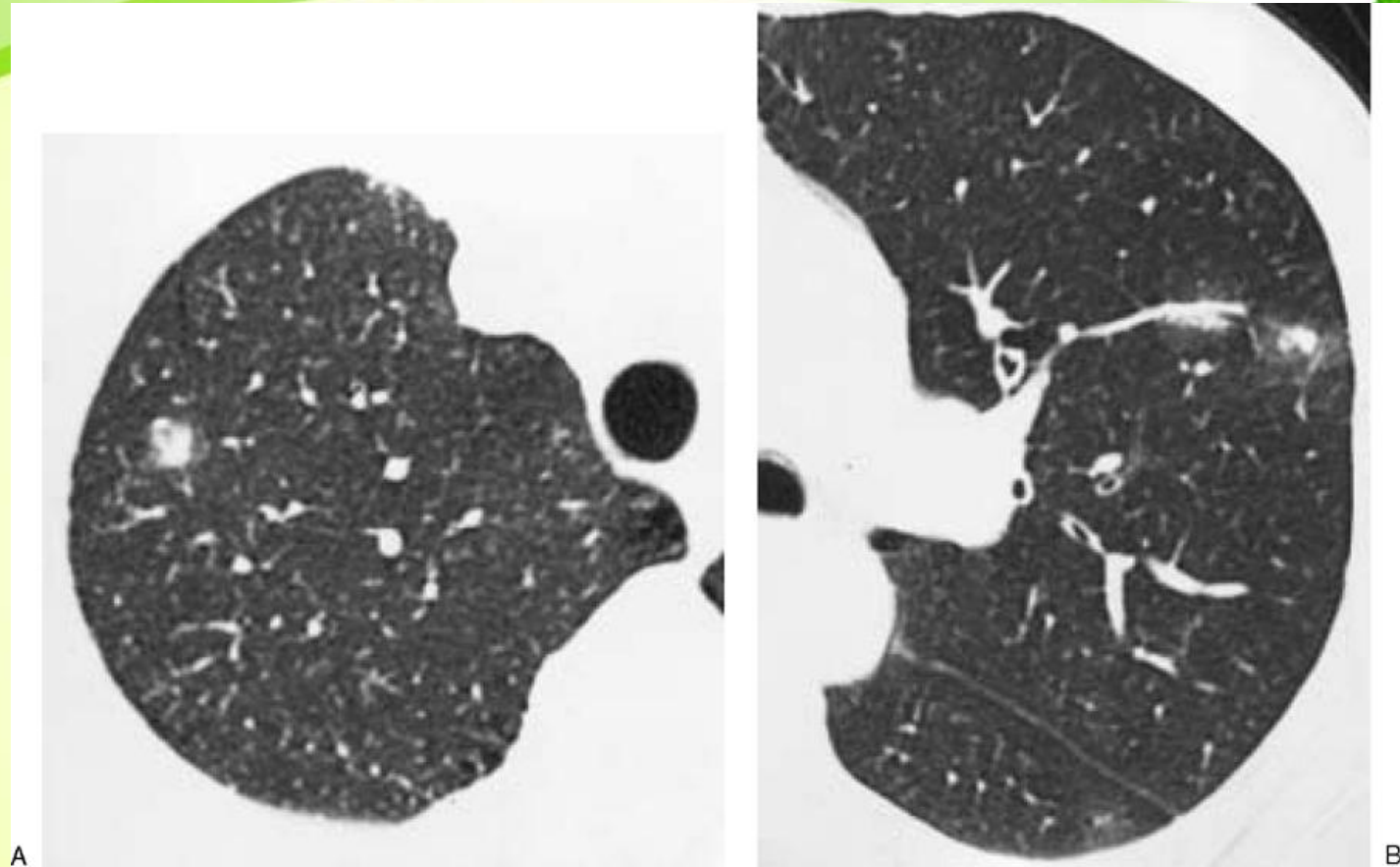
- The chest radiograph may reveal transient focal or diffuse pulmonary infiltrates (with no predilection for any particular distribution) and/or pleural effusion(s).
- Histopathological examination of affected lung specimens most commonly reveals intense interstitial infiltration with eosinophils.
- Less commonly, necrotic areas of parenchyma are found. These are believed to be due to pulmonary microemboli.
- In contrast to CSS, significant vasculitis is not present.



**Chest X-ray showing
symmetric bilateral alveolo-
interstitial infiltrates in the
central parts of the lungs**



Computed tomography showing dense patchy alveolar shadows and interstitial infiltrates in HES



Hypereosinophilic syndrome. Views of the right (A) and left (B) upper lobes from an HRCT demonstrate small nodules surrounded by a halo of ground glass attenuation.



- The organ damage in IHS is believed to be due both to eosinophilic infiltration of tissues and to tissue injury caused by thromboembolic events.
- Eosinophils probably contribute to tissue damage via antibody-mediated cytotoxicity and the release of toxic granule products such as major basic protein and eosinophil cationic protein.

Differential diagnosis



- Parasitic infection
- Acute eosinophilic leukemia
- CSS
- Episodic angioedema with eosinophilia
- Tuberculous or fungal infection
- Allergic or autoimmune disease
- Other acute or CEPs
- TPE
- Lymphoproliferative disorders

TREATMENT



- The mainstay of therapy for IHS with organ involvement includes corticosteroids
- prednisone at 1 mg/kg/day for several weeks, with taper of dose attempted to an every-other-day regimen once eosinophil levels are reduced
- If the disease stabilizes or resolves, alternate-day corticosteroids should be continued for approximately 1 year at the minimal dose that effectively controls disease activity.
- Hydroxyurea (0.5 to 1.5 g per day) may be added to the regimen if there is evidence of further disease progression
- Etoposide and chlorambucil are effective alternative agents for cases that prove refractory to standard treatment with corticosteroids



- Cyclosporine with corticosteroids
- IFN- α *as a* second-line agent among patients with IHS who fail to respond to corticosteroid treatment
- Imatinib tyrosine kinase inhibitor may also be beneficial for treatment of the myeloproliferative variant of HIS
- Leukapheresis
- Allogeneic bone marrow transplantation

PROGNOSIS



- **Favourable prognostic features include**
 - A rapid clinical response to treatment with reduction in blood eosinophilia
 - Presence of angioedema
 - An elevated IgE
 - Absence of findings associated with myeloproliferative disorder.
- **Factors associated with a poor prognosis include**
 - Presence of total blood WBC greater than 100,000/mm³,
 - Myeloblasts in the peripheral blood
 - Refractory CHF
 - Basophilia above 3 percent,
 - Chromosomal abnormalities in bone marrow
 - Elevated serum B12 levels

Summary of Comparative Features of the Chronic Pulmonary Eosinophil Syndromes



	CEP	ABPA	CSS	IHS
<i>Clinical course</i>	Subacute	Acute, subacute, chronic	Acute, subacute, chronic	Subacute, chronic
<i>H/o allergic disease/asthma</i>	+ (30–60%)	Nearly 100%	100%	—
<i>Blood eosinophilia</i>	Mild–mod. in most	Typical	Extreme, fluctuating	Extreme, persistent
<i>Sputum/BAL eosinophilia</i>	Striking	In some	Prominent	Striking
<i>Elevated serum IgE</i>	Mod.–elev. in 30%	Marked elev., fluctuates w/disease	Mod.–elev.	Mod.–elev. in some
<i>Etiologic agent</i>	Unknown	<i>Aspergillus</i> (or other fungus)	Unknown	Unknown
<i>Radiographic findings (CXR, CT)</i>	Predominately, peripheral consolidation and GGO; “photographic negative of pulmonary edema”	Upper lobe predominant proximal bronchiectasis	Transient, migratory peripheral, rarely diffuse; patchy peribronchial and septal thickening, patchy parenchymal GGO or consolidation	Transient, focal or diffuse

<i>PFTs</i>	Normal, OVD, or RVD	OVD +/- RVD	OVD +/- RVD	Mild RVD in some
<i>Characteristic diagnostic findings</i>	None	See Table 72-4	Histopathology plus appropriate clinical setting	Extreme persistent eosinophilia and multi-organ dysfunction (no other evident cause)
<i>Vasculitis</i>	Occasionally mild, non-necrotic	None	Characteristic (see text)	None
<i>Extrapulmonary manifestations</i>	Very rare reported	None	Typical of vasculitic phase	Cardiac, neurological, GI, hematological, other
<i>Therapy</i>	Corticosteroids	Corticosteroids, bronchodilators, antibiotics, antifungals	Corticosteroids, other immunosuppressives (see text)	Corticosteroids, other immunosuppressives (see text)
<i>Chronic/recurrent disease</i>	Common	Typical	Infrequent after Rx	Chronicity typical



Thank
You!