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Secondary causes of pulmonary Eosinophilia: A comprehensive literature review on Loeffler's Syndrome

Abigail Ulil Albab Affendi [1], Ryan Nur Fikri [1] and Wiwin Is Effendi [2,*]

[1] *Medical Study Program, Faculty of Medicine, Universitas Airlangga, Surabaya – Indonesia.*
[2] *Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya – Indonesia.*

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Abstract

Loeffler's syndrome, also known as simple pulmonary eosinophilia, represents a distinctive clinical entity characterized by transient pulmonary infiltrates accompanied by peripheral blood eosinophilia. Loffler syndrome is an uncommon, self-limited, benign pulmonary eosinophilia that usually lasts less than a month. This literature review synthesizes current evidence from peer-reviewed publications between 2014 and 2024, examining the etiology, pathophysiology, clinical manifestations, diagnostic approaches, and therapeutic strategies for Loeffler's syndrome and its cardiac variant. The review also addresses the differential diagnosis with other eosinophilic lung diseases and highlights emerging treatment modalities, including targeted biological therapies.

Keywords: Loeffler's Syndrome; Pulmonary Eosinophilia; Parasitic Infection; Hypereosinophilic Syndrome; Ascaris Lumbricoides.

1. Introduction

Eosinophilic pulmonary diseases constitute a heterogeneous group of disorders characterized by the accumulation of eosinophils in the lung parenchyma, airways, and/or peripheral blood. Acute and chronic eosinophilic pneumonia (AEP and CEP) include a group of rare interstitial lung diseases characterized by peripheral blood eosinophilia, increased eosinophils in bronchoalveolar lavage fluid, or eosinophilic infiltration of lung parenchyma (Carbone et al., 2024) [1]. Among these conditions, Loeffler's syndrome occupies a unique position as a self-limiting form of pulmonary eosinophilia most commonly associated with parasitic infections. Eosinophilic pulmonary disease (EPD) is a heterogeneous group of disorders including the accumulation of eosinophils in the lung parenchyma. All have common characteristics, such as eosinophilia of the blood and/or bronchoalveolar lavage (BAL), the presence of areas of increased pulmonary attenuation on high-resolution computed tomography (HRCT), and eosinophilic infiltration of the lung tissue, which can be detected during biopsy (Averyanov et al., 2020) [2].

Loeffler's syndrome was first described by Wilhelm Löffler in 1932, who observed patients with transient pulmonary infiltrates and peripheral eosinophilia. The syndrome is classically defined as simple pulmonary eosinophilia characterized by migratory pulmonary infiltrates on chest radiography, peripheral blood eosinophilia, and mild or absent respiratory symptoms that resolve spontaneously within one month. Loeffler's syndrome (LS) is a transient respiratory ailment characterised by pulmonary infiltration along with peripheral eosinophilia and commonly follows parasitic infestation (Sil et al., 2023) [3]. The self-limiting nature of this condition distinguishes it from chronic eosinophilic pneumonia and hypereosinophilic syndrome, which require more aggressive and prolonged treatment.

* Corresponding author: Wiwin Is Effendi.

The clinical significance of Loeffler's syndrome extends beyond its pulmonary manifestations. Loeffler syndrome can be caused by such factors and pathological conditions as idiopathic hypereosinophilic syndrome, allergic diseases, parasitic infections, autoimmune processes, cancer (Yashin et al., 2023) [4]. Understanding this condition is crucial for clinicians, particularly in endemic areas where parasitic infections remain prevalent, as timely diagnosis and appropriate treatment can prevent complications and unnecessary interventions.

2. Material and methods

This literature review was conducted using peer-reviewed publications spanning the decade from 2014 to 2024. The primary search strategy involved querying major medical databases. Publication types were strictly limited to articles, reviews, and conference papers focusing on the etiology, pathophysiology, diagnosis, and management of Loeffler's syndrome and related eosinophilic lung diseases as per the predetermined selection criteria.

Ethical approval and informed consent were not required for this study, as it is a literature review that does not involve primary research on human or animal subjects.

3. Results and discussion

3.1. Etiology and Causative Agents

Parasitic infection, particularly helminths that undergo a pulmonary migration phase during their life cycle, is a well-recognized cause of Loeffler's syndrome. Loeffler's syndrome initiated by *Ascaris lumbricoides*, mimicked the clinical picture of community-acquired pneumonia (CAP) and bronchial asthma (Özdemir, 2020) [5]. *Ascaris lumbricoides* (AL), popularly known as roundworm, is a nematode species belonging to the Ascarididae family, involved in the most common worldwide intestinal helminthic infection (Ascariasis). This nematode reaches gastrointestinal tract (GI) through ingestion of food/fluids contaminated with faeces, and in small intestine they migrate into pulmonary circulation, where they mature causing capillaries and alveolar walls destruction (Santos et al., 2019) [6]. An allergic response is responsible for the presence of respiratory symptoms and radiological manifestations, which can be seen as a transient nodular or diffuse pulmonary infiltrates (Loeffler's syndrome) or as a chronic eosinophilic pneumonia (Santos et al., 2019) [6].

Other parasites implicated in Loeffler's syndrome include:

- Hookworm species (Ancylostoma duodenale, Necator americanus).
- Strongyloides stercoralis.
- Toxocara species (causing visceral larva migrans).

Toxocariasis is a zoonotic infection caused by *Toxocara canis*, or less commonly, *Toxocara cati*, which is one of the most common zoonotic infections worldwide. It commonly affects the pediatric and immunocompromised population; however, it has rarely been reported in the immunocompetent adults. With an increase in migration and travel, physicians should have an index of suspicion for parasitic infection. Parasitic worms that can affect the lung include trematodes, protozoa and nematodes. Diagnostic investigations such as serology are prone to cross-reactions. In addition, *Ascaris* eggs are only passed in the stool following pulmonary symptom resolution, and many non-infectious causes of pulmonary eosinophilia have been described (Singh et al., 2023) [7].

While not classic Loeffler's syndrome, drug-induced eosinophilic pneumonia represents an important differential diagnosis. Eosinophilic pneumonia comprises a group of lung diseases in which eosinophils appear in increased numbers in the lungs and sometimes in the bloodstream. Among several causes of pulmonary eosinophilia, drug-induced pulmonary eosinophilia and subsequent pneumonia is a well-known side effect of many medications (Raza et al., 2019) [8]. Eosinophilic pneumonia comprises a rare and potentially serious group of lung diseases characterized by abnormal accumulation of eosinophils in the lungs. Many medications including the anticonvulsant phenytoin, have been implicated in the development of eosinophilic pneumonia. Attributing eosinophilic pneumonia to a medication or toxin can be difficult and may only be achieved by exclusion (Gordon & Silhan, 2019) [9]. The presence of a potential offending drug/agent, exclusion of other causes of eosinophilic pneumonia, clinical improvement after cessation of the offending agent, or return of eosinophilic pneumonia after re-challenge are strong indicators for a drug-induced diagnosis (Gordon & Silhan, 2019) [9]. Eosinophilic lung diseases may also be associated with systemic conditions. Pulmonary eosinophil infiltrates in lung biopsy specimens present a broad differential diagnosis, including eosinophilic pneumonia; hypersensitivity reactions, such as allergic bronchopulmonary fungal disease; and pulmonary

manifestations of systemic diseases, such as eosinophilic granulomatosis with polyangiitis. An additional important consideration in the differential diagnosis is pulmonary involvement by HES (Zimmermann & Wikenheiser-Brokamp, 2018) [10].

3.2. Pathophysiology

The pathophysiology of Loeffler's syndrome involves a complex interplay between parasitic antigens and the host immune response, predominantly mediated through type 2 (Th2) inflammatory pathways.

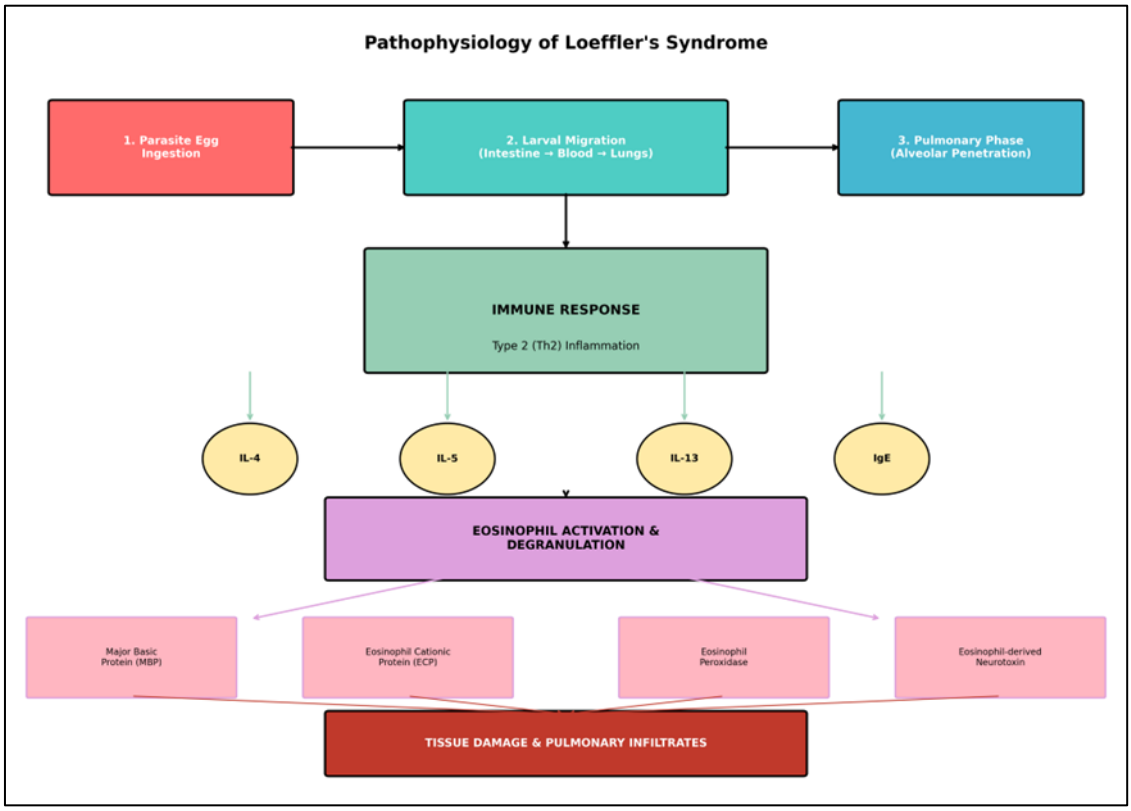

Figure 1 Pathophysiological mechanisms underlying Loeffler's syndrome, illustrating the cascade from parasitic infection through eosinophil activation to tissue damage.

During their life cycle, certain helminths undergo obligate pulmonary migration. After ingestion of parasite eggs, larvae hatch in the small intestine, penetrate the intestinal wall, and enter the bloodstream. They are carried to the lungs where they penetrate alveolar capillaries, enter the airways, and migrate up the tracheobronchial tree before being swallowed to complete their development in the gastrointestinal tract.

The presence of parasitic antigens triggers a robust type 2 immune response characterized by the production of interleukin-4 (IL-4), IL-5, and IL-13. Interleukin 5 (IL-5) to be a crucial cytokine in several asthma phenotypes. In fact, IL-5 exerts selective action on eosinophils, which, in turn, sustain airway inflammation and worsen asthma symptoms and control (Bagnasco et al., 2017) [11]. IL-5 is the principal cytokine responsible for eosinophil proliferation, differentiation, activation, and survival. Elevated IL-5 levels lead to peripheral blood eosinophilia and recruitment of eosinophils to the pulmonary parenchyma. Upon activation, eosinophils degranulate and release cytotoxic proteins including major basic protein (MBP), eosinophil cationic protein (ECP), eosinophil peroxidase, and eosinophil-derived neurotoxin. These proteins cause direct epithelial damage and contribute to the inflammatory response observed in affected tissues.

When eosinophilic inflammation affects the heart, it manifests as Loeffler's endocarditis or cardiac syndrome. Loeffler's cardiac syndrome, a rare and often severe form of hypereosinophilic syndrome, is characterized by endomyocardial damage and restrictive cardiomyopathy secondary to eosinophilic infiltration and degranulation. This condition progresses through three distinct pathological phases: an acute necrotic stage, a thrombotic stage, and finally, an endomyocardial fibrotic stage, leading to significant cardiac dysfunction (López & Montes, 2024) [12]. The pathophysiological underpinnings are driven by eosinophil-mediated cytotoxicity, resulting in cardiac inflammation,

endomyocardial fibrosis, and subsequent heart failure manifestations (López & Montes, 2024) [12]. Loeffler's endocarditis (LE) represents a frequent cardiac manifestation of HES, caused by infiltration of the myocardium by eosinophilic cells, which determines endocardial damage, with subsequent inflammation, thrombosis, and fibrosis of either one or both ventricles (Padoan et al., 2023) [13].

3.3. Clinical Manifestations

The clinical presentation of pulmonary Loeffler's syndrome is variable. Clinical presentation may vary from malaise, fever, loss of appetite, myalgia and headache to respiratory symptoms, which includes sputum-productive cough, chest pain, haemoptysis, shortness of breath and wheezing (Santos et al., 2019) [6]. A 14-year-old male child was hospitalized with complaints of a bronchial wheezing, cough, dyspnea, and sputum and a preliminary diagnosis of bronchial asthma and pneumonia. The patient was treated empirically for bronchial asthma and pneumonia, but gave neither clinical nor radiological response to treatment (Deveci et al., 2013) [14].

Key clinical features include:

- Respiratory symptoms: Dry cough, mild dyspnea, wheezing, and occasionally hemoptysis.
- Constitutional symptoms: Low-grade fever, malaise, and fatigue.
- Physical examination: May be unremarkable or reveal scattered rhonchi and crackles.

When he presented to us, he seemed to be in a good general condition, but his physical exam revealed coarse polyphonic rhonchi, especially on the upper zone of the left lung (Özdemir, 2020) [5]. Children represent a significant proportion of Loeffler's syndrome cases, particularly in endemic areas. We present clinical features, radiological, and pathological findings of Loeffler's syndrome with secondary bacterial pneumonia in a child. He presented with dry cough, hemoptysis 2 times, chest pain for 1 week. Blood tests revealed high C-reactive protein levels and eosinophilia (Tran et al., 2022) [15].

Clinical presentation of cardiac Loeffler's syndrome varies based on the disease stage, ranging from nonspecific symptoms like fatigue and fever to advanced signs of congestive heart failure, thromboembolic events, or restrictive cardiomyopathy (López & Montes, 2024) [12]. Cardiovascular involvement in HES is most commonly associated with Loffler endocarditis (cardiac HES). Cardiac HES is typically characterized by progressive subendocardial fibrosis with overlying mural thrombus formation, leading to restrictive dysfunction of the left ventricle (Ono et al., 2021) [16].

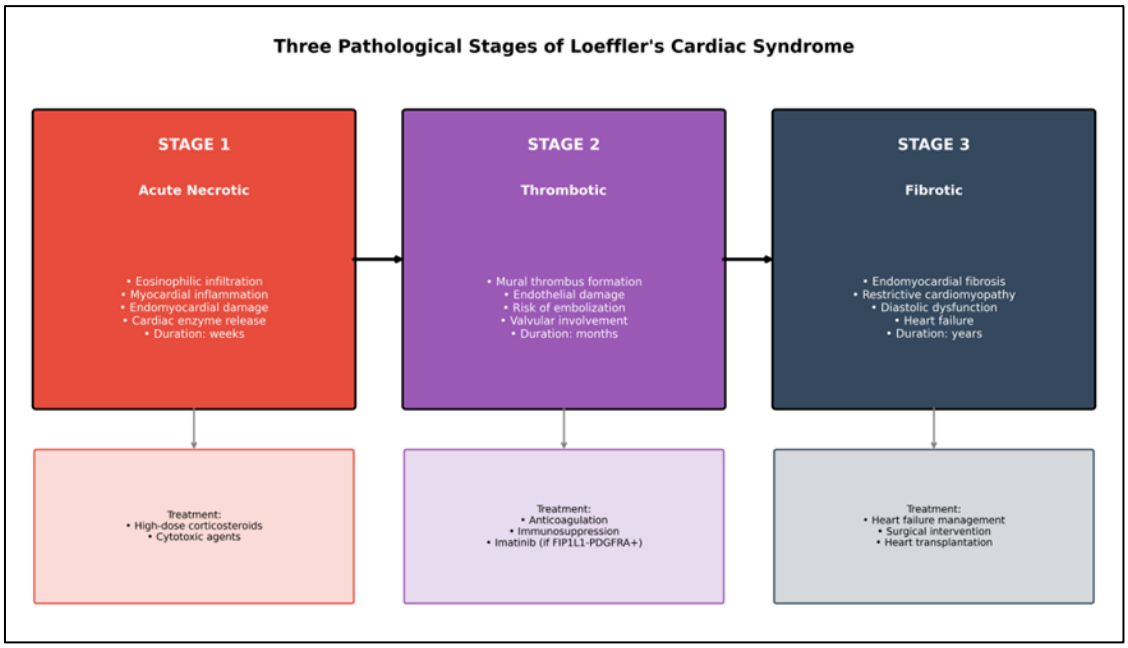

Figure 2 The three pathological stages of Loeffler's cardiac syndrome with corresponding treatment approaches.

When coronary artery is involved, known as eosinophilic coronary periarteritis, the clinical presentation, electrocardiographic changes and troponin level are extremely nonspecific and may mimic acute coronary syndrome. It is very important to make differential diagnosis for ECPA in order to avoid the unnecessary further invasive coronary angiography (Kong et al., 2020) [17]. The thrombus from cardiac HES could result in cardiogenic stroke; however, most of the stroke cases with HES were not associated with huge thromboembolism rather multiple infarcts in the watershed area (Ono et al., 2021) [16]. Compared to HES patients without cardiac involvement, thromboembolic events occurred significantly more frequently (63.6% vs. 24.0%, P=0.02) (Reeder et al., 2024) [18].

3.4. Diagnostic Approach

Peripheral blood eosinophilia is the hallmark laboratory finding in Loeffler's syndrome. Evaluation of the peripheral blood smear of the patient demonstrated mounting eosinophilia (from 0.2% to 2.06%-338/mm3-), while IgE was 50 IU/mL (Özdemir, 2020) [5]. Examination of the peripheral blood smear of the patient revealed eosinophilia (40%), while IgE was measured as 350 IU/mL (Deveci et al., 2013) [14]. Eosinophils are a type of granulocyte key to immune system modulation seen in a number of disease processes. Nearly every major organ system can be connected to peripheral eosinophilia through a number of different disease processes, ranging from benign conditions to malignancy (Weaver et al., 2024) [19]. The recent diagnostic criteria for idiopathic HES require an elevated absolute eosinophil count (AEC) above 1500 cells/mcL with evidence of tissue damage (Sullivan et al., 2024) [20].

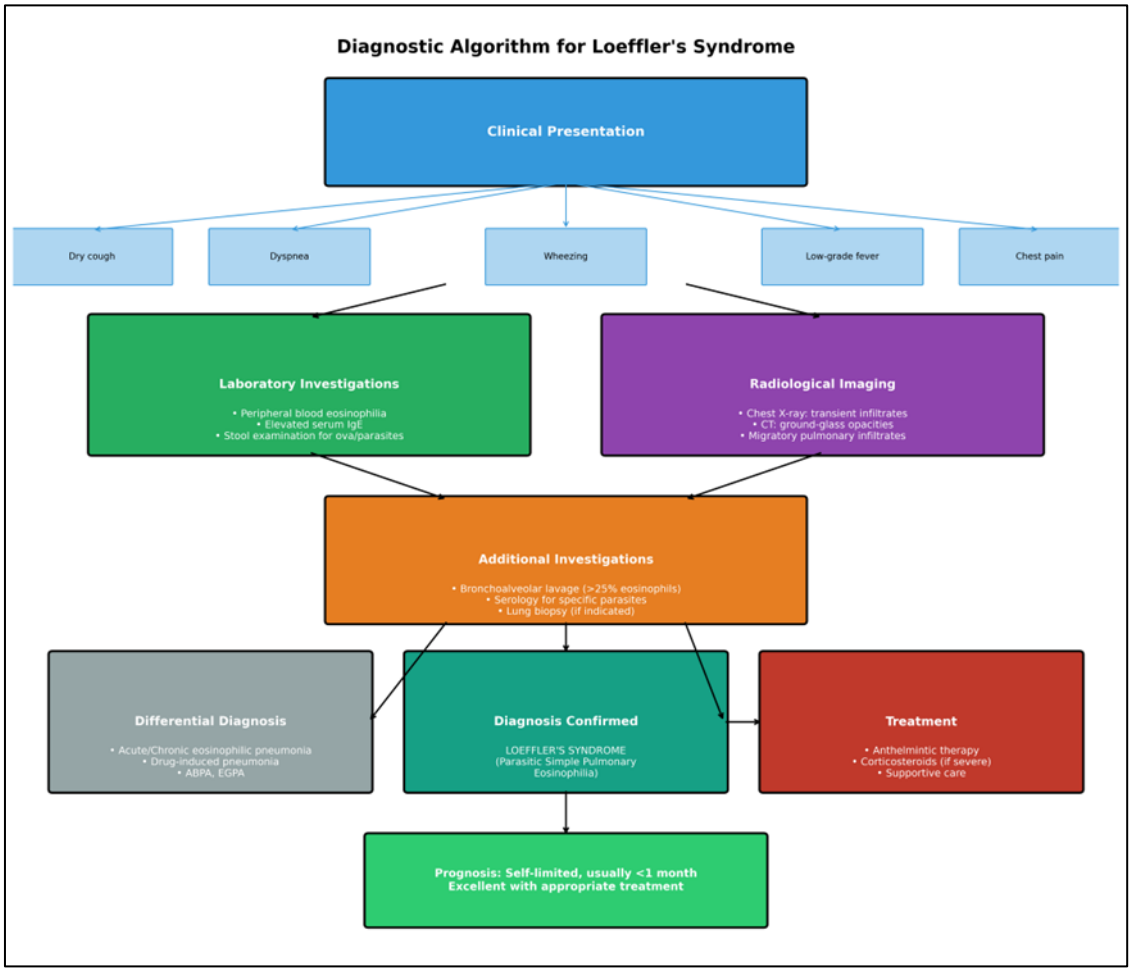

Figure 3 Diagnostic algorithm for Loeffler's syndrome, outlining the systematic approach to clinical evaluation, laboratory investigations, and imaging.

Stool examination for ova and parasites is essential but has important limitations. *Ascaris* eggs are only passed in the stool following pulmonary symptom resolution, and many non-infectious causes of pulmonary eosinophilia have been described. Therefore, direct microscopy is a valuable option to identify the parasite when larvae migrate to the lungs, which is common for many parasitic infections (Singh et al., 2023) [7].

Abnormal chest radiography occurs in 95% of patients; however, computed tomography findings are not well described (Tran et al., 2022) [15]. Chest radiograph findings usually demonstrates peripherally basal opacities, although they can be present in different ways (Santos et al., 2019) [6]. A chest X-ray demonstrated unilateral upper zone patchy consolidation (pneumonic infiltrations) of the left lung (Özdemir, 2020) [5]. High-resolution computed tomography (HRCT) provides superior characterization of pulmonary infiltrates. On the high-resolution computerized tomography, a typical spiral image of *Ascaris lumbricoides* was identified inside a cavity in the upper lobe of the left lung with a diameter of 8x7 cm. Also, migratory pneumonic infiltrations progressing between the lower lobe and hilary region of the left lung were seen (Deveci et al., 2013) [14]. On the initial computed tomography (CT) scan, a lesion was discovered at the upper edge of the right lung hilum. The lesion developed in size, together with right pleural effusion, on the repeated CT scan (Tran et al., 2022) [15]. Ground-glass opacification/opacity is a non-specific sign with a wide etiology including infection, chronic interstitial disease and acute alveolar disease. HRCT is essential diagnostic tool for diagnosis and characterization of diffuse ground glass opacities (Hafez et al., 2023) [21].

Idiopathic and secondary EPDs are usually identified via bronchoalveolar lavage. This chapter describes the most frequent EPD such as eosinophilic granulomatosis with polyangiitis, idiopathic chronic eosinophilic pneumonia, allergic bronchopulmonary aspergillosis, and hypereosinophilic syndrome (Averyanov et al., 2020) [2]. Bronchoalveolar lavage showing eosinophilia greater than 25% strongly supports the diagnosis of eosinophilic lung disease. A lung biopsy revealed a substantial number of inflammatory cells, including eosinophils and neutrophils. After ruling all other possibilities, Loffler's syndrome was confirmed (Tran et al., 2022) [15].

For suspected Loeffler's cardiac syndrome, multimodality cardiac imaging is essential. The diagnosis of cardiac involvement is based on a multimodality approach (i.e., two-dimensional transthoracic echocardiography [2D-TTE], speckle-tracking echocardiography [STE], and cardiac magnetic resonance [CMR]), with different findings depending on the stage of disease. STE may be useful in the initial phase when traditional imaging techniques may result negative, whereas CMR allows myocardial tissue characterization along with a better definition of the right ventricle (Padoan et al., 2023) [13]. The diagnosis of Loeffler's cardiac syndrome requires a high index of suspicion, particularly in patients with persistent eosinophilia, and relies on multimodal imaging techniques, including echocardiography and cardiac magnetic resonance imaging (MRI), coupled with laboratory studies and endomyocardial biopsy when indicated (López & Montes, 2024) [12]. Echocardiography showed severe left ventricle apical endomyocardial thickening, apical thrombus, and left ventricular hypertrophy compatible with a Loeffler's syndrome. To confirm the diagnosis, a cardiac magnetic resonance was performed corroborating these findings and excluding associated myocardial oedema (Mapelli et al., 2022) [22]. Echocardiography was performed in all patients and cardiac magnetic resonance (CMR) imaging was performed in eight patients. Left ventricular (LV) thrombus was detected more frequently by CMR (5/8, 62.5%) compared to echocardiography (3/10, 30%). Subendocardial pattern of late gadolinium enhancement (LGE) was observed in the majority of patients on CMR (6/7, 85.7%) (Reeder et al., 2024) [18]. Quick echocardiography showed endomyocardial thickening with normal regional wall motion, which corresponded to the characteristics of Loeffler's endocarditis. Emergent blood analysis showed marked increase in eosinophils and computed tomography angiography found no significant stenosis of coronary artery. Manifestations of magnetic resonance imaging consisted with findings of echocardiography (Kong et al., 2020) [17]. Patients with LE had significantly lower left ventricular global longitudinal strain (LV-GLS) (-9.7% vs. -15.5%, p=0.001), left atrial (LA) reservoir strain (21.0% vs. 32.1%, p=0.021) and LA conduit strain (-9.7% vs. -19.2%, p<0.001), compared to patients without LE (Okushi et al., 2024) [23].

3.5. Differential Diagnosis

AEP is characterized by rapid onset, fast response to steroid treatment, and no relapse. CEP is characterized by marked tissue and peripheral blood eosinophilia, rapid response to steroid therapy, and tendency to disease recurrence. In addition, we briefly describe other eosinophilic lung diseases that must be considered in differential diagnosis of AEP and CEP. Eosinophilic pneumonias may be idiopathic or due to known causes such as medications or environmental exposure (Carbone et al., 2024) [1]. HES is a rare syndrome that comprises a heterogeneous group of conditions characterized by persistent blood and/or tissue eosinophilia associated with organ dysfunction. Approximately one-third of HES cases are caused by neoplastic diseases, with the remaining cases classified as reactive or idiopathic. Lung involvement is seen in up to 67% of cases and may be the presenting manifestation of the disorder (Zimmermann & Wikenheiser-Brokamp, 2018) [10]. Hypereosinophilic syndrome is a rare, chronic hematological disease characterized by a persistently elevated eosinophil count exceeding 1.5x10^9/L following the exclusion of other potential etiologies. The systemic involvement of the disease causes tissue damage through eosinophil infiltration, and may affect various organs; cardiac complications are observed in 50-60% of cases, which are predominately attributed to endomyocardial fibrosis (Dal Berto et al., 2018) [24]. Idiopathic hypereosinophilic syndrome (IHES) is a disorder characterized by abnormal and persistent peripheral blood hypereosinophilia (eosinophil count >= 1.5x10^9/L and >= 10% eosinophils) with duration >= 6 months, associated organ damage, and/or dysfunction attributable to tissue eosinophilic infiltrate

of unknown cause. IHES affects different organs such as the heart, lungs, nervous system, and skin, with renal involvement being rare in this condition (Cieza-Terrones et al., 2024) [25]. Eosinophilic granulomatosis with polyangiitis (EGPA) is a systemic ANCA-associated vasculitis, characterized by peripheral eosinophilia, neuropathy, palpable purpuras or petechiae, renal and cardiac involvement, sinusitis, asthma, and transient pulmonary infiltrates (Maranini et al., 2023) [26]. Loeffler's endocarditis should be suspected when physicians encounter restrictive cardiomyopathy accompanied by mural thrombus in a patient with eosinophilia. Prompt immunosuppressive and anticoagulant medication can bring the disease under control (Lin et al., 2021) [27]. Loeffler's pneumonia should be considered when patients with bronchial asthma and pneumonia do not respond to specific treatment in developing countries. Radiological investigations may be available in the diagnosis of parasitic infections. In this case, early diagnosis by radiologic methods have prevented unnecessary drug use and related complications (Deveci et al., 2013) [14]. The differential diagnosis of pulmonary eosinophilia is broad and requires a multidisciplinary approach with clinicopathologic-radiologic correlation (Zimmermann & Wikenheiser-Brokamp, 2018) [10].

3.6. Treatment Approaches

For parasitic-induced Loeffler's syndrome, anthelmintic treatment is the cornerstone of therapy. Both albendazole and mebendazole have a low rate of absorption in the human intestine. These drugs primarily target parasites in the stomach's lumen, and their metabolites are effective against parasites in the stomach's muscles and tissues. Albendazole and mebendazole are highly effective against *Ascaris lumbricoides*, with a single dose of albendazole showing a cure rate of 96% and mebendazole showing a cure rate of 92.3% (Mohammed et al., 2024) [28]. The patient was diagnosed as "Loeffler's syndrome" due to *A. lumbricoides*, and successfully treated with mebendazole 2x100 mg/day for three days (Deveci et al., 2013) [14]. Treatment with seven-day course of oral albendazole (400 mg daily) coupled with nebulisation (levosalbutamol and budesonide) led to complete resolution of cutaneous lesions and respiratory complaints within two weeks. There was complete resolution of pulmonary pathology at four-weeks follow-up (Sil et al., 2023) [3]. The combination of albendazole with ivermectin showed superior efficacy against *T. trichiura* compared to albendazole alone, both in terms of cure rates (31.3% versus 12.3%, difference 18.9%-points, 95% CI 6.2-31.2, $p<0.004$) and in terms of egg reduction rates (ERRs; 91.4% versus 52.7%) (Palmeirim et al., 2024) [29]. Among participants with persistent or recurrent infections with *Trichuris*, the combined therapy of albendazole (400 mg) and ivermectin at 600 ug/dose increased overall CR for *Trichuris* infection to 75.2% (95% CI: 67.3-83.2%) with an ERR of 84.2% (95% CI: 61.3-93.8%). Albendazole administration alone for the control of STH was associated with high rates of treatment failure, especially for *Trichuris*. Combined single doses of albendazole and ivermectin was observed to have improved efficacy (Curico et al., 2024) [30].

Corticosteroids are indicated in severe cases or when symptoms persist despite anthelmintic treatment. As a result of antibiotic treatment, favorable outcomes were confirmed by improving clinical symptoms and follow-up chest CT scans (Tran et al., 2022) [15]. The alternative non-conventional drug was immediately discontinued and the patient was treated with systemic corticosteroids, leading to a rapid improvement in her symptoms and radiographic abnormalities. A repeat CT of the chest after 15 days revealed significant resolution of the ground-glass opacities and complete resolution of pneumomediastinum (Agarwal et al., 2024) [31]. Hypoxemia was refractory despite conventional treatment of ARDS, but the evolution was satisfactory after corticosteroid therapy. This case demonstrates that acute eosinophilic pneumonia should be included in rigorous etiological research before any ARDS, in order to start the appropriate treatment as soon as possible (Houba et al., 2022) [32].

Current treatment strategies for cardiac syndrome focus on eosinophil-lowering therapies, including corticosteroids and cytotoxic agents, to prevent progression to irreversible fibrosis. In cases with established cardiac damage, therapeutic options may extend to surgical interventions, heart transplantation, or advanced heart failure management (López & Montes, 2024) [12]. The patient was treated with corticosteroids and subcutaneous heparin, and rapid clinical picture and eosinophil values normalization was observed. At 3-month follow-up, he is asymptomatic, and the echocardiogram demonstrated almost complete thrombosis resolution (Mapelli et al., 2022) [22]. The therapy with methylprednisolone 24 mg/day azathioprine 75 mg/day was started. Six months after the operation, the symptoms of heart failure are completely absent, the thrombosis did not recur (Blagova et al., 2019) [33].

The presence of the Fip1-Like1-platelet-derived growth factor receptor alpha (FIP1L1-PDGFRa) fusion gene represents a rare cause of hypereosinophilic syndrome (HES), which is associated with organ damage (Varga et al., 2023) [34]. The treatment is based initially on determining the presence of the FIP1L1-PDGFRA fusion. Patients with positive results for this mutation tend to achieve a complete response with imatinib treatment, which is thus the first line of treatment for this condition. However, patients who are negative for this mutation initially undergo treatment with corticosteroids (Dal Berto et al., 2018) [24]. We present a rare case of LE with isolated right ventricular involvement in a patient with HES caused by chronic eosinophilic leukemia with constitutively activated fusion tyrosine kinase on chromosome 4q12,

successfully treated with imatinib mesylate (Padoan et al., 2023) [13]. Selective, biological eosinophil-reducing agents provide treatment options that improve clinical symptoms associated with eosinophilic inflammation and reduce OCS use. Mepolizumab is a humanized monoclonal antibody that binds to and neutralizes interleukin-5, the major cytokine involved in eosinophil proliferation, activation, and survival. Mepolizumab is approved for the treatment of severe eosinophilic asthma, eosinophilic granulomatosis with polyangiitis and hypereosinophilic syndrome (Pavord et al., 2022) [35]. Regarding treatment complications, 71 (73%), 28 (29%), and 16 (16%) patients were treated with steroids, anticoagulants, and antiplatelets, respectively. The overall mortality and recovery rates were 11% and 89%, respectively (Ono et al., 2021) [16]. Steroids were utilized in 90.9% of cases, and aspirin in all patients (Reeder et al., 2024) [18].

3.7. Prognosis and Outcomes

The prognosis of uncomplicated pulmonary Loeffler's syndrome is excellent. Loffler syndrome is an uncommon, self-limited, benign pulmonary eosinophilia that usually lasts less than a month (Tran et al., 2022) [15]. A close combination of pulmonary symptoms, peripheral blood eosinophilia, abnormal chest imaging, and histopathological findings must be taken to confirm the diagnosis of Loeffler's syndrome (Tran et al., 2022) [15]. Timely diagnosis of cardiac conditions will prevent the rapid development of severe complications and carry out appropriate therapy, which will significantly prolong the life of patients with Loeffler syndrome. However, in the presence of nonspecific symptoms, the diagnosis of this disease may be diagnostically difficult for the physician (Yashin et al., 2023) [4]. Loeffler's endocarditis remains is a very rare disease, develops due to eosinophilic inflammation predominantly of the endocardium with an outcome in fibrosis and massive thrombus formation. He is generally characterized by an unfavorable prognosis (Blagova et al., 2019) [33]. Despite hematological improvement under corticosteroid and imatinib therapy, anticoagulant, and patient-oriented HF treatment, there was further clinical progression and subsequent multiple complications (including embolization), which led to patient death. HF is a severe complication that diminishes the demonstrated effectiveness of imatinib in the advanced phases of Loeffler endocarditis (Varga et al., 2023) [34]. Loeffler's endocarditis is a cardiac manifestation of hypereosinophilia leading to diastolic dysfunction, valvulopathy, or as in this case embolic events. Promptly recognizing signs and symptoms allows the correct treatment to be initiated, usually ensuring rapid improvement (Mapelli et al., 2022) [22].

3.8. Special Considerations

COVID-19 infection, although paucisymptomatic, may have functioned as a trigger for developing a previously completely silent eosinophilic syndrome (Mapelli et al., 2022) [22]. A clinical case of Loeffler syndrome in an 84-year-old patient with heart, lung, liver, kidney and pancreatic lesions is presented. Difficulties of differential diagnostics of this syndrome because of individual clinical picture and signs of the course are discussed in the article (Yashin et al., 2023) [4]. The patient showed an AEC of 4500 cells/mcL on admission associated with high inflammatory markers. Cardiac imaging demonstrated acute myocarditis with heart failure and a reduced ejection fraction. Chest imaging was initially suggestive of community-acquired pneumonia. Our case illustrates the importance of considering hypereosinophilia as a precipitating factor for acute heart failure in an otherwise healthy adult. An expeditious diagnosis can lead to early initiation of steroids to avoid progression toward multi-organ failure (Sullivan et al., 2024) [20]. Spontaneous pneumothorax has also been described in literature in the context of *Ascaris* infection, but it constitutes a rare event (Santos et al., 2019) [6].

3.9. Research Gaps

The need for an accurate identification of heart failure etiology in the absence of endomyocardial biopsy is particularly important for ensuring effective treatment (Varga et al., 2023) [34]. Ivermectin and moxidectin, two macrocyclic lactones, are potent antiparasitic drugs currently registered and mainly used against filarial diseases; however, their potential value for improved soil-transmitted helminth control has been acknowledged (Hürlimann et al., 2023) [36]. This study underscores the key role of ivermectin-based MDA in addressing limitations in current global STH guidelines in terms of limited efficacy against *S. stercoralis* and *T. trichiura*. Based on these findings, revising international STH guidelines to include ivermectin is a promising option to progress the control and eventual elimination of STHs and other NTDs (Le et al., 2024) [37]. Further research is needed to establish standardized diagnostic criteria for Loeffler's syndrome that distinguish it from other eosinophilic lung diseases. The development of more sensitive and specific biomarkers would aid in early diagnosis and monitoring of disease progression.

4. Conclusion

Loeffler's syndrome remains an important clinical entity, particularly in regions where parasitic infections are endemic. This literature review has synthesized current evidence demonstrating that the syndrome is characterized by its self-

limiting nature, association with helminth pulmonary migration, and excellent prognosis with appropriate anthelmintic therapy.

Clinicians should maintain a high index of suspicion for Loeffler's syndrome in patients presenting with pulmonary symptoms and eosinophilia, particularly in endemic areas or those with potential parasitic exposure. Early recognition and appropriate treatment ensure favorable outcomes and prevent unnecessary diagnostic procedures and treatments.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declared there is no conflict of interest.

Statement of ethical approval

Ethical approval and informed consent were not required for this study, as it is a literature review that does not involve primary research on human or animal subjects.

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