Hypereosinophilic syndrome and eosinophilic granulomatosis with polyangiitis: Eosinophilic-associated inflammatory conditions with a challenging diagnosis and treatment

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In their recently published clinical vignette, Gil and Zaręba [1] reported an interesting case of hypereosinophilic syndrome (HES) with Loeffler's endocarditis in a 60-year-old female with a medical history of eosinophilia, asthma, allergic rhinitis, chronic obstructive pulmonary disease, hypertension, coronary artery disease, and embolic stroke, presenting with hemorrhagic stroke and persistent hypoxemia. As eosinophilic-associated inflammatory conditions are an extremely rare heterogeneous group of diseases characterized by high tissue infiltrating and/or circulating eosinophils, which potentially affect multiple organs without a recognized cause [2], we would like to write a short comment.

Allergic bronchopulmonary aspergillosis may present with an elevated eosinophil count, and the diagnosis does not require positive *Aspergillus spp.* cultures and can be based on immediate skin test reactivity to *Aspergillus* antigens and elevated levels of serum IgG and IgE antibodies [3]. However, multiple organ damage combined with eosinophilia should trigger a search for an alternative diagnosis, as was done in the reported case [1].

Hypereosinophilic syndrome is a collection of disorders characterized by chronic hypereosinophilia (circulating eosinophil count >1.5 × 10^9/ml documented on at least 2 occasions) or marked tissue eosinophilia, as well as clinical manifestations specifically related to or assumed to be the result of eosinophilia for which no other cause can be found. This is a broad definition that includes all patients with clinical manifestations of eosinophilia regardless of the underlying etiology. In patients with suggestive symptoms, the diagnostic "step-by-step" procedure for HES begins with screening for the various secondary causes of (reactive) eosinophilia (secondary HES), followed by a careful investigation of primary, clonal subtypes (primary or myeloid HES). The latter investigation is based mainly on a variety of molecular and cytogenetic analyses. The prognosis of the disease varies depending on the HES variant and the availability of targeted therapy [2].

The diagnosis of HES requires differentiation from eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg–Strauss syndrome. This is another uncommon primary systemic necrotizing vasculitis of the small vessels that frequently affects the skin and other organ systems and manifests as eosinophilia, asthma, and pulmonary infiltrates. Eosinophilic granulomatosis with polyangiitis typically manifests itself in three partially overlapping phases: a prodromal phase dominated by respiratory tract symptoms, asthma, and rhinosinusitis; a second phase characterized by blood eosinophilia, tissue infiltration of eosinophils, and organ inflammation; and a third phase characterized by systemic necrotizing vasculitis. Palpable purpura, peripheral nervous system involvement (e.g., mononeuritis multiplex), scleritis, alveolar hemorrhage, glomerulonephritis, pulmonary infiltrates, pleural effusion, urticarial papules, eosinophilic tubulointerstitial nephritis, and eosinophilic myocarditis are the main clinical manifestations of EGPA. Anti-neutrophil cytoplasmic antibodies (ANCA) are often directed against myeloperoxidase and can be found in up to 40% of patients with EGPA [2].

Clinical signs and symptoms of HES and EGPA greatly overlap. In the analysis by Maino

et al. [4] arterial thrombosis was more common in HES than in EGPA. On the contrary, in EGPA there was a predominance of venous thrombosis. It should be noted that, especially in young patients, thrombophilia tests should be performed. Furthermore, the occurrence of asthma is less common in EGPA, while splenomegaly and lymph node enlargement are more frequent in HES [2]. We wonder if the patient [1] presented other signs and symptoms suggestive of HES and EGPA, and if she had ANCA, molecular or cytogenetic tests performed.

We would also like to draw attention to the damage to the cardiac structure caused by eosinophils. Unfortunately, despite great improvements in management and survival, some patients continue to develop severe cardiomyopathy and heart failure [2, 5]. We would like to emphasize that cardiologists play a fundamental role in the early detection and treatment of these conditions. Loeffler's endocarditis is the cardiac manifestation of HES, which is usually diagnosed by transthoracic and/or transesophageal echocardiography. These imaging modalities are also used later in follow-up for prognostic stratification and to assess response to treatment. New imaging modalities, such as strain imaging and particularly cardiac magnetic resonance imaging sequences, give the possibility of identifying minor changes and discriminating between inflammatory and fibrotic processes. Endomyocardial biopsy can be useful in problematic situations, but it may be ineffective due to sampling difficulties, eosinophil degranulation, or fibrosis replacement and must always be performed after a careful assessment of the risk-benefit balance [5]. The nature of clinical manifestations arising from eosinophil-related organ dysfunction should influence the choice of treatment [2].

In conclusion, eosinophilic-associated inflammatory conditions should be treated by experienced physicians; however, cardiologists are crucial in the early diagnosis and management of the accompanying cardiomyopathy. We would also like to emphasize the importance of ANCA, molecular or/and cytogenetic testing.

Article information

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