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Letter to the editor

Hypereosinophilia with asthma and systemic (non-vasculitic) manifestations: Eosinophilic granulomatosis with polyangiitis or hypereosinophilic syndrome?

Dear Editor,

It was with great interest that we read the article entitled “Revisiting the systemic vasculitis in eosinophilic granulomatosis with polyangiitis (Churg-Strauss)” by Cottin and al. [1].

This retrospective analysis of 157 cases of eosinophilic granulomatosis with polyangiitis (EGPA) by two groups of experts (the Groupe d'Etudes et de Recherche sur les Maladies Orphelines Pulmonaires and the European Respiratory Society Taskforce on EGPA (Churg-Strauss)) provides useful new information on the heterogeneity of EGPA [1]. In particular, the work enables better characterization of ANCA-negative patients with systemic manifestations but who do not fulfill the criteria for vasculitis. The suggested revision of the nomenclature (with the term “EGPA” being reserved for patients with polyangiitis) makes sense with regard to treatment, prognostic assessments and clinical trials in this field.

However, we were surprised to see that Cottin et al. did not mention hypereosinophilic syndrome (HES) as an important differential diagnosis for EGPA. HESs share many features with EGPA, such as peripheral hypereosinophilia (an eosinophil count > 1.5 G/L) and tissue eosinophilia with systemic manifestations (once classical eosinophilic disorders have been ruled out). HESs are usually divided into clonal, reactive and idiopathic subtypes. Reactive HES refers to conditions in which a Th2 T-cell subset overproduces interleukin-5 (IL-5). In patients with reactive HES, the lymphoid variant (L-HES) is characterized by high peripheral and tissue counts of clonal T-cells with abnormal phenotypes (e.g. CD3-CD4+, CD3 + CD4 + CD7- or CD3 + CD4-CD8-TCRαβ+) [2].

In the larger international case series, dermatological, pulmonary and gastrointestinal symptoms were reported in respectively 37%, 25% and 14% of HES patients. Interestingly, the upper respiratory tract and pulmonary manifestations reported in 47 HES patients included asthma ($n = 21$, 45%), sinusitis ($n = 9$, 19%), pulmonary infiltrates ($n = 4$, 8%) and rhinitis ($n = 2$, 4%). Overall, asthma was reported in 11% ($n = 21/188$) of the cases of HES [3].

In CD3-CD4+ L-HES, 48% of the patients studied by the French Eosinophil Network ($n = 10/21$) were atopic, and around 25% had developed asthma prior to the diagnosis of HES [2]. These findings suggest that HES (and particularly L-HES) should be considered as a diagnosis in patients with asthma, hypereosinophilia (an eosinophil count above 1.5 G/L) and systemic manifestations. This was clearly suggested in the recent European Task Force guidelines (which involved many of Cottin's co-authors) on the evaluation and management of EGPA [4].

Differentiating between non-vasculitic EGPA and HES has therapeutic repercussions. In both diseases, corticosteroids constitute the first-line treatment. In EGPA, patients with life- and/or organ-threatening disease manifestations (e.g. acute eosinophilic myocarditis) usually receive a remission-induction regimen with cyclophosphamide and then maintenance treatment with azathioprine or methotrexate [4]. In contrast, these immunosuppressants are rarely effective in HES, and therefore are not recommended [3]. The anti-IL-5 monoclonal antibody mepolizumab is a well-tolerated, effective, long-term, corticosteroid-sparing agent in HES [5]; interestingly, several case reports and the results of uncontrolled trials suggest that mepolizumab is of value in severe and/or refractory EGPA [6–8].

For all these reasons, we propose that patients who present with asthma, an eosinophil count above 1.5 G/L, and systemic manifestations but no vasculitis or ANCA (as identified by Cottin et al.) may be considered as suffering from HES – as indicated by the 2012 consensus expert workshop [9], and the 2015 update on WHO-defined eosinophilic disorders [10]. Further studies are required to determine (i) whether or not patients with undefined HES can progress to “true” EGPA with vasculitis, and (ii) which clinical and/or biological characteristics may be predictive of disease progression.

Conflicts of interest

None.

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None.

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