

Correspondence

Idiopathic, asymptomatic, and durable blood hypereosinophilia—still many unknowns

To the Editor:

With great interest we read a recently published article by Chen et al¹ presenting the clinical and laboratory characteristics of subjects with hypereosinophilia of undetermined significance (HE_{US}). HE_{US} is a new and provisional term that relates to patients with idiopathic and sustained blood hypereosinophilia (HE) (>1500/μL) and no eosinophilia-attributable organ damage. Its clinical relevance needs to be elucidated.² Until now there were no studies analyzing this poorly characterized patient subgroup, and therefore we really enjoyed reading this article. Nevertheless, many questions still remain open and several issues need clarification. The authors showed data of 8 asymptomatic patients with HE_{US} and compared their results with those of a hypereosinophilic syndrome (HES) cohort. Only patients with blood HE of a minimum of 5 years duration were included in this analysis, and the maximum observation exceeded 29 years. We wonder what were the reasons of choosing this time criterion? We may only speculate that the longer the observation the more likely is HE_{US}. This is also more time for comprehensive evaluations. But one may ask why, for example, 6 months' time limit is not enough to exclude primary and secondary blood HE? When we assumed a 6-month cutoff, 40 patients with asymptomatic and sustained blood HE have been identified in our database and they remain idiopathic after a median follow-up of 5 years. This number represents about 25% to 30% of *FIP1L1-PDGFR*A-negative asymptomatic subjects (data not published) and is comparable with that showed in the Chen study.¹

The authors did not find any significant difference between subjects with HE_{US} and subjects with HES in regard to eosinophil counts, cytokines, and surface markers of eosinophil activation. In line with the Chen study,¹ we have found no difference in serum levels of IL-4, IL-5, IL-13, IL-17, thymus activation and regulated chemokine, and eotaxin between on and off therapy subjects with HE_{US}, *FIP1L1-PDGFR*A-negative HES, and *FIP1L1-PDGFR*A-positive HES (data not published). No patient from the Chen study¹ developed HES despite the long-term follow-up. There was a single report on HES development after 9 years of sustained HE.³ Moreover, 1 patient from our cohort after 11 years of asymptomatic blood HE transformed into HES (data not published).

What surprised us in the Chen study¹ is the high proportion of subjects with an aberrant T-cell population on flow cytometry. Despite a small number of included patients with HE_{US}, half of them had a lymphocytic variant. In the up-to-date largest study,

clonal T cells were detected in 17% of the patients with HES,⁴ but data for HE_{US} are still lacking. Personally, we did not detect clonal blood T cells on flow cytometry in our 40 subjects with HE_{US}. Another concern regarding these data is how to classify asymptomatic patients with HE and the presence of T-cell clone. Are they still patients with unknown pathogenesis? We would like to note that lymphocytic HES is classified as secondary HES not idiopathic in the newest classification.²

Currently, we have no reliable data supporting the use of corticosteroids in patients with HE_{US}. However, some experts recommend that corticosteroids be used when blood HE is extremely high, for example, 20,000/μL.⁵ Such high blood eosinophilia was not observed in the Chen study.¹ The upper blood HE threshold was 7,100/μL, and corticosteroids were not administered in her patients. Personally, we offer corticosteroids in selected patients with a high number of circulating blood eosinophils to prevent organ damage. However, every physician should be aware of the adverse events of the prolonged use of corticosteroids and only the minimal effective dose should be offered. We think that it would be interesting for the readers to know the authors' opinion on this topic.

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