

When is Asymptomatic Peripheral Eosinophilia Early-Onset Hypereosinophilic Syndrome?



P. Ogbogu¹, B. Kahwash¹, C. Curtis¹, N. Boggs², J. Li³, E. Erwin¹, R. Scherzer¹,
P. Khoury², S. Mathur³, A. Klion²

¹Division of Allergy and Immunology, The Ohio State University/Nationwide Children's Hospital, Columbus, OH; ²National Institutes of Health/NIAID, Bethesda, MD; ³Division of Allergy, Pulmonary and Critical Care Medicine, University of Wisconsin, Madison, WI



RATIONALE

- Hypereosinophilia of uncertain significance (HEus) is defined as asymptomatic hypereosinophilia (AEC ≥ 1500 cells/mm³) on two occasions one month apart, without evidence of end organ manifestations.
- Although relatively uncommon, HEus presents a diagnostic challenge: both risk of progression and predictors of progression to hypereosinophilic syndrome (HES) are unknown.
- Based on previous investigations of HES, it is estimated that 5% of patients who develop end-organ eosinophilic disease present initially without symptoms (Figure 1).
- Objective: to identify demographic and clinical features, as well as baseline laboratory findings, in patients with HEus that are associated with progression to HES.**

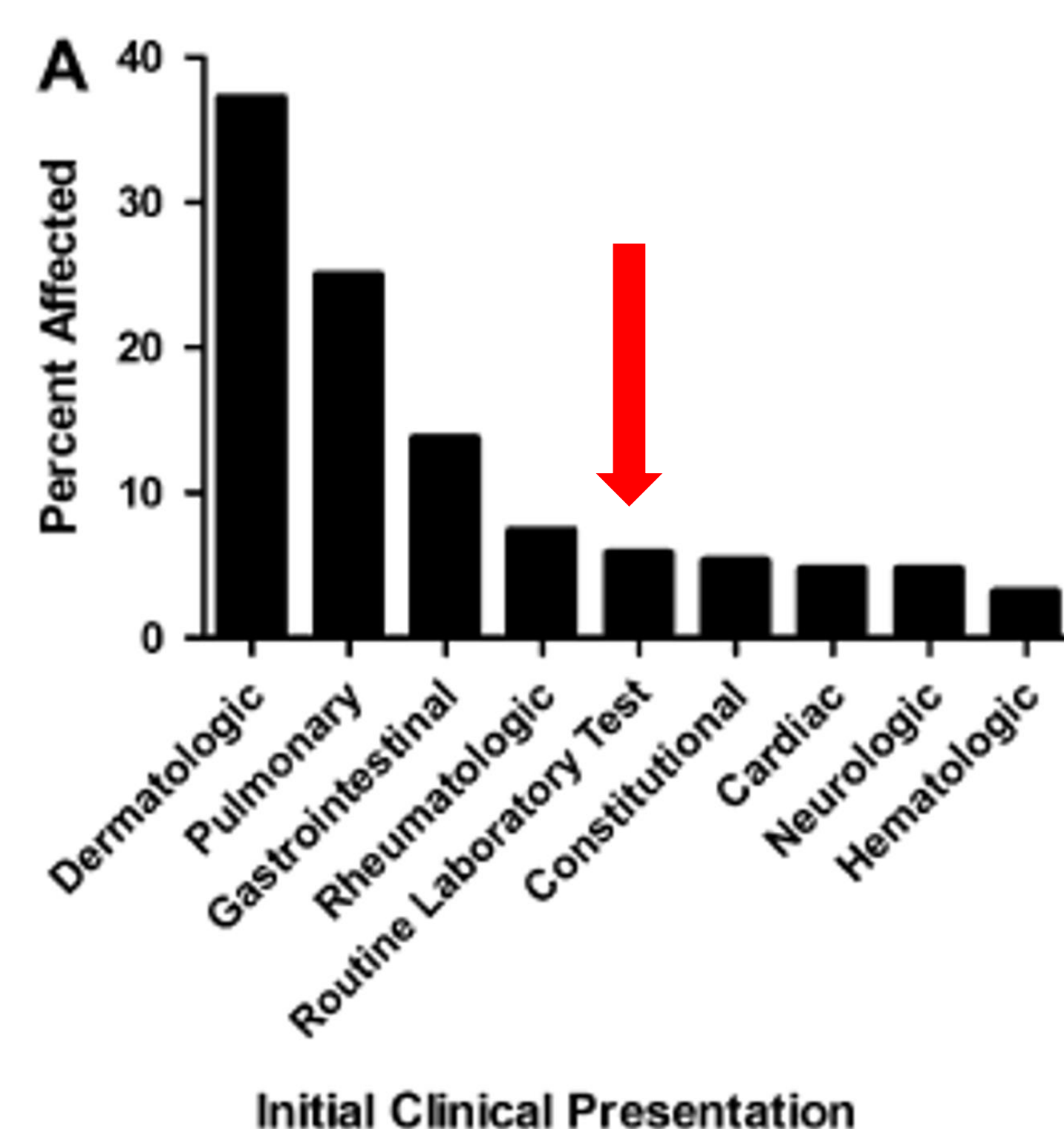


Figure 1. Clinical manifestations of HES at initial presentation (published data)¹.

RESULTS

Characteristic	Male	Female	Total
Number of Patients	30	9	39
Median Peak AEC (Cells/ μ l)	3850	3682	3700
Number of Patients with Clonal T-Cell Population	6	3	9
Eventual Diagnosis			
HES	6	1	7
Other Diagnosis/No Diagnosis	24	8	32

Table 2. Preliminary data from patients with HEus.

- 39 patients with asymptomatic peripheral hypereosinophilia were included in the preliminary analysis (Table 2).
- 9 out of the 39 patients had clonal T lymphocyte populations detected by PCR. Interestingly, none of these 9 patients progressed to HES.
- 7 of 39 patients eventually progressed to hypereosinophilic syndrome with end-organ disease. 4 of these 7 patients had myeloid-variant HES as determined by detection of a PDGFRA gene rearrangement.

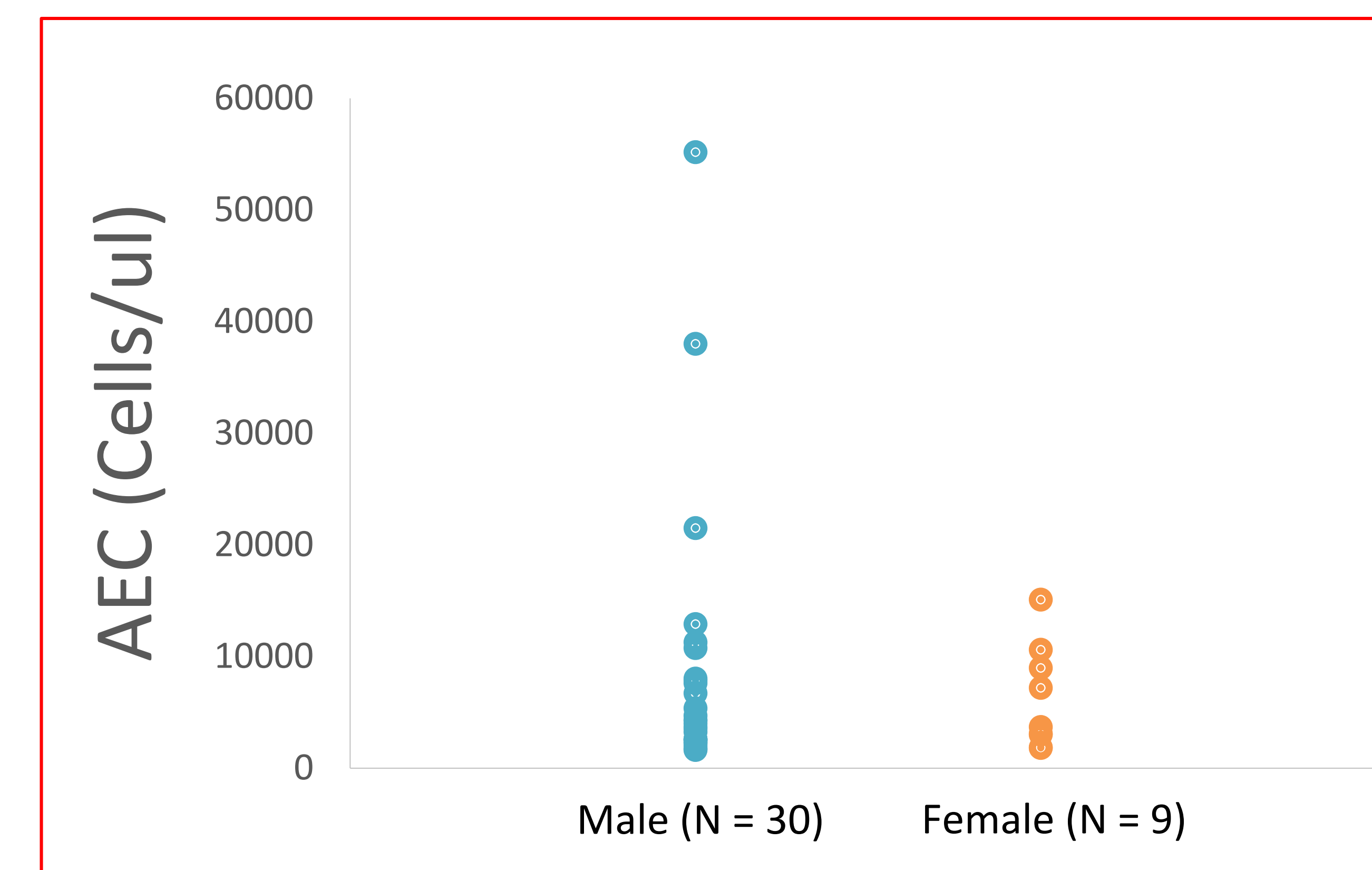


Figure 2. Peak peripheral blood absolute eosinophil count by biological sex.

- 30 out of the 39 patients with HEus were male. Median AEC did not appear to vary by biological sex, however all 3 patients who recorded AEC > 20,000 cells/ul were male (Figure 2).
- 6 of the 7 patients who progressed to HES from asymptomatic hypereosinophilia were male.

METHODS

- A multicenter retrospective study was initiated at 17 medical centers in the United States and Europe. Preliminary data from 39 adult and pediatric patients evaluated between January 1st, 2000 and January 30th, 2019 at 3 centers in the United States (Table 1) are presented here.
- Inclusion criteria: 1) patient presented with asymptomatic AEC ≥ 1500 cells/mm³ of unknown cause without evidence of end organ manifestations on at least 2 occasions at least 1 month apart, and 2) patient was followed for at least 1 year after the diagnosis of presumptive HEUS.
- Exclusion criteria: 1) patient was found to have a defined etiology of HE (AEC ≥ 1500/mm³), such as parasitic infection, malignancy or drug hypersensitivity, or 2) patient was treated with an agent that affects eosinophil count (with the exception of inhaled or topical steroids) within 1 month of the diagnosis of HEUS, or within 3 months if the treatment was a biologic.

Demographics	Age at presentation; Biological sex; Racial/ethnic category
Clinical Features	Concomitant medical diagnoses; clinical manifestations
Baseline Laboratory Findings	Peripheral blood AEC at presentation; Serum B12, tryptase, IgE, troponin, ESR, CRP; Serum Strongyloides antibody; Stool ova/parasite assay; Peripheral blood flow cytometry for lymphocyte subsets; Peripheral blood T cell clonality by PCR; Cytogenetics
Peak Laboratory Findings	Peak peripheral blood AEC; CBC with differential at peak AEC; Serum B12, tryptase, IgE, troponin, ESR, CRP
Diagnostic Test Results	Echocardiogram; Spirometry/PFT; Imaging (eg. CT Chest); Tissue Biopsy; Bone Marrow Biopsy

Table 1. Data points collected.

CONCLUSIONS

- Preliminary data from patients who presented with asymptomatic peripheral blood eosinophilia confirm that HEus is a rare disorder.
- Early data suggests that HEus has a male predominance and that while progression to HES can be observed, most patients remain asymptomatic.
- Further analysis of demographic, clinical, and diagnostic data is needed to identify potential risk factors for progression to HES.

REFERENCES

1. Ogbogu PU et al. Hypereosinophilic syndrome: a multicenter, retrospective analysis of clinical characteristics and response to therapy. *JACI*. 2009; 124(6):1319-25.