

Challenges in Diagnosing and Managing Hypereosinophilia in Pediatric Patients: A Case Report

S. Azitoune¹, Z. Isfaoun², L. Hessissen³

^{1,2,3}Pediatric Hematology and Oncology Department, Rabat Children's Hospital

Abstract: *Hypereosinophilia HE is a condition with various potential etiologies, posing diagnostic and treatment challenges, especially in pediatric cases. This article presents a case study of a child with major hypereosinophilia and emphasizes the complexities of diagnosis and the importance of continuous disease monitoring to prevent potentially fatal complications. The diagnostic approach involves a thorough examination, additional tests, and consideration of various underlying causes beyond the common parasitic, allergic, or medicinal factors. The article discusses the management of the patient, including corticosteroid therapy and dietary restrictions, as well as the role of genetic studies in identifying potential genetic mutations. Furthermore, it explores the prevalence and common causes of hypereosinophilia in children, highlighting the significance of early diagnosis and management in preventing adverse outcomes.*

Keywords: Hypereosinophilia, Pediatric Patients, Diagnosis, Case Study, Complications

1. Introduction

Peripheral hypereosinophilia (HE) is defined by an eosinophilia rate greater than 1500 cells/mL on at least two samples with a minimum time interval of 4 weeks.

Tissue HE is diagnosed in the presence of at least one of the following criteria:

- 1) Eosinophils constitute more than 20% of all nucleated cells in the bone marrow.
- 2) And/or the presence of significant tissue infiltration by eosinophils, as determined by a pathologist,
- 3) And/or marked deposition of eosinophilia granular proteins is present (with or without major tissue infiltration).

Hypereosinophilic syndrome (HES) is defined by:

- 1) Blood hypereosinophilia, >6 months
- 2) And an organic lesion or dysfunction secondary to hypereosinophilia,
- 3) Without any other argument for another cause for the organic damage.

Alongside the parasitic, allergic, or medicinal causes, which are most frequently observed, we also find blood diseases or cancers. (1.2.3)

In this work, we present the clinical observation of a child with severe hypereosinophilia.

2. Observation

Child aged five and a half; history: repeated infections (ear infections and urinary infections), episodes of epigastralgia and heartburn, personal and family atopy, non-consanguineous parents

Follow-up for etiological research on hypereosinophilia syndrome

History: Goes back to 7 months before his admission with the appearance of a febrile torticollis with an assessment revealing hyperblood and marrow eosinophilia, whose evolution was marked by a decrease in the eosinophil level after deworming and reappearance after 7 months of an afebrile torticollis with a re-increase in eosinophils.

Examination at admission: good general condition, right torticollis, moderate limitation in opening the mouth, with tonsillar hypertrophy and bilateral cervical lymphadenopathy less than 1 centimeter

Additional Tests:

| NFS | 28/08/2018 | 25/09/2018 | 22/01/2022 | 04/05/2022 | 16/07/2022 | 07/31 | 08/22 | 22/11/22 | 02/01/23 | unit |
|---------|------------|------------|------------|------------|------------|--------|--------|----------|----------|-----------------|
| HB | 9,7 | 9,7 | 9,3 | 10,4 | 11,4 | 9,7 | 10 | 10.4 | 10.5 | g/dl |
| VGM | 64,9 | 61,8 | 54,5 | 60,5 | 67,2 | 63,7 | 62 | 61 | 66.1 | mm ³ |
| GB | 30200 | 19280 | 98210 | 12260 | 90940 | 11780 | 14070 | 43900 | 5500 | /ul |
| PNN | 15220 | 9717 | 10606 | 4950 | 11820 | 5390 | 6050 | 6716 | 1400 | /ul |
| LYM PH | 8400 | 5745 | 12767 | 4540 | 13640 | 4500 | 5346 | 5443 | | /ul |
| EOSI NO | 0 | 231 | 70514 | 1370 | 60020 | 200 | 703 | 29237 | 600 | /ul |
| PLQ | 34400 | 278000 | 439000 | 412000 | 398000 | 385000 | 347000 | 328000 | 210000 | /ul |

Medullogram: marrow eosinophilia 66% eosinophils; 55% after treatment with corticosteroid therapy; Immunophenotyping presence of 3% of blast population

Esophago-duodenal fibroscopy: micro abscess in the esophagus Esophageal biopsies: fibrino-leukocyte block showing polynucleareosinophils and neutrophils indicating nearby ulceration. Gastric biopsy: chronic mild to moderate slightly active non-atrophic antropfunditisJejunal biopsy: edematous duodeno-jejunitis with hemorrhagic character, IgE 321.12 u/ml; skin test normal; Unremarkable specific IgE

Normal stool coproparasitology; normal serologies, normal weight dosage of IgA, IgG and IgM, normal lymphocyte typing

Normal lung radiology,

Cervical CT: laterocervical lymph nodes and adenomegalyThoraco-abdominopelvic CT: homogeneous hepatomegaly 10 cm;

Normal transthoracic ultrasound;

Normal ophthalmological examination; otolaryngological examination: no otitis, presence of tonsillar hypertrophy

Genetic study absence of the PDGRF gene. PDGFRA, PDGFRB, FGFR1; 46XY karyotype no genetic mutation

And subsequently, a cow's milk protein diet whose research framework for a restriction diet is started,

Observation of a clear reduction in the level of blood eosinophils

A negative skin test, specific IGE dosages without particularity. Positive milk and cheese patch test



Treatment:

Oral Corticotherapy for 3 months with a clear reduction in the rate of eosinophilia and re-increase in eosinophils is after stopping corticosteroid therapy

Moreover, given the absence of the PDGFRA ET B gene and the re-increase in eosinophils after stopping corticosteroid therapy, the decision was to seek a diet with possible restriction; diet without cow's milk protein was started

The evolution marked by a clear reduction in the rate of eosinophilia

3. Discussion

The incidence of hypereosinophilia in children is approximately 0.4 cases per 1, 000, 000. (4)

Secondary HE: eosinophils considered as non-clonal cells. Polyclonal expansion of eosinophils through increased production of eosinophil-promoting cytokines, such as interleukin (IL)-3, IL-5, and granulocyte-macrophage colony-stimulating factor (GM-CSF). (4 5 6)

The most common causes:

- Allergic disorders (asthma, atopic dermatitis),
- Infections (fungal, viral [HIV], bacterial) Drug hypersensitivity, Primary immunodeficiency
- Neoplasms (leukemia, lymphoma),
- Chronic inflammatory bowel/autoimmune diseases: Systemic lupus, Vasculitis, Sarcoidosis, Other chronic inflammatory diseases

Primary Hyper-Eosinophilic: Primary (8% and 11%): results from an underlying stem cell, myeloid, or eosinophilic neoplasm, in which eosinophils represent the predominant cell type or are one of several proliferating cell lineages; eosinophils are considered malignant.

Myeloid/lymphoid tumors associated with eosinophilia and PDGFR, PDGFR-b, or FGFR1, or with PCM1-JAK2 rearrangementsFamily HE

A cohort done at Texas Children's Hospital between January 1, 2011 and December 31, 2019 of 771 patients under the

age of 18 who were evaluated. The most common cause of eosinophilia was allergy (46%), with atopy and drug reaction being the most common subcauses. Next, come unknown etiology (36%), infectious causes (9%) and parasitic causes (6%). (6,7)

The diagnosis of hypersensitivity reaction syndromes to foods is clinical and is based on the history, symptoms and possible link with a food.

Among reactions to food, eosinophilic enteropathy is of particular importance.

According to the EuroPrevall study, the prevalence of non-IgE-mediated and challenge-confirmed cow's milk protein allergies was low, at approximately 1%. In the UK birth cohort of this study, the cumulative incidence of all allergens was 2.4% (cow's milk 1.7%). (8)

However, the true prevalence of non-IgE-mediated allergies is believed to be higher, as it is often misdiagnosed/unrecognized as these symptoms frequently occur during infancy and in breast-fed infants. (9)

4. Conclusion

This observation highlights the difficulty of establishing a cause, hence the need to follow a methodical approach and regular monitoring for early management of complications, which can be fatal.

References

- [1] AD Klion. How I treat hypereosinophilic syndromes. *Blood* 2015;126:1069-77 Valent
- [2] P, Klion AD, Horny HP, Roufosse F, Gotlib J, Weller PF, et al. Proposed contemporary consensus on the criteria and classification of eosinophilic disorders and related syndromes. *J Allergy Clin Immunol* 2012;130:607-612.e9
- [3] Diagnosis and management of pediatric hypereosinophilic syndrome
- [4] Chen E. Rosenberg, MDun, Patricia C. Fulkerson, MD, PhD, and Kelli W. Williams, MD, MPHcBoston, Mass; Bethesda, Maryland; and Charleston, SCCABINET J ALLERGY CLIN IMMUNOLMAY 2022J ALLERGY CLIN IMMUNOL PRACT VOLUME 10, NUMBER 5
- [5] Shomali W, Gotlib J. World Health Organization and defined eosinophilic disorders: 2022 update on diagnosis, risk stratification and management. *Am J Hematol* 2022;97:129-48
- [6] Helbig .G, Klion AD. Hypereosinophilic syndromes – an enigmatic group of disorders with an intriguing clinical spectrum and challenging treatment. *Blood Rev* 2021;49:100809. *Am J Hematol* 2022; 97:129-48
- [7] Burris D, Rosenberg CE, Schwartz JT, Zhang Y, Eby MD, Abonia JP, et al. Pediatric hypereosinophilia: characteristics, clinical manifestations and diagnoses. *J Allergy Clin Immunol Pract* 2019; 7:2750-2758.e2
- [8] Pediatric Eosinophilia: A Review and Multiyear Investigation into Etiologies, Tara E. Ness, MD, MPH, Timothy A. Erickson, PhD, MSPH, Veronica Diaz,

MD, Amanda B. Grimes, MD, Ryan Rochat, MD, PhD, Sara Anvari, MD, MS, Joud Hajjar, MD, MS3, and Jill Weatherhead, MD, PhD THE JOURNAL OF PEDIATRICS, Volume 253, February 2023.

- [9] Schoemaker AA, Sprickelman AB, Grimshaw KE, et al. Incidence and natural history of challenge-proven cow's milk allergy in European children – Euro Prevall birth cohort. *Allergie* 2015;70(8):963-972.
- [10] Grimshaw K, Bryant T, Oliver EM, et al. Incidence and risk factors for food hypersensitivity in British infants: results from a birth cohort study. *Clin Transl Allergy*. 2015;6:1