DOI:10.21276/sjpm.2017.2.3.9

Saudi Journal of Pathology and Microbiology
Scholars Middle East Publishers
Dubai, United Arab Emirates
Website: http://scholarsmepub.com/

ISSN 2518-3362 (Print)
ISSN 2518-3370 (Online)

Case Report

Idiopathic hypereosinophilic syndromes and diagnostic difficulties

A. Taghouti*, S. Figuigui, Z. Bennani, H. khalki, Z. Amhaouch, F. Aich, I. Tlamçani, M. Amrani Hassani
Laboratory of Medical Analysis, Department of Hematology, Hassan II Hospital of Fez, Morocco

***Corresponding Author:**
A. Taghouti
Email: taghoutiamal@gmail.com

Abstract: Hypereosinophilia is defined by blood eosinophil count greater than 0.5 x 109 / L, it is a biological symptom which should not be neglected given the risk of visceral complications. However, any eosinophilia should be thoroughly investigated in order to define the etiology and treat it. Diagnosis of idiopathic hypereosinophilic syndrome HES can be retained after elimination of parasitic, allergic and haematological causes in the presence of a blood eosinophilia greater than 1.5 x 109 / L evolving over a period of at least six months and complicated by at least one visceral lesion. The visceral sites observed are not specific among which the cardiac and neurological attacks are the most dangerous compared to the other attacks: bronchopulmonary, liver, digestive, renal, cutaneous. We report an observation of persistent hypereosinophilia in a patient with exclusively digestive signs and the diagnostic difficulties encountered.
Keywords: hypereosinophilic syndromes, digestive tract, corticosteroid therapy.

INTRODUCTION

HES are classically divided between lymphoid forms with Th2 lymphocytics abnormalities (CD3-CD4 +), myeloproliferative forms associated or not to a FIP1L1-PDGFRα fusion transcript and idiopathics HES which constitutes a diagnosis of elimination [1, 2]. Several organs can be affected in hypereosinophilic syndromes: the skin, the lungs, the nervous system, the heart and the digestive tract. Hypereosinophilia with only one visceral involvement is rarely found, we report the case of a patient who has persistent major blood eosinophilia with exclusively digestive signs, which makes a diagnostic problem in view of the non-specific clinical picture.

CASE REPORT

It is a 65-year-old male patient with no significant pathological history (no diabetes, no allergy or atopy and no travel concept in the tropics) who consults for one Weight loss at 15 kg over 2 months with digestive signs of abdominal pain, vomiting without diarrhea or fever, in physical examination does not find adenopathies or hepatosplenomegaly; An initial balance sheet revealed isolated hypereosinophilia at 4500 x 109 / L for a leukocyte rate of 9720 x 109 / L without anemia or thrombocytopenia and was confirmed on several hemograms. Considering the clinical picture of more thorough examinations are requested: stool examination for parasites is negative, distomatosis serology, trichinosis, ascariasis, and toxocarose serologies are negative, thus eliminating a parasitic etiology. Negative allergic tests with normal IgE at 7 KIU / L. Abdominal ultrasound did not show splenomegaly, hepatomegaly, adenopathy, ascites or intestinal thickening. The medullary smear shows a marrow massively infiltrated by eosinophilic elements (precursors and mature elements) of normal morphology with 2% blasts cell (Figure 1). The karyotype performed on bone marrow is normal (Philadelphia chromosome negative). Immunophenotyping of lymphocyte subpopulations is also normal. Cardiovascular examination, electrocardiogram and echocardiography did not reveal any secondary abnormalities. The diagnosis of essential hypereosinophilic syndrome has been suggested by default of the realization of a molecular cytogenetics for lack of means that could show cytogenetic abnormalities. The clinical and biological evolution of the patient was favorable under corticosteroid therapy with disappearance of the digestive signs, weight gain and return to normal of the blood eosinophilic rate at 380 / mm³.

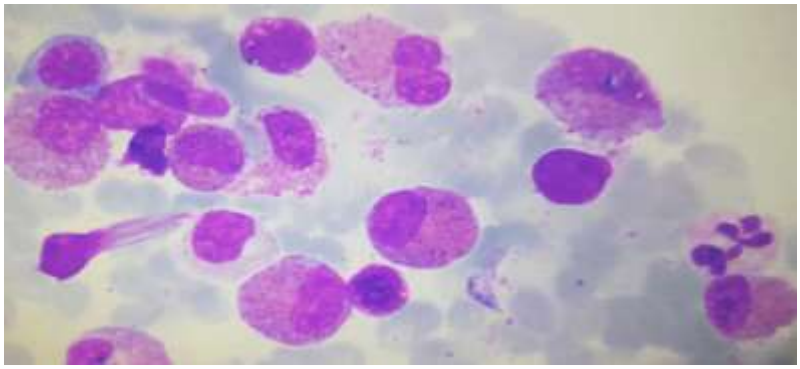

Fig-1: Medullary smear with Wright Giemsa stain, magnification x100 in optical microscop, showing massive medullary infiltration by eosinophils.

DISCUSSION

Major hypereosinophilia are defined by a rate of eosinophilic granulocyte greater than 1500 x 109 / L [2]. Eosinophils produced in the bone marrow make a passage of a few hours in the bloodstream and then migrate to the tissues, especially the lungs, skin and digestivetract. Their half-life is about ten days [3]. They release inflammatory mediators at the tissues such as cationic proteins (eosinophil cationic protein, eosinophil derivated neurotoxin, eosinophil peroxidase and major basic protein) that havea direct tissue toxicity [4]. The hypereosinophilic syndrome is defined according to the diagnostic criteria of Chusid since 1975 by a rate of eosinophils greater than 1500 x 109 / L, chronic over a period of 6 months with no obvious cause and with visceral involvement; But in the new classification adopted by the Hypereosinophilic Syndromes Working Group in 2005 and revised in 2010 with respect to the Chusid classification the visceral involvement criterion became optional for early diagnosis before irreversible visceral complications [5-7]. Significant advances in knowledge of the physiopathology of hypereosinophilic syndromes, such as the identification of a FIP1L1-PDGFRA fusion gene in certain myeloproliferative forms and the presence of Th2-type lymphocyte abnormalities responsible for hypersecretion of interleukin -5, the main element in eosinophilopoiesis; But despite this progress more than half of the HES remain unexplained [8, 9]. In patients with lymphoid hypereosinophilic syndromes, patients often have cutaneous manifestations including angioedema, erythroderma, pruritic or urticaria, however, cardiac involvement is rare. Biologically, there is a polyclonal elevation of gammaglobulins and total IgE, whereas lymphocytes are cytologically normal, hence the interest of lymphocyte immunophenotyping which shows abnormal phenotypic T profiles and variable from one patient to another. A good therapeutic response to corticosteroids is usual with the risk of corticodependence [1, 4]. Chronic eosinophilic leukemia is characterized by a male predominance. The affected organs are identical to those of HES with predominance of cardiac involvement and mucosal ulcerations whereas digestive tract disorder remains rarer. The medullogram seeks an increase in the rate of blast cells but remains less than 20%, with in parallel an increase in tryptase and vitamin B12 which is quasi-constant. The osteomedullary biopsy shows an excess of mast cells, the FIP1L1-PDGFRA fusion transcript is identified by FISH or RT-PCR and the karyotype in this case is normal. Therapeutically, hypereosinophilia does not improve under corticosteroid therapy; On the other hand, imatinib has totally changed the prognosis of these patients [10-12]. The HES is seen mostly at ages between 20 and 50 years with a male predominance (9/1). They are presented by general signs in 50% of the patients with visceral involvement in the heart, the skin, the lungs, the digestive tract and the nervous system [2]. The etiologic examinations are: radiological assessment (ultrasound, CT scan ...), myelogram, osteomedullary biopsy, T lymphocyte immunophenotyping, medullary karyotype and FISH, without forgetting the evaluation of the Impact on organs of hypereosinophilia [1]. The blood smear explores the morphology of eosinophils: dystrophic or not, and looks for possible abnormalities such as the presence of blast cells, early myeloid cells or atypical lymphocytes thus helping to etiologic orientation. The diagnosis of idiopathic HES can be retained after elimination of parasitic, allergic and haematological causes. Medullary cytology should not show signs of myelodysplasia, myeloproliferative syndrome, or excess blast cells with cytogenetics and molecular biology without abnormalities [13]. (Table I) The digestivetract constitutes 38% of the damage found during HES but it is rarely isolated as the case of our patient. These effects are usually accompanied by general signs of asthenia, emaciation or fever, but the severity of the manifestations is not proportional to the level of eosinophils. Digestive manifestations are non-specific: abdominal pain, diarrhea and ascites [14]. The diagnoses to be evoked in front of an hypereosinophilia with digestive signs are digestive helminthiasis; parasitoses that have a larval or adult phase located in other tissues are accompanied by significant hypereosinophilia: bilharziasis, ascariasis, anguillulose, toxocarose, trichinosis, hookworm disease, celiac disease, crohn's disease and eosinophilic gastroenteritis, where the need for a complete assessment including an ultrasound, an abdominal scan and an endoscopy with biopsies [15, 16]. The syndrome of idiopathic

hypereosinophilia with a digestive localization constitutes a differential diagnosis of eosinophilic gastroenteritis. The latter may be presented under different clinical tables depending on the location of the eosinophilic infiltrate. The involvement of the mucosa gives a table of enteropathy with a malabsorption syndrome. The involvement of the muscularis is in the form of subocclusion and the involvement of the serous results in an ascitic array with pseudoperitonitis [17]. Eosinophilic gastroenteritis has no specific clinical signs. Usually, there is a personal or family history of atopy with increased total IgE, but hypereosinophilia of blood is only present in 50% of cases. Gastric involvement is frequent, mainly affecting the antrum and results in abdominal pain, vomiting, nausea and weight loss [15]. The prognosis of HES is related to cardiac involvement because of resulting high mortality, hence the interest of a systematic exploration as part of his impact assessment (electrocardiography, echocardiography). It evolves in several phases: initially, it is a myocarditis with eosinophils often silent; Then thrombi may be formed in the left ventricle with risk of progression to endomyocardial fibrosis and restrictive cardiopathy, whereas other explorations are required according to the symptomatology [14]. Corticosteroid therapy is usually effective because circulating eosinophils are usually carriers of glucocorticoid receptors, which explains their high corticosensitivity but where appropriate, the use of second-line therapies is necessary: hydroxyurea or alpha interferon. For patients with hypereosinophilia with recurrent deletion 4q12; Imatinib significantly improved their prognosis at a dose clearly lower than that used to treat chronic myeloid leukemia (CML) (100 mg / day versus 400 mg / day in the case of CML). However, some patients responded well to imatinib treatment even in the absence of this molecular abnormality [18, 19].

Table-I: Etiologies to be evoked in front of hypereosinophilia.

Parasitoses: helminthoses +++ Distomatose, Trichinose, Anisakiase, visceral Larva migrans (toxocarose) ; Tæniasis and threadworm (eosinophils < 1 500 x 109/L)
Allergies: asthma, allergic rhinitis, atopic dermatitis
Drug toxicity: amphotéricin B, Beta lactams, isoniazid, Alpha methyl-dopa
Autoimmune disorders : Churg Strauss syndrome, rheumatoid arthritis, Wegener's Granulomatosis, Periarteritis nodosa, Shulman's syndrome, Bullous pemphigoid, scleroderma, Crohn's disease …
Cancers: paraneoplastic sundromes
Infections: HIV, tuberculosis…
Hemopathies : Hodgkin's disease, T lymphomas, systemic mastocytosis, myeloproliferative syndromes …

CONCLUSION

Hypereosinophilic syndrome (HES) is a diagnosis of elimination in front of any unexplained chronic hypereosinophilia after numerous clinical and paraclinical investigations leading to no pathology, Hence the interest of regular monitoring to prevent the mostly cardiac complications that are the cause of high mortality in these patients [20].

REFERENCE

1. Malfuson, J. V., Fagot, T., Konopacki, J., Mangouka, L., Souleau, B., & de Revel, T. (2009). Hyperéosinophilies et affections hématologiques. *La Revue de médecine interne*, *30*(4), 322-330.
2. Kahn, J. E., Girszyn, N., & Blétry, O. (2006). Causes non parasitaires des grandes hyperéosinophilies. *La Presse Médicale*, *35*(1), 144-152.
3. Bourée, P., & Lançon, A. (2000). Diagnostic d'une hyperéosinophilie sanguine. *Revue Française des Laboratoires*, *2000*(321), 67-71.
4. Kahn, J. E., Grandpeix-Guyodo, C., Ackermann, F., Charles, P., Legrand, F., & Blétry, O. (2010). Syndromes hyperéosinophiliques: actualités physiopathologiques et thérapeutiques. *La Revue de médecine interne*, *31*(4), 268-276.
5. Chusid, M. J., Dale, D. C., West, B. C., & Wolff, S. M. (1975). The hypereosinophilic syndrome: analysis of fourteen cases with review of the literature. *Medicine*, *54*(1), 1-27.
6. Klion, A. D., Bochner, B. S., Gleich, G. J., Nutman, T. B., Rothenberg, M. E., Simon, H. U., ... & Hypereosinophilic Syndromes Working Group. (2006). Approaches to the treatment of hypereosinophilic syndromes: a workshop summary report. *Journal of Allergy and Clinical Immunology*, *117*(6), 1292-1302.

7. Simon, H. U., Rothenberg, M. E., Bochner, B. S., Weller, P. F., Wardlaw, A. J., Wechsler, M. E., ... & Klion, A. D. (2010). Refining the definition of hypereosinophilic syndrome. *Journal of allergy and clinical immunology*, *126*(1), 45-49.
8. Cogan, E., Schandene, L., Crusiaux, A., Cochaux, P., Velu, T., & Goldman, M. (1994). Clonal proliferation of type 2 helper T cells in a man with the hypereosinophilic syndrome. *New England Journal of Medicine*, *330*(8), 535-538.
9. Cools, J., DeAngelo, D. J., Gotlib, J., Stover, E. H., Legare, R. D., Cortes, J., ... & Cross, N. C. (2003). A tyrosine kinase created by fusion of the PDGFRA and FIP1L1 genes as a therapeutic target of imatinib in idiopathic hypereosinophilic syndrome. *New England Journal of Medicine*, *348*(13), 1201-1214.
10. Vandenberghe, P., Wlodarska, I., Michaux, L., Zachée, P., Boogaerts, M., Vanstraelen, D., ... & Maerevoet, M. (2004). Clinical and molecular features of FIP1L1-PDFGRA (+) chronic eosinophilic leukemias. *Leukemia*, *18*(4), 734-742.
11. Klion, A. D., Noel, P., Akin, C., Law, M. A., Gilliland, D. G., Cools, J., ... & Nutman, T. B. (2003). Elevated serum tryptase levels identify a subset of patients with a myeloproliferative variant of idiopathic hypereosinophilic syndrome associated with tissue fibrosis, poor prognosis, and imatinib responsiveness. *Blood*, *101*(12), 4660-4666.
12. Vallentin, B., Barlogis, V., Doréb, E., & Chambosta, H. (2016). Mise au point: diagnostic d'hyperéosinophilie chez l'enfant. Revue d'oncologie hématologie pédiatrique, 4 (4) , 246-252.
13. Bain, BJ. (2004). Relation ship between idiopathic hypereosinophilic syndrome, eosinophilic leukemia and systemic mastocytosis. American Journal of Hematology, 77(1), 82–85.
14. Kahn, J. E., Schoindre, Y., Legrand, F., Bletry, O., & Ackermann, F. (2011). Hyperéosinophilies chroniques inexpliquées syndromes hyperéosinophiliques. *Revue des Maladies Respiratoires Actualités*, *3*(2), 108-113.
15. Desreumaux, P., Seguy, D., Dutoit, E., Dubucquoi, S., & Colombel, JF. (1996). La gastroentérite à éosinophiles. Hépato-Gastro & Oncologie Digestive, 3(4), 279-286.
16. Talley, NJ., Shorter, RG., Phillips, SF., & Zinsmeister, AR. (1990). Eosinophilic gastroenteritis: a clinicopathological study of patients with disease of the mucosa, muscle layer, and subserosal tissues. Gut, 31(1), 54-58.
17. Prin, L., Lepers, S., Roumier, AS., & Dubucquoi, S. (2002). Suivi d'une hyperéosinophilie persistante. Revue Francaise d'Allergologie et d'Immunologie Clinique, 42 (3), 219-230.
18. Ogbogu, PU., Bochner, BS., Butterfield, JH., Gleich, GJ., Huss-Marp, J., Kahn, JE., Leiferman, KM., Nutman, TB., Pfab, F., Ring, J., Rothenberg, ME., Roufosse, F., Sajous, MH., Sheikh, J., Simon, D., Simon, HU., Stein, ML., Wardlaw, A., Weller, PF., & Klion, AD. (2009). Hypereosinophilic syndrome : a multicenter, retrospective analysis of clinical characteristics and response to therapy. Journal of Allergy and Clinical Immunology, 124 (6), 1319-1325.
19. Moles, MP., Landry, J., Roche-Lestienne, C.,Godon, A, Schmidt-Tanguy, A., Gardembas, M., Le Clech, C., Verret, JL., Zandecki, M., & Blanchet, O. (2005). Hyperéosinophilie essentielle : nouvelle thérapeutique ciblée et nouvelle définition cytologique et moléculaire. Annales de Biologie Clinique, 63 (3), 317-322.
20. Prin, L., Gatault, S., Lefèvre, G., & Kahn, JE. (2014). Le polynucléaire éosinophile : nouveautés en physiologie et implications diagnostiques. Revue Francophone des Laboratoires. 462, 73-85.