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Eosinophilic Variant Of Acute Myelomonocytic Leukemia Revealed By Necrotizing Myocarditis : Case Report.

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Abstract*: Acute myeloid leukemia are a heterogeneous group of hematological malignancies that account for more than 80% of acute adult leukemia, with a worldwide incidence rate of 2.6 per 100.000 population. The myelomonocytic subtype with eosinophilic component accounts for 5 to 8% of these acute myeloid leukemias and can occur at any age, but especially in young adults. It is associated with chromosome 16 inversion. Inaugural cardiac involvement during these hemopathies is rare, and seems to be related to eosinophilia associated with AML4 vEo. We report a case of acute necrotizing myocarditis revealing acute hypereosinophilic eosinophilic myelomonocytic leukemia in a young patient with congestive heart failure, in the absence of progressive coronary or valvular disease. The biological assessment, myelogram and molecular biology have allowed to diagnose acute myelomonocytic leukemia with eosinophilic variant, and to establish a rapid and effective therapeutic management.*

Keywords: hypereosinophilia; acute myelomonocytic leukemia; necrotizing myocarditis

1. INTRODUCTION :

Eosinophilic variant acute myelomonocytic leukemia, classified as AML 4 Eo according to the Franco-American-British international classification, is a rare hematological malignancy, characterized by myeloid blast proliferation, associated with monocytosis and dystrophic eosinophils. It differs from all acute myeloid leukemias by its better prognosis, with a remission rate of about 80% [1].

We report the case of an eosinophilic variant acute myelomonocytic leukemia in a 36-year-old patient, revealed by an acute necrotizing myocarditis, which we will discuss in the light of the data in the literature.

2. CASE REPORT :

Mr D.J, 36 years old, with no previous history, was referred to the emergency department for acute chest pain and aggravation of respiratory distress. The history of his illness revealed NYHA stage II dyspnea evolving for one month, without palpitations or loss of consciousness, in a patient whose only cardiovascular risk factor was the male sex. The physical examination found a conscious patient, hemodynamically and respiratory stable, apyretic. Physiological parameters showed 112/88 mmHg blood pressure in both arms, a heart rate of 98 beats per minute, and 96% ambient air saturation. The cardiovascular examination showed present and symmetrical peripheral pulses and normal cardiac auscultation. The rest of the examination showed a skin paleness, bilateral inguinal lymphadenopathy and homogeneous hepatosplenomegaly, with a liver arrow at 12cm.

The electrocardiogram performed on admission showed anterior subepicardial ischemia. The chest X-ray showed cardiomegaly and bilateral perihilar vascular overload. Biological assays confirmed myocardial necrosis (troponin: 12 mg/l) and heart failure (pro-BNP: 10850 pg/ml). There was also a major leukocytosis at 112000 leukocytes/mm3 with aregenerative normochromic normocytic anemia at 8g/dl, and thrombocytopenia at 90 G/L. The blood smear was used to perform a count with verification of circulating cells, which showed the presence of a 43% blastosis, monocytosis at 5G/L, and an excess of dystrophic eosinophilic polynuclear (monolobate, fragmented or hypersegmented nucleus; immature granulations, cytoplasmic vacuoles) (figure 1).

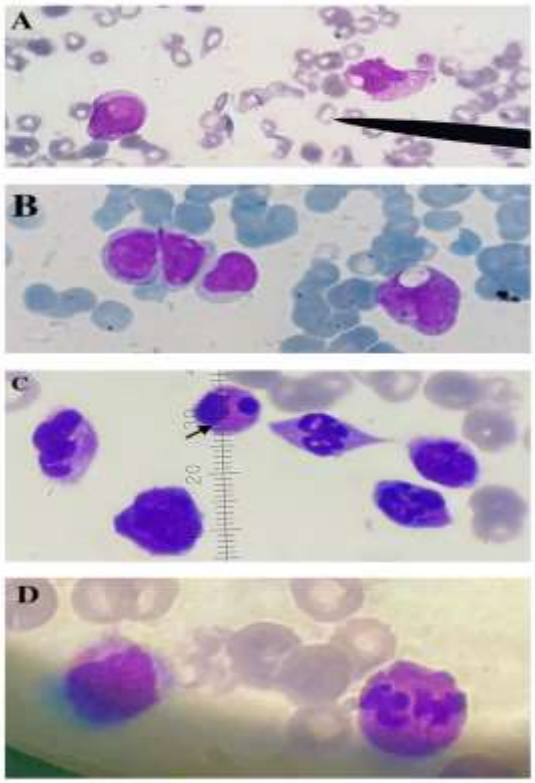

Figure 1: Hematology laboratory, Hassan II University Hospital, Fez, Morocco, Blood smear (May-Grünwald-Giemsa, read under light microscope, objective x100) showing:

(A): one blast on the left and one monocyte on the right;

(B): three undifferentiated blasts on the left and one monocyte on the right;

(C): dystrophic eosinophilic polynuclear cells with fragmented nuclei (arrow);

(D): eosinophilic polynuclear cells with fragmented and hypersegmented nuclei on the right, and one monocytic blast on the left.

A myelogram was performed and showed marrow invasion by 80% blasts made of myeloblasts and undifferentiated monocytic-like blasts. The eosinophilic component was estimated at 12%, the majority of which were dystrophic (figure 2).

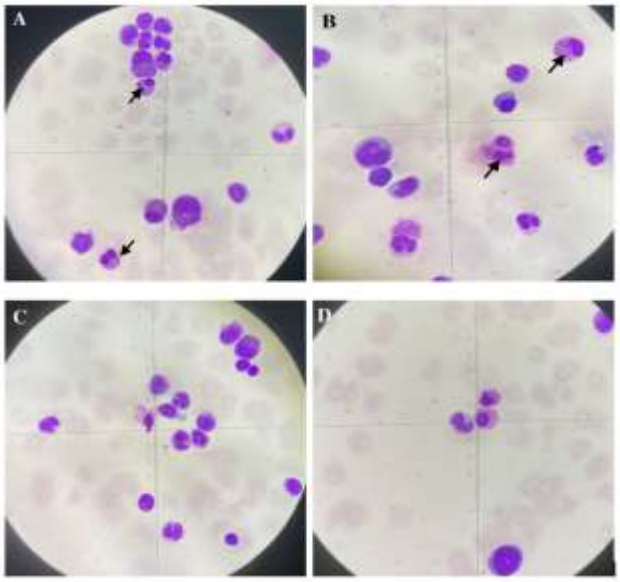

Figure 2: Hematology laboratory, Hassan II University Hospital, Fez, Morocco, Medullary smear (May-Grünwald-Giemsa, read under light microscope, objective x100) showing:

(A): clusters of monocytic-like blasts, and dystrophic eosinophilic polynuclei (arrows). (B): numerous eosinophilic precursors, sometimes dystrophic, with monocytic blasts and a plasma cell.

(C): monocytic blasts, undifferentiated blasts and an eosinophilic precursor containing basophilic granulations (arrow).

(D): a monolobed eosinophilic polynuclear and a blast.

Cytochemical staining with myeloperoxidase affirmed the myeloid origin of blast cells. Flow cytometry phenotyping showed the existence of blasts expressing CD33, CD13 and CD65 markers. Others express CD14, CD4 and CD11c (figure 3).

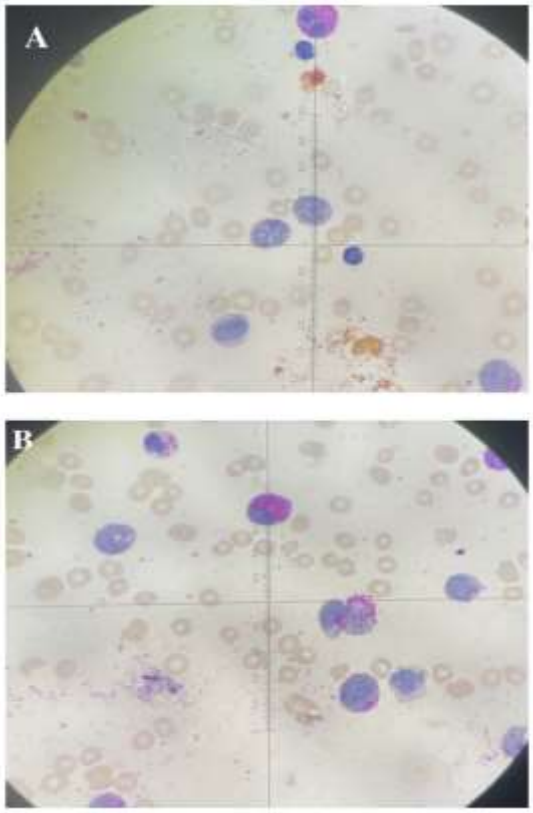

Figure 3: Hematology laboratory, Hassan II University Hospital, Fez, Morocco, Medullary smear (Cytochemical staining by alphanaphthol-pyronine, read under optical microscope, objective x100) showing:

(A): many bright red granulations reflecting the presence of myeloperoxidase, characterising granulocytes, and to a lesser degree, monocytes.

(B) : enzyme activity observed in most elements.

The conventional medullary karyotype showed the presence of an isolated inv(16); the chromosomal formula was 46,XY,inv(16)(p13,q22). The fluorescence in situ hybridization (FISH) study confirmed the previous result by showing that 67% of the cells examined had a remodeling of the CBFb locus at 16q22[inv(16)][134/200].

Trans-thoracic echocardiography showed left ventricular dilatation and diffuse hypokinesia (LV ejection fraction [LVEF]=40%).

The presentation was a left heart failure following myocardial necrosis concomitant with Eo AML4.

The evolution was quickly favorable after a first cure of chemotherapy, started on the seventh day after diagnosis. A cardiac treatment including a beta-blocker, an angiotensin-converting enzyme inhibitor and a loop diuretic was

associated. At one month, we observed a decrease in the leukocyte count. The evaluation performed immediately after aplasia confirmed complete remission by normalization of the CBC and a bone marrow blastosis less than 5%.

3. DISCUSSION:

Acute myeloid leukemias are a heterogeneous group of hematological malignancies, characterized by clonal proliferation of myeloid precursors blocked in their differentiation. They represent 80% of acute leukemias in adults, with a worldwide incidence rate of 2.6 per 100,000 population [2]. The myelomonocytic subtype constitutes about 15% of these AMLs, and its association with eosinophilia occurs in about one third of cases [2]. In our hospital, AML 4 has approached 22% of acute myeloid leukemias in the last 4 years, 31% of which are eosinophilic variant AML 4.

Pathophysiologically, chromosome 16 inversion is a recurrent cytogenetic abnormality usually associated with eosinophilic variant M4 AML [3]. The presence of numerous immature eosinophilic precursors with dark granulations on the myelogram should suggest the anomaly. It results in the fusion of the CBF beta genes located at 16q22 and the MYH1 gene, coding for the myosin heavy chain [4]. This fusion would have two major consequences: sequestration of the protein encoded by the AML1 gene, which would be involved in the control of hematopoietic differentiation, and a repression of the transcription of factors involved in normal hematopoiesis, resulting in a blockage of differentiation [5 ; 6]. The presence of this genetic rearrangement seems to improve the prognosis of patients and allows this hemopathy to be classified in group 1 of the 2008 WHO classification (with favorable cytogenetic abnormality Inv (16)) [7].

Clinically, cardiac manifestations related to hematological malignancies are much more frequently described with acute promyelocytic leukemias classified as AML3 according to the FAB classification and correspond most frequently to ischemic manifestations of the myocardial infarction or acute coronary syndrome type [8]. Myocarditis is much more exceptional and seems to be related to the hypereosinophilia linked to eosinophilic variant of VEo AML4. Indeed, in the case of associated hypereosinophilia, cardiac involvement is frequently found and should be systematically investigated because it increases the morbidity and mortality of affected patients [9]. Hypereosinophilia is also seen in parasitic infections and allergic conditions, and may also have several other causes (inflammatory and autoimmune diseases, asthma, cancer, myeloproliferative syndromes, leukemia and lymphoma, drugs, dermatoses...) [4,5]. The hypereosinophilic syndrome includes various clinical situations such as eosinophilic pneumopathy, eosinophilic gastroenteritis or eosinophilic cellulitis. Myocardial involvement is equally common. Among patients with hypereosinophilia, 40 to 50% develop cardiac involvement detected by ultrasound [10]. This damage does not correlate with the extent of eosinophilia but rather with the duration of exposure to hypereosinophilia; it is the consequence of granular extracellular deposition of eosinophils, which through their chemical mediators, directly induce myofibrillar damage and myocyte necrosis [11]. These lesions also reach the endocardium and the vascular endothelium to evolve towards endomyocardial fibrosis [11,12].

While the diagnosis of myeloid leukemia and its classification is based on the examination of the count and the reading of the myelogram, AML4 veo is closely associated with chromosome 16 inversion and is classified according to the 2008 WHO classification as an acute myelomonocytic leukemia with recurrent cytogenetic abnormalities. Chromosome 16 inversion is a visible abnormality on standard R-band karyotype, but requires a good quality of prior chromosome preparation to be authenticated on karyotype [6]. However, cytogenetics is not the tool of choice for the diagnosis and follow-up of Inv(16), due to the difficulty of identifying the abnormality. In situ hybridization techniques are much more sensitive, the detection of the CBF/MYH11 gene rearrangement can then be detected by fluorescence (FISH), and its fusion transcript can be revealed by RT-PCR, allowing, in addition to a diagnostic help, a follow-up of the residual disease [7; 8].

The treatment of this hematological malignancy is based on a classical two-phase treatment regimen: a tumor reduction phase or intensive induction treatment according to the 3+7 regimen (three days of anthacyclines overlapping with 7 days of AraC), with the objective of complete morphological remission, and a consolidation phase consisting of several cycles of high-dose AraC, with 4 consolidation courses [9]. In case of associated myocarditis, the treatment is based on the treatment of the cause and on the rapid and intensive initiation of corticosteroid therapy that could reduce the cytotoxic effects of eosinophilic degranulation [12;13].

This treatment regimen proved to be effective in our patient, in whom the evolution was quickly favorable after a first course of chemotherapy. At one month, the normalization of the CBC and a bone marrow blastosis < 5% allowed us to confirm complete remission. AML with IVC is indeed a cytogenetic group associated with a good response to chemotherapy. Our patient is therefore no exception to the rule reported by numerous studies, which report survival rates varying between 50 and 70% in this subgroup of AML [14, 15, 16].

4. CONCLUSION:

This case illustrates a typical case of eosinophilic variant acute myelomonocytic leukemia. The presumptive diagnosis was suspected by the presence of dystrophic-looking eosinophilic elements containing abnormal granulations (particularly evident in the promyelocytic and myelocytic stages), and was confirmed by a multimodal diagnostic approach including morphology, cytochemistry, flow

cytometry, conventional cytogenetics and molecular biology. While the presence of a chromosome 16 inversion (Inv (16)) predicts a good response to therapeutic induction and improves prognosis, the association of this hemopathy with persistent blood eosinophilia exposes to potentially lethal visceral complications, justifying rapid and effective therapeutic management and prolonged ultrasound follow-up.

5. REFERENCES:

[1] Alessandro Pulsoni, Simona Iacobelli, Massimo Bernardi, Marco Borgia, Andrea Camera. M4 acute myeloid leukemia: the role of eosinophilia and cytogenetics in treatment response and survival: the GIMEMA experience. Haematologica. 2008;93(7):1025–1032.

[2] Pierre BORIES. leucémies aiguës myéloblastiques, recherche clinique, phases précoces. Horizons Hémato // Octobre / Novembre / Décembre 2018 // Volume 08 // Numéro 04.

[3] Appelbaum FR, Kopecky KJ, Tallman MS, et al. The clinical spectrum of adult acute myeloid leukemia associated with core binding factor translocations. Br J Haematol. 2006 Oct;135(2):165–73.

[4] Nozomu Kawashima, Akira Shimada, Takeshi Taketani. Childhood acute myeloid leukemia with bone marrow eosinophilia caused by t(16;21)(q24;q22) Int J Hematol. 2012;95(5):577–80.

[5] Roumier C, Fenaux P, Lafage M. New mechanisms of AML1 gene alteration in hematological malignancies. Leukemia. 2003 Jan;17(1):9–16.

[6] Reilly JT. Pathogenesis of acute myeloid leukaemia and inv(16)(p13;q22): a paradigm for understanding leukaemogenesis? Br J Haematol. 2005 Jan;128(1):18–34.

[7] Huret JL. +22 or trisomy 22 (solely?). Atlas Genet Cytogenet Oncol Haematol 2000 ; 4(1) : 19.

[8] Paulson K, Serebrin A, Lambert P, Bergeron J, Everett J, Kew A et al. Acute promyelocytic leukaemia is characterized by stable incidence and improved survival that is restricted to patients managed in leukaemia referral centres: a pan-Canadian epidemiological study. Br J Haematol. 2014 Sep;166(5):660-6.

[9] Ommen SR, Seward JB, Tajik JA. Clinical and echocardiographic features of hypereosinophilic syndromes. Am J Cardiol 2000;86:110–3.

[10] Corradi D, Vaglio A, Maestri R, Legnane V, Leonardi G, Bartoloni G. Eosinophilic myocarditis in a patient with idiopathic hypereosinophilique syndrome: insights into mechanisms of myocardial cell death. Hum Pathol 2004;35:1160–3.

[11] Cohen A, Abergel E, Blanchard B, Chauvel C, Habib G, Hagege A. Recommandations de la Société française de cardiologie concernant les indications de l'échocardiographie-doppler. Arch Mal Cœur Vaiss 2003; 96:223–63

[12] Fourcade L, Heno P, Nguyen Hy Thuy G, Mourot S, Cloix JJ, Bonnet D, et al. Myocardite aiguë éosinophilique : diagnostic et traitement d'urgence. Med Trop 1998;58:465–70.

[13] 13. Hayashi S, Isobe M, Okubo Y, Suzuki J, Yazaki Y, Sekiguchi M. Improvement of eosinophilic heart disease after steroid therapy: successful demonstration by endomyocardial biopsied specimens. Heart Vessels 1999;14:104–8.

[14] Nguyen S, Leblanc T, Fenaux P et al. A white blood cell index as the main prognostic factor in t(8;21) acute myeloid leukemia (AML): a survey of 161 cases from the French AML Intergroup. Blood 2002;99:3517-23.

[15] Schlenk RF, Benner A, Krauter J et al. Individual patient data-based meta-analysis of patients aged 16 to 60 years with core binding factor acute myeloid leukemia: a survey of the German Acute Myeloid Leukemia Intergroup. J Clin Oncol 2004;22:3741-50.

[16] Delaunay J, Vey N, Leblanc T et al. Prognosis of inv(16)/t(16;16) acute myeloid leukemia (AML): a survey of 110 cases from the French AML Intergroup. Blood 2003;102:462-9.

[17] Maxwell, J. C. (1892). A Treatise on Electricity and Magnetism, 3rd ed., vol. 2. Oxford: Clarendon, pp.68-73.

[18] Nicole, R. (2016). Title of paper with only first word capitalized, Journal Name Stand. Abbrev., in press.

[19] Media and plastic substrate interface," IEEE Transl. J. Magn. Japan, vol. 2, pp. 740-741, August 1987 [Digests 9th Annual Conf. Magnetics Japan, p. 301, 1982].

[20] Young, M. (1989). The Technical Writer's Handbook. Mill Valley, CA: University Science.