

## Case Report

# Association of Acute Myeloid Leukemia and Systemic Lupus Erythematosus: A Case Report

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**Abstract:** Systemic lupus erythematosus is an autoimmune inflammatory disease that can affect multiple systems and organs of the body including skin, kidneys, lungs, joints and nervous system. Some previous studies up light that SLE was associated with increased risk of Acute leukemia (SIR = 2.3). The incidence of the association of AML and SLE is not known but there are few case reports in literature. The aim of this report was to up light the difficulties which occurred in the diagnosis and the management of acute myeloid leukemia in patient with systemic lupus erythematosus. Patient, 43 years old, diabetic treated with insulin, whose sister is followed for Behcet's disease, was admitted for AML with trisomy of chromosome 4 and 8 and thrombophlebitis of the superior sagittal sinus. Chest CT-Scan showed minimal bilateral pleural effusion. She was treated according to Morocco National protocol AML-MA-2011. CT-Scan was done at day 12 of chemotherapy and noticed the persistence of the minimal bilateral pleural effusion. At day 19 the patient presented malar rash, and right axillary adenitis. The biopsy of the adenitis show the presence of LE cells. According to internal physician recommendations we add steroids to the treatment. The cough and fever disappear. The CT-scan for control was normal after two weeks of steroids. Patient is in complete remission after induction I. After a following-up of five months, the patient still well, but present severe infections during chemotherapy cycles and a bad tolerance for the treatment. The association SLE-AML is rare. The diagnosis of the association SLE-AML is difficult. Its management is also difficult according to comorbidity, severe infectious because of decline of immunity, and less tolerance to AML chemotherapy.

**Keywords:** Acute Myeloid Leukemia, Systemic Lupus Erythematosus, Association

## 1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease that can affect multiple systems and organs of the body including skin, kidneys, lungs, joints and nervous system. Some previous studies up light that, SLE increase the risk of Hematologic malignancies which are defined as a heterogeneous group of diseases characterized by the abnormal (malignant) growth and/or accumulation of hematopoietic cells in the blood, bone marrow and/or lymph

nodes.

In 2005, a meta-analysis conducted by Zintzaras and al, had shown that there was a moderate risk of lymphoma incidence in patients with SLE with an estimated standardized incidence ratio (SIR) 7-times higher compared with the general population [1]. In 2014, in a meta-analysis, including 401 cases of hematologic malignancies identified in a total cohort of 67,929 individuals with a diagnosis of SLE, Emmanuel Apor and al had shown that SLE was associated with increased SIR of Acute leukemia (SIR = 2.3) [2]. The incidence of the

association of Acute Myeloid Leukemia and SLE is not known but there are few case reports in literature. The first case had been reported by Lee in 1955[3].

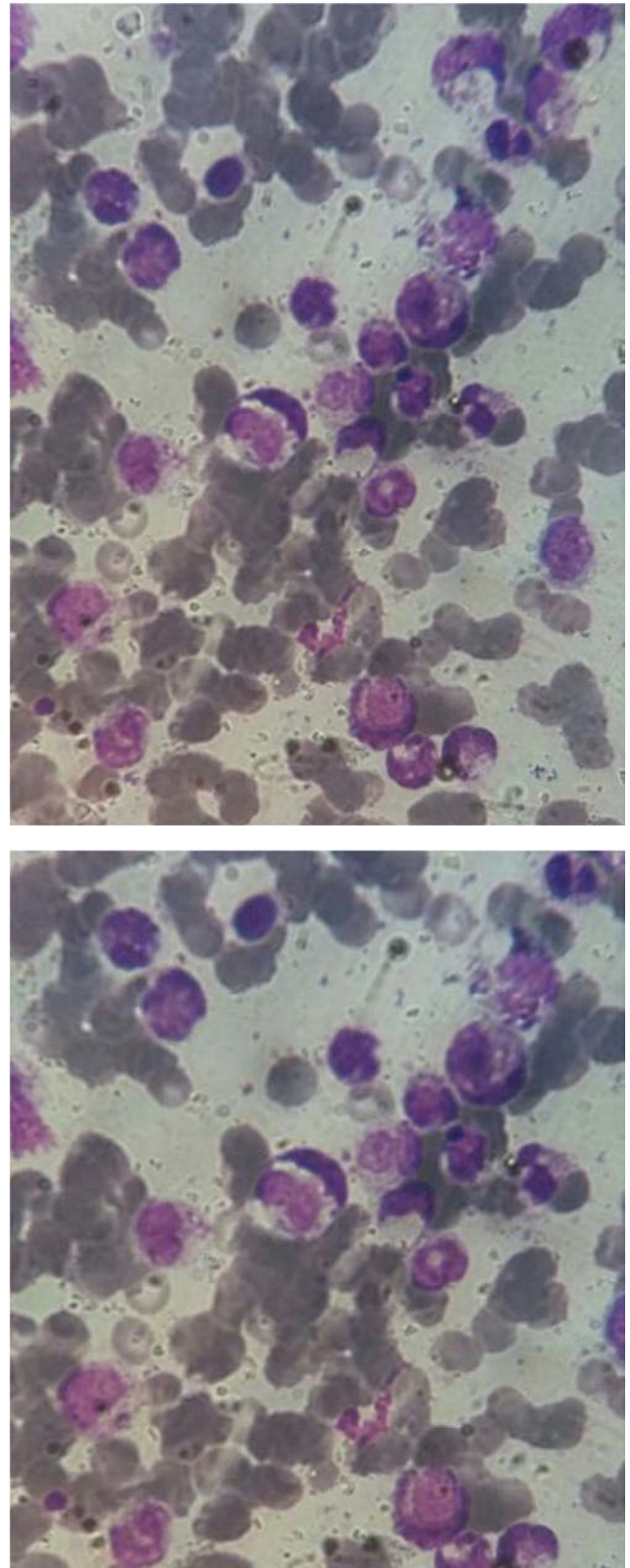
This is a report of a case of systemic lupus erythematosus associated with Acute Myeloid Leukemia in a young woman.

## 2. Case Presentation

Patient, 43 years old, mother of 02 children, diabetic treated with insulin, whose sister is followed for Behçet's disease, presented one month before the first consultation, asthenia, cutaneous pallor, recurrent headache, multiple arthralgia, cough and fever. The initial clinical examination had noticed a patient with Performans status (WHO) at 2, febrile at 39°C, blood pressure was at 110/80 mmHg, respiratory rate was at 20 cycles/min. Heart and lung auscultation was normal. No hemorrhagic syndrome, no lymph nodes, no splenomegaly, no hepatomegaly. CBC showed hemoglobin level at 7.8 g/dl, white blood cells at 24300/ml with 54% blasts, platelet count was at 56000/ml. The bone marrow aspiration and immunophenotyping concluded to AML 2. The karyotype found trisomy of chromosomes 4 and 8. The viral serology were negative. Tuberculosis PCR and Galactomannan antigenemia was negative. Blood cultures were negative. The research for lupus antibodies, nuclear and DNA antibodies were negative. MRI found thrombophlebitis of the superior sagittal sinus (Figure 1). Chest CT-Scan showed minimal bilateral pleural effusion.



**Figure 1.** Thrombophlebitis of the superior sagittal sinus.



**Figure 2.** LE Cells.

A multidisciplinary consensual meeting of hematologists, pulmonologists, neurologists decided to treat the patient according to protocol AML-MA-2011, recommended to administer 0.6 ml of enoxaparin twice a day, to maintain by

iterative transfusion, platelet rate  $\geq 30.000/\text{mL}$  because of the use of enoxaparin, and hemoglobin level  $\geq 10\text{g/dl}$  because of the rebels headache. The evolution was marked by a significant decline of headache but a persistent fever and cough despite the administration of multiple drugs (Ceftazidim, Amikacin, Imipenem, Ciprofloxacin, Voriconazol, Cicloviral). Another CT-Scan was done at day 12 of chemotherapy and noticed the persistence of the minimal bilateral pleural effusion. At day 19 the patient presented malar rash, and right axillary adenitis. The biopsy of the adenitis show the presence of LE cells (Figure 2). To summary it is a patient treat for AML with present also some ACR criteria for the diagnosis of SLE: malar rash, arthritis, pleural effusion, thrombopenia less than  $100.000/\text{ml}$ , leucopenia and LE cells. According to internal physician recommendations steroids was added to the treatment. The cough and fever disappear. The CT-scan for control was normal after two weeks of steroids. Patient is in complete remission after induction I. After a following-up of five months, the patient still well, but present severe infections during chemotherapy cycles and a bad tolerance for the treatment.

### 3. Discussions

Cancer risk in SLE is a topic of increasing interest, but to date much of the focus has been directed at lymphoma, especially Non-Hodgkin's lymphoma. The studies on the association AML-SLE are rare. In 2013, Mary Lu and al in a cohort of 16, 409 patients with SLE observed 33 cases of non-lymphoma hematological malignancies [4]. Of these 33 non-lymphoma cases, 13 were of lymphoid lineage: multiple myeloma (N=5), plasmacytoma (N=3), B-cell chronic lymphocytic leukemia, B-CLL (N=3), precursor cell lymphoblastic leukemia (N=1), and unspecified lymphoid leukemia (N=1).

The remaining 20 cases were of myeloid lineage: myelodysplastic syndrome, MDS (N=7), acute myeloid leukemia, AML (N=7), chronic myeloid leukemia, CML (N=2), and 4 unspecified leukemias. This study up light that the association SLE-AML is very rare because only seven cases of AML were diagnosed in 16,409 patients with SLE. Most of the hematological malignancies developed in SLE were female, which reflected the fact that 90% of SLE patient are female [5]. That is also the same think in this report.

In 2009, Bjorn L and al conducted a meta-analysis completed by a nested case control study based on Swedish registers among 6438 patients with SLE. They identified eight cases of AML in SLE but only three were female. In female SLE cases with SLE, the median age at AML diagnosis was 48 years (range 34 – 72) [6]. That is also what was noticed in this case. The case of this report had 43 years old. All the cases of AML in SLE were diagnosed during the following of SLE. In Bjorn L and al cohort, the median of following-up before the diagnosis was 77 months [29-110 months].

The difficulty in this case, is that the patient was not

followed for SLE before the diagnosis of AML. She had some SLE manifestations (Pleuritis, arthritis, thrombopenia) but this signs are not specific for SLE and can be present in AML also. Its the persistence of symptomatology despite all drugs which were administered, the apparition of malar rash and the identification of LE cells which permit for to update the diagnosis. So, when steroids were administered all clinical and radiological signs disappear and confirm the diagnosis.

The presence of haematological abnormalities, anaemia, leucopenia and to a lesser extent thrombocytopenia are common clinical manifestations of the SLE disease, often independent of disease severity and can be present also in AML.

So it is necessary that SLE patients be subject to regular check-ups for clinical manifestations and laboratory tests, to show if a possible transition had occurred from cytopenias via MDS to AML. Interestingly, leucopenia was the only clinical SLE-associated finding with a significantly elevated OR for leukaemia development.

The frequency of a preceding myelodysplastic phase before leukaemia was at least comparable with the estimated 25% that has been observed in the general leukaemia population [7]. Some previously known associations between rheumatic diseases and leukaemia do exist. In a population-based cohort of Wegener's granulomatosis, a more than 5-fold increased risk of leukaemia was found [8] [9].

The relation between SLE and leukemia is rather unclear. One could hypothesize that some of the drugs used to treat SLE, such as the alkylator cyclophosphamide among others, can increase the risk of developing myeloid neoplasms such as myelodysplastic syndrome (a pre-leukemic state) and acute myeloid leukemia [10] [11].

So chemotherapeutic drugs, constitute one of the relatively few known aetiological risk factors for leukaemia. Azacytidin is an anti-metabolite that has been used in SLE treatment since the 1960s both for treating disease manifestations and as a glucocorticoid-sparing drug. It could induce defective DNA mismatch repair, possibly promoting survival of cells for a leukaemic clone [12]. On the contrary, anti-malarial drugs like chloroquine, are immune modulating drugs often used in patients with SLE that have recently been reported to exert anti-neoplastic properties. They are strongly DNA intercalating, preventing mutations in cells with a high mitotic rate and improving cellular mechanisms of DNA repair after the damage was caused by alkylating therapy [13]. This effect of anti-malarial drugs can explain why AML are rare in SLE patients.

The therapeutic management of AML in SLE is difficult because of comorbidity (kidneys, lungs, nervous system diseases), severe infectious because of decline of immunity, and less tolerance to AML chemotherapy. In fact febrile neutropenia is the most frequent and important complications of chemotherapy during the management of acute myeloid leukemia. It is generally the first factor of mortality. Its incidence had been estimated between 70–100% during the neutropenic phase after intensive chemotherapy. Immune deficiency developed during malignancy and chemotherapy is

the first factor which explain febrile neutropenia in acute myeloid leukemia patient. Because of this immune deficiency serious infection will manifest in neutropenic patient with minimal symptoms. In AML patient with SLE this immune deficiency is more important and patient present graveous infections during neutropenia. It what was noticed also when managed this patient which present several infection during a different phase of chemotherapy.

The median survival time after the diagnosis of AML in SLE patients is 7 months (2-18 months) [14] [15]. In our case, after a following-up of five months, the patient still well, but present severe infections during chemotherapy cycles and a bad tolerance for the treatment.

## 4. Conclusion

The association SLE-AML is rare. The presence of haematological abnormalities, are common clinical manifestations of the SLE disease, often independent of disease severity and can be present also in AML. So the diagnosis of the association SLE-AML is difficult. It is management is also difficult according to comorbidity, severe infectious because of decline of immunity, and less tolerance to AML chemotherapy.

## Abbreviations

Systemic lupus erythematosus (SLE); Acute Myeloid Leukemia (AML).

## Authors' Contributions

RM and MC prepared the draft and BH, ML, BO, and AQ all reviewed and contributed to the final manuscript.

## Conflict of Interest

The authors declare that they have no competing interests.

## Consent for Publication

Written consent to publish this report was obtained from the patient.

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