

# 5Q- SYNDROM A CASE REPORT WITH REVIEW OF THE LITERATURE

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## ABSTRACT :

5q syndrome - is a unique paradigm of myelodysplastic syndrome (MDS) characterized by the correlation between cytology and cytogenetics and the low risk of clinical progression.

It is a category apart in myelodysplastic syndromes (MDS) because of hematological peculiarities, the pathophysiology that remains unknown, and the refractoriness of the anemia with which it is associated. It is a pathology that affects the female sex with predilection.

The prognosis of the disease remains good and the risk of malignant transformation into acute leukemia does not exceed 15%.

In this work, we report a typical case of SMD with deletion of the long arm of chromosome 5 in order to describe the observation of this particular entity diagnosed in our formation, rare in our Moroccan context and that we must know how to evoke in front of a refractory anemia most often isolated.

**KEYWORDS:** MDS, 5q-, cytology, cytogenetic, prognosis, MLA.

## 1. INTRODUCTION

Myelodysplastic syndromes (MDS) are acquired bone marrow disorders characterized by pancytopenia, morphological and functional abnormalities of hematopoiesis and a risk of transformation into acute myeloid leukemia (AML). The karyotype anomaly identified so far in this group of diseases is a deletion of the long arm of chromosome 5 (del (5q)) occurring in 10 to 15% of patients. This chromosomal anomaly with refractory macrocytic anemia, normal to high platelet count, normal to moderately reduced leukocyte count, and a significant number of hypolobulated megacaryocytes in the bone marrow is highly predictive of the 5q- syndrome.

## 2. OBSERVATION

Our patient is a 67-year-old woman who was hospitalized for a check-up of recurrent episodes of epistaxis over a year with no other bleeding signs associated with asthenia in a context of general state maintenance. The patient was diabetic under oral anti-diabetic drugs and her clinical examination was without particularity.

The blood count indicated a hemoglobin of 9.7 g/dl, a GMV of 98.1 fl, a TCMH of 30.9 pg of leukocytes of 11 G/L, platelets of 673 G/L. The blood smear showed many platelet aggregates.

The myelogram showed a very rich bone marrow with many megacaryocytes all dystrophic with mono lobed round eccentric round nuclei with sometimes micro-megacaryocytes and many platelet aggregates. The remaining lines did not show any significant cytological abnormalities except for a few signs of dysgranulopoiesis (Figure 1).

The cytogenetic study carried out on medullar blood showed a clonal structural anomaly. 5 of the 11 mitoses classified had a del(5)(q13q33).

The diagnosis of 5q- syndrome was made before the clinic (refractory anemia), cytological, cytogenetic abnormalities and the patient was placed on recombinant erythropoietin (Epoetin beta 30000 IU/week) with good clinical and cytological progression.

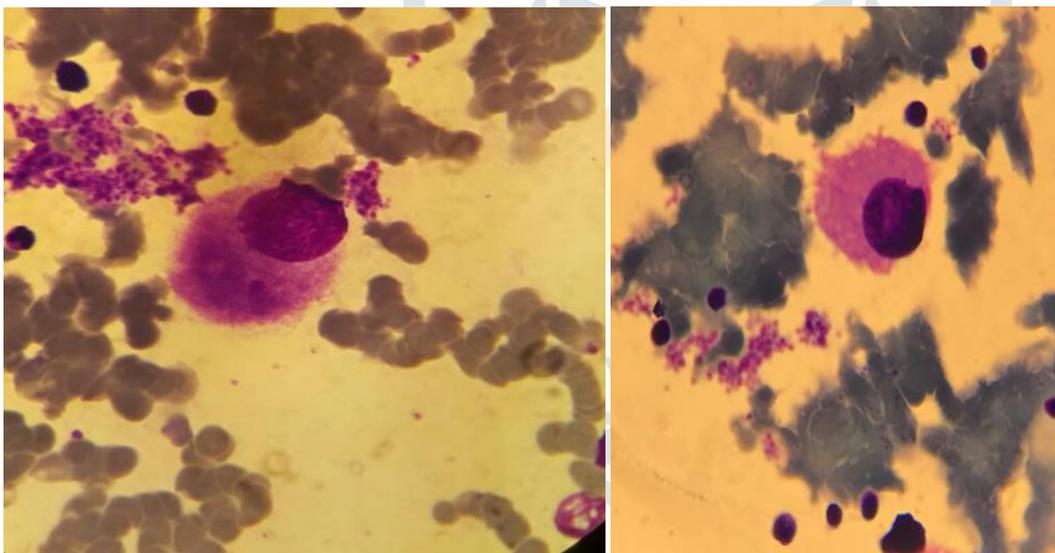


Figure1: Spinal cord smear (objective 100): Mono-lobed mega karyocyte with eccentric nucleus

## 3. DISCUSSION:

5q syndrome - was first described by Van den Berghe in 1974 in three patients with refractory anemia and interstitial deletion of the long arm of chromosome 5[1].

There is a particular interest in 5q- syndrome due to the large number of genes encoding hemopoietic growth factors or their receptors located on the long arm of chromosome 5.

A detailed description of the clinical and hematological characteristics of patients with refractory anemia (RA) and 5q chromosome deletion was provided by Sokal et al[2] The patients were predominantly female and all had refractory macrocytic anemia, moderate leukopenia, normal or high platelet count, hypoplastic erythroid bone marrow with hypolobulated megacaryocytes. The constellation of characteristics described by

these investigators was called 5q- syndrome, which is now recognized as a clinical entity distinct from MDS with a favourable prognosis and a low risk of transformation into acute leukemia.

The average age of patients at the time of presentation is 66 years. Patients under 50 years of age represent only 15% of cases. [1, 2, 3]

One of the most striking aspects of the 5q syndrome is the female preponderance, which is unusual, not only for MDS and leukaemia, but for malignant tumours in general. The preponderance of older women led Van den Berghe et al. to suggest the possibility of a toxic agent in the domestic environment. [1]

The platelet count in 5q- syndrome is generally normal or increased and moderate leukopenia is often associated.

Monolobular megacaryocytes are a consistent conclusion in all reports of 5q syndrome, they are not specific to this syndrome and have been reported in patients with MDS with normal or abnormal karyotypes. [4,5]

5q- is one of the most common karyotypic abnormalities observed in MDS. However, most studies concluded that 5q- is interstitial; the most frequently cited stopping points are 5q12-14 (proximal rupture point) and 5q31-33 (distal rupture). Part of the variability of deletion arrest points may result from difficulties in interpreting some leukemic chromosome preparations. Mitelman et al reported identical stopping points del(5)(q13.3; q33.1) in 15 MDS patients using high resolution techniques, raising the possibility that this particular deletion was common to all cases of 5q syndrome. [6, 7, 8]

In the majority of patients with myelodysplastic syndrome (MDS), 5q deletion was the only abnormality at diagnosis. It remains to be shown whether the proximal rupture point on chromosome 5q has a prognostic impact.

With regard to the latter, all studies confirmed the favourable prognosis of MDS with 5q deletion and without excess blasts, i.e. 5q syndrome - according to the WHO classification. Giagounidis found, and through a study that included 76 patients, that the median survival time of patients is 145 months for a median follow-up period of 67 months. Patients with an additional chromosomal abnormality have a median survival time of 45 months. Interestingly, among patients with an additional chromosomal abnormality (14 patients), only one patient had advanced MDS (RAEB). The remaining 13 patients had an increase in the number of spinal cord blasts. Patients with spinal blastosis greater than 5% have significantly shorter overall survival (24 months) compared to those with blastosis of less than 5%. The cumulative development of AML in patients with less than 5% blast cells in the bone marrow and with an isolated deletion (5q) did not exceed 9% [9]. This probability reaches 80% in patients with more than 5% blasts in the bone marrow. There is no significant difference in overall survival between men and women (P0.09). However, the Düsseldorf group showed that the median survival of patients with 5q- syndrome was significantly lower than that of a population of the same age and sex, both in women and men [10,11].

Although basic morphological abnormalities have been provided and the disease has been recognized as a separate entity by the WHO Neoplastic Disease Classification Committee, a detailed description of this subgroup of patients is missing to date.

A complex issue is the relationship between 5q- syndrome and other associated myeloid disorders, particularly secondary leukaemias. The frequent association of chromosome abnormalities with these malignant tumours was first reported by Rowley [12]. The overall proportion of patients with MDS 5q- and secondary leukaemia is no greater than the proportion of patients with MDS 5q- and primary leukaemia. In addition, 5q- syndrome in secondary leukaemias usually occurs in the context of a complex karyotype, for example, only 2 out of 300 cases in 4 large series were found to have del 5q- as the only anomaly [3, 8, 13].

Treatment of 5q- syndrome was largely dominated by erythrocyte transfusions before the advent of lenalidomide, with other therapeutic modalities rarely applicable or of limited efficacy. Allografting of stem cells may be proposed in relatively young patients with an identical HLA donor, who do not respond to other treatments, or who are at high risk of hematological progression [11,6].

#### 4. CONCLUSION

Little is known about the relationship between 5q- syndrome and other MDS subtypes. The history of these disorders is very different, suggesting the presence of different underlying anomalies. Importantly, the good prognosis of 5q- syndrome and its rare transformation into leukaemia contrasts with the poor prognosis and clinically aggressive course of other MDS.

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