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Original Article

Cytogenetic profile of a representative cohort of young adults with de novo acute myéloblastic leukaemia in Morocco

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ABSTRACT

Background: We analyzed the cytogenetic characteristics of a representative population of young adults with de novo acute myéloblastic leukemia (AML) treated in a single center institution.
Methods: Patients with de novo AML included were aged between 20 and 60 years. Cytogenetic analysis was done at diagnosis. Twenty cells were analyzed, although examination of lower numbers of metaphases was also acceptable if an abnormal clone was detected.
Findings: From 1/1/04 to 31/12/2014, among 1315 adult patients, 1055 (80%) patients were aged between 20 and 60 years. Karyotype was done in 927 (88%) patients and cytogenetic analysis failed in 32 cases (3·4%). Clonal abnormalities were observed in 520 (58%) patients. 175 (19·5%) were classified in the favorable group, 609 were in the intermediate group and 111 (12·5%) were in the adverse group. The most frequent chromosomal abnormality observed was *t*(8;21) in 112 (12·5%). Thirty three (3·7%) patients had *t*(15;17) and 30 (3·3%) had inv16, trisomy 8 was found in 47 (5·2%), 11q23 rearrangements in 32 (3·6%), 67 (7·4%) had a complex karyotype, −5/del(5q) and −7/del(7q) were seen in, respectively, 11(1%) and 27 (3%). Monosomy occurred in 115 (13%) patients, 70 (8%) responded to the definition of monosomal karyotypes.
Interpretation: This is the largest study done in Morocco, Africa and Middle East. Epidemiological studies involving different ethnic populations and geographic regions of the world should help unfold the true nature of environmental and genetic interplay in the development of AML. Our cytogenetic profile reveals some particularities when compared to other populations; it does not seem to be similar neither to eastern or western countries.

Introduction

In the last decade cancer has been given more scrutiny in developing countries and has become a more attentive focused global public health initiative [1]. Acute myeloblastic leukemia (AML) is a relatively rare disease but it represents the most common acute leukemia in adults [2]. The incidence of AML varies between 3·2 and 3·8 per 100,000 individuals and increases with age, with the majority of patients being older than sixty years old. The disease is heterogeneous and constitute a complex group of hematologic neoplasms characterized by distinctive morphologic, immunophenotypic, cytogenetic and molecular abnormalities. The clinical outcome is extremely variable, with survival from a few days to a definitive cure for patients with some clinical and biological aspects [3]. Cytogenetic abnormalities are crucial for the diagnosis, prognosis of patients and for therapy decisions; they are recognized in approximately 56% of de novo AML in adults and up to 80% in children [4,5]. At present, cytogenetic aberrations detected at the time of AML diagnosis constitute the most common basis for predicting clinical outcome [6].

Geographic heterogeneity of cytogenetic patterns in hematological malignancies has been reported occasionally but there have been limited data on the cytogenetic profile of AML in adult patients in low-income countries especially in Africa and the Middle East. Similarities in ethnicity were reported between North Africa and Middle East countries because of the immigration.

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Such data could aid to define the cartography of cytogenetic abnormalities and to describe the role of ethnic and geographic variability [7].

Geographically, Morocco is a North African country with a population of 33 millions. It is considered a middle-income country and ranks 114th out of 169 countries in the Human Development Index. Morocco's per capita GDP is $2769, with $202 per person spent on healthcare per year. Access to medical care is difficult and unfair between urban and rural areas [8].

Taking care of adults with haematological malignancies started in Morocco on 1980 in the city of Casablanca with special attention to patients with AML; steps and protocols were developed to increase the prognosis and to improve our knowledge about our patient's characteristics such as defining our cytogenetic profile. Assessing the prognosis by cytogenetic classification was done systematically since 2004. Adult patients with AML were treated from 2003 to 2010 by a uniform protocol called AML-MA 03 which included two inductions $(7+3)$, two consolidations and a maintenance treatment without any stratification. On 2011 another protocol, AML-MA 11 was developed with two risk groups stratification based on the age (more or less than thirty years old) and cytogenetic finding as favorable, core binding factor (CBF) leukemias with *t*(8;21) or inv(16)/*t*(16;16) versus all the others groups, the favorable group was receiving intensive chemotherapy involving cytarabine at a range of doses. Patients with acute promyelocytic leukemia were treated by the APL-2004 protocol. Because the worst survival in AML elderly patients, the lack of resources and beds availability, we concentrate all our efforts to treat patients aged between 20 and 60 years old by improving the diagnosis, risk stratification and supportive care. Patients aged more than sixty years old goes systematically to the palliative care. Even if our Hospital is in Casablanca, the biggest city in the country, patients comes from different regions around Morocco. In 2010, a second unit in Marrakech started to treat patients with AML, especially those coming from the south of Morocco.

A little is known about the cytogenetic profile of AML in Morocco, there was one study published in 1996 about cytogenetic profile of 53 Moroccan patients with AML [9,10]. The aim of this study is to report the cytogenetic findings of the largest series in Africa and Middle East population of young adults aged between 20 and 60 years old with the novo AML and to compare our cytogenetic profile with those reported from other populations.

Methods

Participants

Patients were aged between 20 and 60 years old, followed in our department for de novo AML diagnosed from January 2004 to December 2014. Patients with secondary AML and AML with Myélodysplasia were excluded.

Morphologic and cytochemical analysis

Diagnosis of AML was confirmed by bone marrow aspiration and stained with May-Grunwald-Giemsa, and myeloperoxidase (MPO). The marrow blast count of 20% was required and AML was classified into eight subtypes M0–M7 according to the French American British (FAB) classification [11,12].

Immunophenotyping

The immunophenotyping was done *earlier* in case of AML with minimal differentiation (AML-M0), acute megakaryoblastic leukemia (AML-M7), erythroblastic leukemia (AML-M6) and acute leukemia of ambiguous lineage. To improve our diagnosis criteria, immunophenotyping has been done systematically for all patients since 2011.

Cytogenetic studies

Cytogenetic analysis was done at diagnosis according to standard techniques with RHG banding. The bone marrow cells were cultured for 24–48 h. Twenty cells were analysed, although examination of lower numbers of metaphases was also acceptable if an abnormal clone was detected. An abnormality was considered clonal when at least two metaphases had the same aberration in case of a structural abnormality or an extra chromosome. If there was a monosomy, it had to be present in at least three metaphases.

All the samples were sent at time of diagnosis, to a single reference laboratory who worked in collaboration with the university hospital.

Chromosome identification and classification of chromosomal abnormalities were made according to the International System for Human Cytogenetic Nomenclature 2013 (ISCN) [13]. The cytogenetic findings were classified into three prognostic risk categories: favorable, intermediate and adverse, according to the classification proposed by Mrozek in 2006 [14]. The favorable included patients with *t*(8;21)(q22;q22), *t*(15;17)(q24;q21) and inv(16)(p13·1q22)/t(16;16)(p13·1;q22), whether alone or in combination with other abnormalities. The intermediate includes patients with normal karyotype and other aberrations excluded in the favorable or adverse group. The adverse included those with complex karyotypes defined with 3 or more abnormalities, inv(3)(q21q26)/*t*(3;3)(q21;q26), *t*(6;9)(p23;q34), *t*(6;11)(q27;q23), *t*(11;19)(q23;p13·1), del (5q) and monosomies 5 and 7.

Cytogenetic abnormalities such as *t*(8;21), t(15;17), inv(16)/*t*(16;16), 11q23,+8, t(9;11), −5/del(5q) and −7/del(7q) were further evaluated as sole or in combination with other anomalies. For the *t*(8;21) the characteristics and associated abnormalities were detailed.

To investigate the frequency of monosomal karyotype defined by the presence of at least 2 autosomal monosomies or a single autosomal monosomy associated with at least one structural abnormality, we studied the distribution of autosomal chromosomal monosomies among patients with cytogenetic abnormalities other than core binding factor.

Rare and novel abnormalities were also detailed. Research was done in the Atlas of Genetics and Cytogenetics in Oncology and Hematology [15] and Pubmed.

Statistics

All statistical analyses were evaluated using SPSS 16·0 software.

Results

Patient's characteristics, morphology and immunophenotyping

From January 2004 to December 2014, 1315 patients aged more than 19 years old, with the novo AML were followed in our depart-

Table 1
Patients characteristics.

	N	%
Age	Median: 40·49 [20–60]	
Sex Ratio	1·06	
Median WBC count	120 G/L [0.150–844 G/L]	
FAB AML classification		
AML-M0	48	4·4
AML-M1	337	32
AML-M2	271	26
AML-M3	33	3
AML-M4	110	10
AML-M5	59	6
AML-M6	42	4
AML-M7	8	0·6
NOS	147	14

FAB: French-American-British, NOS: not otherwise specified.

ment. One thousand and fifty five patients (80%) were aged between 20 and 60 years old and 260 (20%) more than sixty years old. The total number of patients with de novo AML aged between 20 and sixty years old entered the hospital per year varied between 73 patients on 2005 and 132 patients on 2012 with an overall of 96 new patients per year. On the 1055 patients, 544 (52%) were male and 511 (48%) were female; the sex-ratio was at 1·06. The median age was 40·5 [20–60] years old and distribution of patients' ages per decade did not show any difference of frequency: 269 (25·5%) patients were aged between 20 and 30 years, 242 (23%) between 31 and 40 years, 275 (26%) between 41 and 50 years and 269 (25·5%) were between 51 and 60 years old. AML-M1 was the most frequent subtype with 337 (32%) patients followed in AML-M2 in 271 (26%) of cases. Immunophenotyping was performed in 46% of cases. Patient's characteristics are showed in Table 1.

Cytogenetic analysis

Among the 1055 patients, 927 (88%) patients performed the karyotype, cytogenetic analysis failed in 32 cases (3·4%). Eight hundred and ninety five patients with cytogenetic analysis results were eligible. One hundred and twenty eight (12%) patients lacked a cytogenetic study because of the cost of this laboratory test or because of death or abandonment before completing laboratory analysis.

Clonal abnormalities were observed in 520 (58%) of the 895 patients. Cytogenetic findings were classified as shown in Table 2.

The most recurrent abnormality was *t*(8;21), found in 112 patients, 48 (43%) were females and 64 (57%), their median age was 33 years old, the sex ratio was at 1·33. The median of Wight blood cells is 20 with range from 1 to 100 G/L. *t*(8;21) was associated with AML-M2 in 70 (62·5%) cases, with AML-M1 in 32 (20·5%) and AML-M4 in 2. *t*(8;21) was equally distributed as sole or with other chromosomal aberrations, it was associated with loss of a sexual chromosome in 24 (43%), del (9q) in 12 (21%), +8 in 2 (3%), +4 in 2 (3%) and associated in 4 (7%) with 3 or more chromosomal abnormalities.

The *t*(15;17) was sole in 25 (76%) patients and in combination in 8 (24%) cases. Inv16 was a sole abnormality in 17 (61%) of cases. Trisomy 8 was sole in 34 (72%) and 11q23 abnormalities in 21 (66%). −5/del(5q) and −7/del(7q) were in combination with other anomalies in 5 (46%) and 14(52%), respectively.

Table 2
Risk group assignments' of young adults aged between 20 and 60 years old with acute myeloid leukemia (AML) with the more frequent cytogenetic findings.

Risk Group	*N*	%
Favorable Risk Group	**175**	**19·5**
t(8 ;21)(q22;q22)	112 12·5	
t(15 ;17)(q24;q21)	33	3·7
inv(16)/t(16;16)(p13.1;q22)	30	3·3
Intermediate Risk Group	**609**	**68**
Normal karyotype	375 42	
t(9 ;11)	10 1	
del(9q)	6 0·7	
del(11)(q23)	23 2·6	
−Y	21 2·3	
+8	41 4·5	
+21	12 1·3	
Unfavorable-Risk Group	**111**	**12·5**
Complex karyotype	67 7·4	
inv(3)(q21;q26)	4	0·4
t(3;3)(q21;q26)	2	0·2
del5q	5	0·5
−5	6 0·7	
−7	26 2·9	

Table 3
Distribution of 115 autosomal chromosomal monosomy among 345 non-core binding factor AML patients with cytogenetic abnormalities.

Autosomal chromosome monosomies	Single	Multiple
Total	45	70
−1	0	0
−2	1	2
−3	1	1
−4	1	2
−5	1	7
−6	1	1
−7	12	14
−8	2	9
−9	0	2
−10	1	2
−11	0	7
−12	1	6
−13	0	6
−14	1	4
−15	1	8
−16	3	4
−17	1	8
−18	1	6
−19	0	1
−20	7	5
−21	7	15
−22	3	8

Among the 345 karyotypes with non-core binding factor abnormalities, 115 (12·8%) had a monosomy which was sole in 45 (5%) and combined to other monosomies or abnormalities corresponding to the definition of a monosomal karyotype in 70 (8%). A monosomy 7 was the most frequent in 26 (2·9%), followed by 21 in 23 (2·6%). The distribution of autosomal monosomies among 345 patients with non-core binding factor cytogenetic abnormalities is shown on Table 3. The frequency of those karyotypes was different from each cytogenetic group: 50 (43%) in the intermediate risk group and 65 (57%) in the adverse group.

Rare and novel cytogenetic abnormalities are showed in Table 3.

Table 4
Frequency of rare and novel abnormalities observed in this study.

Cytogenetic abnormality	Age	FAB	Number of patients	References
Rare abnormalities				
47,XY,+6[8]/46,XY[12]	42	1	(1	(16)
46,XX,*t*(10;17)(p15;q21)[20]	40	NOS	(2	(17)
47,XY,*t*(10;17)(p13;q21),+6[20]/46XY[8]	48	7		
46,XY,*t*(2;14)(p13 ;q32),del(11)(q23)[20]	46	1	(1	(18)
47,XX,+7[6]/46,XX[14]	26	3	(1	(19)
47,XY,*t*(1 ;11)(p32;q23),+8[12]/47,idem,add(9)(q34)[8],XY[1]	22	5	(1	(20)
46,XY,*t*(3;5)(q25;q34)[20]	33	6	(1	(21)
47,XX,+2[6]/46,XX[14]	54	2	(1	(22)
44,XX,−5,−12,t(11;21)(q21;q22),*i*(17)(q10),[10]/46,XX[10]	53	2	(1	(23)
46,XY,*t*(7;11)(p15;p15)[8]/46,XY[12]	47	2	(1	(24)
46,XX,*t*(3;4)(p21;q34)[12]/46,XX[6]	49	3	(1	(25)
47,XX,+4[7]/46,XX[13]	52	1	(2	(26)
47,XY,+4[2]/46,XX[8]	50	0		
47,XX,+16[3]/46,XX[17]	34	4	(2	(27)
47,XX,+16[11]/46,XX[9]	24	2		
46,XX,*t*(10;11)(p12;q14)[20]	46	5	(1	(28)
47,XX,+9[7]/46,XX[13]	47	1	(6	(29)
47,XX,+9[6]/46,XX[20]	31	NOS		
47,XY,+9[20]	34	2		
47,XX,+9[13]/46,XX[7]	45	4		
47,XY,+9[20]	60	0		
47,XX,+9[20]	56	0		
46,XX,*t*(11;19)(q23;p13)[20]	60	NOS	(1	(30)
46,XY,*t*(1;8;21)(p36;q22;q22)[20]	28	2	(1	(31)
46,XX,*t*(8;16)(p11·2;p13·3),add(16)(p13)[20]	22	5	(1	(32)
46XX, *t*(8;13;21)(q22;q14;q22)[18]/46XX[2]	40	NOS	(1	(33)
Novel abnormalities				
46,XX,*t*(10;14)(q24;q32)[20]	56	1	2	
46,XX,*t*(10;14)(q24;q32)[20]	49	0		
47,XX,*t*(X ;2)(q11 ;q13),inv(3)(q21 ;q26),del(9)(q22q32),+9, del(17)(p10p12)[14]/46,XX[6]	60	1	1	
46,XX,(2;3)(p24;q27),inv(16)(p13;q22)[20]	23	4	1	
46,XX,*t*(5;11)(q15;q23),t(8;9)(p12;q33)[20]	32	NOS	1	
46,XX,*t*(3;18)(q13;q22)[27]/46,XX[3]	32	2	1	
46,XX,*t*(2 ;20)(q14 ;q13)[16]/46,XX[10]	37	2	1	
45,XY,−7,der(14)*t*(1 ;14)(p32 ;q32)[14]/46,XY[1]	34	NOS	1	
46,XY,der(15)(14;15)(q11.2;q26)[20]	35	2	1	
45,XX,−16,t(3;21)(q26;q22)[23]	41	1	1	
46,XX,*t*(7;8;21)(q22;q22;q22)[15]	48	2	1	

NOS: Not otherwise specified.

Images from rare and novel abnormalities are shown in Figs. 1 and 2. Fig. 1 is an example of a novel abnormality: 46,XX, *t*(3;18)(q13;q22)[27]/46,XX[3] and Fig. 2 is an example of a rare karyotype: 47,XY, *t*(10;17)(p13;q21),+6[20]/46XY[8]. Rare and novel abnormalities are showed in Table 4.

Discussion

Diagnostic karyotype is one of the most powerful independent prognostic indicators in AML, which serves to identify biologically distinct subsets of disease and has been widely adopted to provide the framework for risk-adapted treatment approaches [4]. However, descriptive epidemiological reports on AML consider the disease as a single entity, and the description of the genetic lesions can vary between countries. By example, the high incidence of APL in Latin populations or *t*(8;21) in the Japanese population supports the view that there may be geographic variations in tumor-associated genetic aberrations in hematologic malignancies [7].

In this study, we report the cytogenetic results from 895 Moroccan patients' studied in Casablanca. Because of some ethnic origin similarities, our findings can represent a partial view of what can exist in Middle East and North Africa. Overall, our patients were between 20 and 60 years old. Five hundred and eleven (48%) patients were aged between 20 and 40 years old, with a mean age at presentation of 40, reflecting our young population.

The slight predominance of the disease in males among adults (52% versus 48%) was in agreement with previous reports [7,34,35].

Among the FAB subtypes, AML-M1 was the most frequent found in our cohort and accounted for 32% followed by AML-M2 in 26%. Thus, in our series, the AML-M2 is slightly lower with that reported in Tunisia, Oman, and China where AML-M2 was the most frequent with 31·2%, 35%, and 29·9%, respectively [4,34,36]. The frequency of AML-M4 (10%) was similar than the Tunisian cohort with 7·9% but lower than either north America (23%) or Germany (20·4%) series. The AML-M5 subtype at 6% was comparable to that reported in Germany (7.3%) and Oman (6%), but lower than the Tunisian cohort (18·5%) [34,36–38]. The differences of frequencies of FAB subtype may be explained by the geographic, ethnic distribution and the differences in the age population of each of these cohorts [7,34].

Cytogenetic abnormalities were detected in 58% of the cases, compared with that previously reported in the literature ranging from 41·8% to 67% [4,34]. The cytogenetically normal AML is a heterogeneous group in terms of response to treatment, achievement of complete remission, and relapse rate. It is classified as intermediate risk group. Clinical outcome of AML patients with normal cytogenetics has been shown to be affected by other genetics

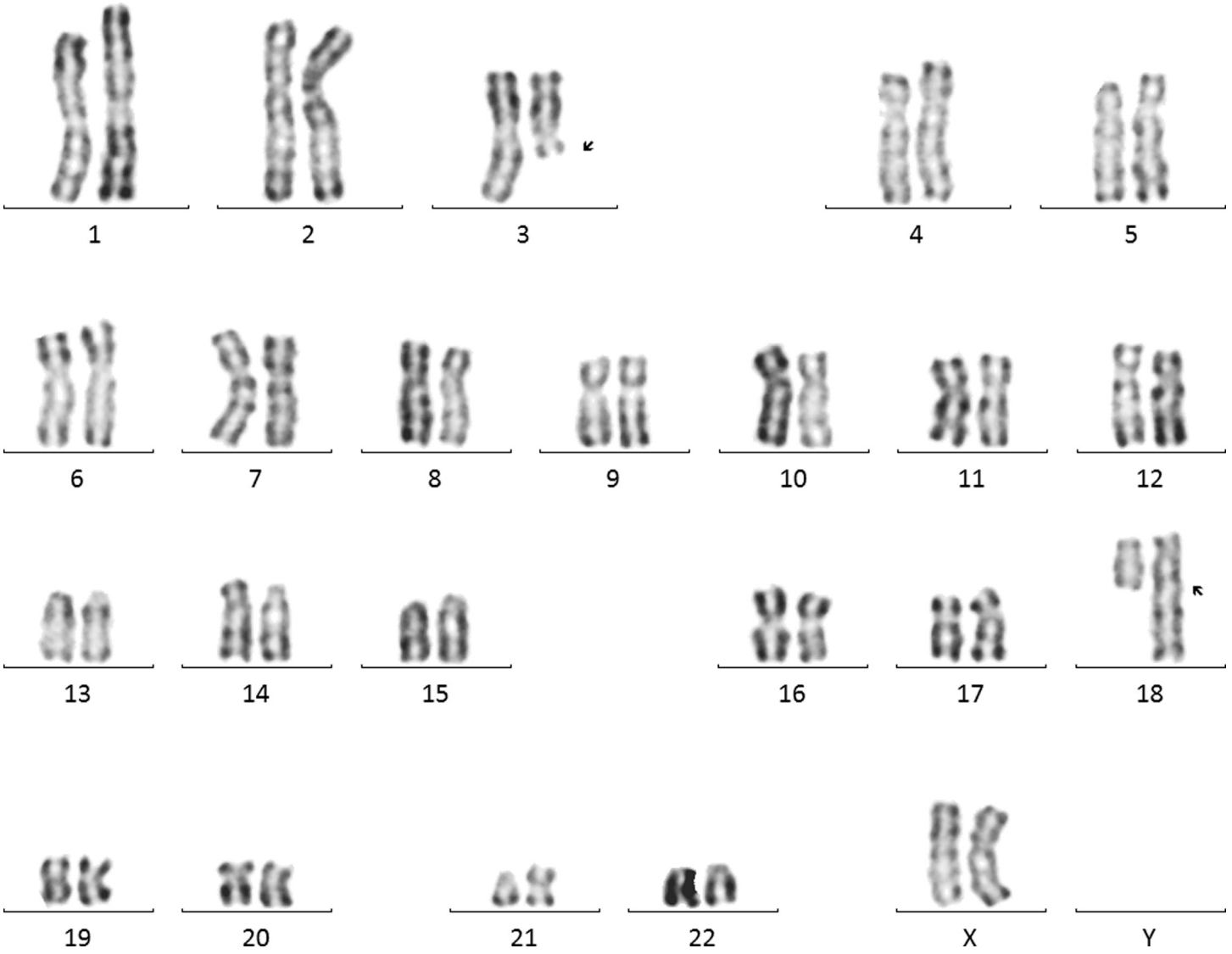

Fig. 1. Karyotype of novel abnormality: 46,XX,*t*(3;18)(q13;q22).

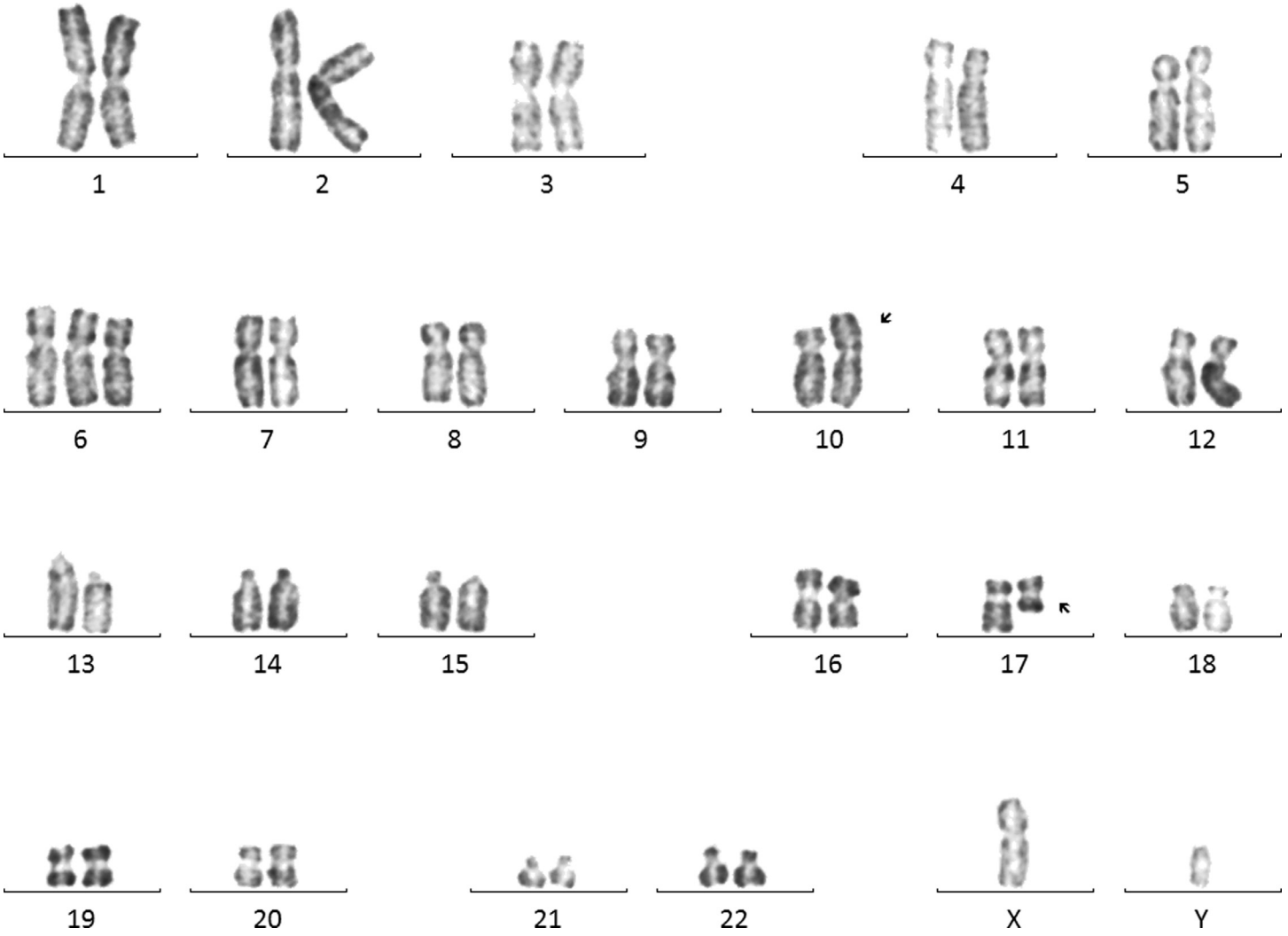

Fig. 2. Karyotype of rare abnormality: 47,XY,+6,*t*(10;17)(p13;q21),+6.

Table 5
Comparison of the caryotypes patterns of the Moroccan AML patients with others from different geographic areas.

Characteristics	This study 2015	Tunisia 2012 [34]	Spain 2006 [7]	Malaysia 2013 [2]	UK 2010 [6]	China 2009 [4]	Japan 2008 [40]	USA 2002 [37]
Total patients	895	631	1129	480	5876	1432	638	1311
Median Age	40·5(20–60)	37(0·08–95)	61(1–94)	39(0·3–81)	44(15–59)	42(4–84)	45(15–66)	52(15–86)
Abnormal karyotypes	58	62·9	63.5	30·4	59	58	58·2	56
t(8;21)	12,5	12·3	2·7	7·3	7	8	17·7	6
t(15;17)	3·7	13·1	14·8	2·3	13	14	NA	7
inv 16	3·3	3·4	2·7	NA	5	NA	4·1	7
11q23	3·6	3·8	3·3	NA	3·6	1	5	4
−5/del5q	1	2·2	9·1	0·8	4·7	1	1	7
−7/del7q	3	3	8·6	1·2	7·2	1	2	7
Trisomy 8	5·2	7	11·4	3	10	2	NA	9

NA: Not available.

alterations that were not evaluated in this study, but we recognize that molecular studies must be integrated with cytogenetic studies for risk stratification at diagnosis to improve therapeutic strategies [34].

In this study of young AML population, the prognostic groups were classified as: favorable (19·5%), intermediate (68%) and adverse (12·5%). Using a similar classification, Medical Research Council (MRC) in United Kingdom reported in patients aged between 16 and 99 years old, that 14% had favorable cytogenetics, 65% had intermediate and 21% had poor risk. Those findings were different in Brazil, with (21%) in the favorable group, (40%) in the intermediate group and (23%) in a poor prognosis [35–39].

The results of this study compared with several population-based and regional studies are detailed in Table 5.

In our study, the *t*(8;21) was the most prevalent aberration found in 12·5% of patients, it was also in Japan (17·7%) and in North America, especially in the African–American population (17%) [40,41]. This finding is closer to that observed in Tunisia (12·2%), but higher than in findings from China (8%), Caucasian American population (6%) and Spain (2·7%) [4,7,37]. Geographical differences have been reported in previous studies for this recurrent translocation [7]. *t*(8.21) was the sole abnormality in 50% of cases and as previously described, was associated to a loss of sex chromosome in 43%, del(9q) in 21%, +8 and +4 in (3%) and in 4 cases with 3 or more chromosomal abnormalities. Reportedly, those additional chromosome aberrations did not have any adverse affect on *t*(8;21) [5,35,42]. Some other reports, suggested a negative impact for del(9q), complex karyotype, or loss of Y [6]. Three variant forms of the classic translocation *t*(8;21) were observed in our study involved chromosomes 1, 7 and 13. The variant forms are uncommon and account approximately 3% of all *t*(8;21) in AML patients [43].

The frequency of *t*(15,17) was observed in only 3·3%, this rate is comparable with Malaysia (2·3%) but is very low when compared to Spain (14·8%), Tunisia (13·1%), and China (14%) [4,7,34]. We hypothesize that in our study, the frequency of this subtle *t*(15;17) may be under estimated by conventional cytogenetic analysis as cells do not have good mitotic division and other essential techniques as fluorescence in situ hybridization (FISH) and/or reverse-transcriptase polymerase chain reaction (RT-PCR) methods were mostly unavailable for evaluation [4]. Accessibility to care may be another reason, if we consider the high rate of early mortality with hemorrhage at diagnosis [44]. An increased frequency has been also reported for Latino patients as compared to Caucasians and race could be one of the reasons for the different incidence of AML but unless they are evaluated thoroughly the comparison regarding geographical differences should be interpreted with caution [7].

Inv(16) was observed in 3·3% of patients, consistent with the results from previous studies ranging from 2% to 8% [34]. The frequency may be also under-estimated because it is a subtle abnormality and the detection of the CBF-MYH11 can be enhanced by FISH or RT-PCR, methods that were not available during this study [2]. Four of our cases had trisomy 22, which is strongly associated with inv(16), with a significantly better outcome.

Trisomy 8 is considered as an intermediate cytogenetic-risk alteration and its pathogenetic role is still unclear, it was the most frequent numerical abnormality occurring in 47 (5·2%) of our subjects, higher than China (3·8%), but lower than that found among Tunisian cohort (7%), north America (9%) and Spain (11·4%) [4,7,34,37].

AML with 11q23 abnormalities is a heterogeneous group with numerous partner chromosomes, the risk stratification is controversial, in general worst than those with normal karyotype, some reports indicated that *t*(9;11) had a relatively favorable prognosis than those with other partner chromosomes genes and *t*(6;11) had an adverse outcome [40]. In our study, 11q23 was observed in 2·6% of adult cases, similar to previous AML studies in which it occurred in no more than 4% in adults and 25% in children [4,6].

The partial and/or complete deletions of chromosomes 5 and 7 accounted for 1 and 3% of our cases, similar to Tunisia (2·2%) and (3%), Malaysia (0·8%) and (1·2%), China (1%) and (1%) and Japan with (1%) and (2%) [2,4,34,40]; those findings have been reported in 6–15% of de novo AML in other adult series [4].

Complex karyotype with 3 or more abnormalities occurred in 7·4% of our patients similar to the Malaysian population with (7·3%). All the cytogenetic classification schemes, adopted 3 or more abnormalities to define the complex karyotype except the MRC. The latest world health organization classification (WHO) defined a complex karyotype as one with 3 or more unrelated abnormalities in the absence of *t*(15;17), *t*(9;11) or CBF leukemias. In general complex karyotypes are found in about 10–12% of adult AML patients and are considered a high cytogenetic risk aberration with a poor prognosis in the absence of *t*(8;21), *t*(15;17) or *t*(16;16)/inv(16), because in most studies increased karyotypes complexity in these subgroups did not adversely affect outcome [2,5]. The complexity frequency increases with age and the mechanisms may be due to age/environmental associated factors.

Negative prognostic impact of autosomal monosomies in AML has been described for chromosomes 5 and 7, but later studies confirmed in multiple comparisons, that any type of monosomy in AML is associated with a dismal outcome. There is no difference regarding the notably adverse prognostic value between an autosomal monosomy in general and the specific −7. Even

more profound is the influence of multiple autosomal monosomies or one autosomal monosomy in combination with at least one structural chromosome abnormality in AML, which results in extremely poor outcome (4 year OS at 4%) [6,45]. Surprisingly, we find that 115 of 345 (33%) patients with cytogenetic abnormalities without core binding factor and (13%) of the 895 patients with eligible karyotypes, had monosomies, they were single in 45 (5%) and in 70 (8%), they were multiple or in conjunction of other abnormalities. Grimwade and all confirmed that the presence of monosomal karyotypes identifies a group of patients with very poor prognosis but noted that the majority of such patients fall within the adverse-risk group as defined by the MRC [6]. These findings are very important; we should consider monosomal karyotypes when elaborating novel diagnosis and therapeutic strategies.

Rare and novel abnormalities can contribute to define novel genes and mutations involved in the leukemic process. We report in this study 10 novel abnormalities not described before as well as rare abnormalities.

In summary, adequate treatment and supportive care are the most critical factors for prognosis, particularly in countries with limited resources. In this context, karyotype of the leukemic cells is important for predicting response to induction therapy and for stratified adapted treatment approach. This is the largest study done in Morocco, Africa and Middle East. Epidemiological studies involving different ethnic populations and geographic regions of the world should help to unfold the true nature of environmental and genetic interplay in the development of AML. Our cytogenetic profile reveals some particularities when compared to others report around the world. Our study confirmed previous reports from around the world and has notable differences with eastern and western countries. The challenge for our future studies is to introduce molecular studies to our practice to enhance the detection of genetic lesions.

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Conflict of interest

The authors declare no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cancergen.2019.06.010.

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