Orijinal Araştırma / Original Investigation
Aegean J Med Sci 2022;2:44 -50

Chromosomal Anomalies in Bone Marrow Samples of Patients Diagnosed With Hematological Cancer: FISH Results of 109 Cases from One Center

Hematolojik Kanser Tanılı Hastaların Kemik İliği Örneklerindeki Kromozomal Anomaliler: Tek Merkezden 109 Olgunun FISH Sonuçları

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ÖZET

AMAÇ: Hematolojik kanserler, kemik iliği, kan ve lenf düğümlerini etkileyen genellikle yapısal ve sayısal kromozom anomalileri ile ilişkili bir neoplazma grubudur. Hematolojik kanserlerde kemik iliği incelemesi, hastalığın tanısı ve prognozu hakkında aydınlatıcı ve yönlendirici bir role sahiptir. Çalışmamızda, hematolojik kanser tanılı hastalarda belirli genetik düzensizliklerin Floresan In Situ Hibridizasyon (FISH) yöntemi kullanılarak elde edilen sonuçlarının retrospektif olarak değerlendirilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Çalışmamızda,1 Ocak 2021-30 Kasım 2021 tarihleri aralığında, Dicle Üniversitesi Tıp Fakültesi Tıbbi Biyoloji ve Genetik Anabilim Dalı'na, Hematoloji anabilimdalı ve diğer kliniklerden yönlendirilen hematolojik kanser ön tanılı 109 hastanın (KML n=14, AML n=40, KLL n=6, ALL n=27, multipl miyelom (n=22) kemik iliği örneklerinden FISH yöntemi kullanılarak elde edilen sonuçları yaş, cinsiyet ve hastalık dağılımı açısından retrospektif olarak incelenmiştir. Çalışma grubuna alınan hastaların tümü kromozomal anomaliler, sayısal ve yapısal değişlikler ya da dengeli translokasyon varlığı açısından değerlendirilmiştir.

BULGULAR: Olguların 47'si kadın 62'si erkek hasta olup yaş ortalaması 48±21,6 olarak tespit edilmiştir. Olguların incelenmesi sonucunda, AML için bilinen; t(15;17), monozomi 7 ve trizomi 8, KML için t(9;22); KLL de del(13q14) ve del(17p13), multipl miyelom için t(11;14)(q13;q32), ALL için (t[9;22]) (bcr-abl) ve t(4;11) yapısal ve sayısal kromozom anomalileri tespit edildi. Ayrıca grupların karşılaştırılmasında kadın ve erkekler arasında anlamlı fark bulunamamıştır.

SONUÇ: FISH yöntemi kullanılarak hematolojik kanser ön tanısı almış hastalarımızla yaptığımız bu retrospektif çalışmada, hastalıklarla ilişkili prognostik olarak önemli anomaliler ile ilgili sonuçlarımızı değerlendirdik. Hastalıkların tanılarının hızlı ve doğru olarak tespitinin, hastalığın tedavi planlaması ve seyrinin ön görüsü açısından çok önemlidir. Sonuç olarak bizim çalışma sonuçlarımıza göre kısıtlı ve zor şartlarda alınan kemik iliklerinden hücre elde etmenin zorluğu göz önüne alındığında FISH yönteminin interfaz hücrelerinde bile çalışma imkânı sağlaması nedeniyle kanser genetiğinde kullanılan güçlü ve etkili bir teknik olduğu kanaatine varılmıştır.

Anahtar Kelimeler: hematolojik kanser, FISH, kemik iliği, kromozomal anomaliler

ABSTRACT

OBJECTIVE: Hematological cancers are a group of neoplasms that affect the bone marrow, blood and lymph nodes, usually associated with structural and numerical chromosomal abnormalities. Bone marrow examination in hematological cancers has an illuminating and guiding role in the diagnosis and prognosis of the disease. In our study, it was aimed to retrospectively evaluate the results obtained by using the Fluorescent In Situ Hybridization (FISH) method of certain genetic disorders in patients with a diagnosis of hematological cancer.

MATERIALS AND METHODS: In our study, between January 1, 2021 and November 30, 2021 The results obtained from bone marrow samples of 109 patients (KML n=14, AML n=40, KLL n=6, ALL n=27, M.Myelom n=22) with pre-diagnosis of hematological cancer, who were referred to Dicle University Faculty of Medicine, Department of Medical Biology and Genetics, Department of Hematology and other clinics, were analyzed retrospectively in terms of age, gender, and disease distribution. All of the patients included in the study group were evaluated in terms of chromosomal anomalies, numerical and structural changes, or presence of balanced translocation.

RESULTS: There were 47 female patients and 62 male patients, and the mean age was 48±21.6 years. As a result of the examination of the cases, known for AML; t(15;17), monosomy 7 and trisomy 8, t(9;22) for CML; Del(13q14) and del(17p13) for CLL, t(11;14)(q13;q32) for M. Myeloma, (t[9;22]) (bcr-abl) and t(4;11) for ALL structural and numerical chromosomal anomalies were detected. In addition, in the comparison of the groups, no significant difference was found between the materials participating in the study, male and female.

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Received/Geliş Tarihi: 19 05 2022 || **Accepted/Kabul Tarihi:** 01 07 2022

CONCLUSION: In this study, which we conducted with our patients who were prediagnosed with hematological cancer with the FISH method, we evaluated our results regarding the prognostically important anomalies associated with the diseases. Rapid and accurate diagnosis of diseases is very important in terms of treatment planning and prognosis of the course of the disease. Considering the difficulty of obtaining cells from bone marrow taken under limited and difficult conditions according to our study results, it was concluded that the FISH method is a powerful and effective technique used in cancer genetics, since it provides the opportunity to work even in interphase cells.

Keywords: hematological cancer, FISH, bone marrow, chromosomal abnormalities

INTRODUCTION

Bone marrow is the nutritious spongy tissue found in the cavities inside long flat bones such as the sternum and hip bones. There are two kinds of bone marrow: red bone marrow and yellow bone marrow. Both types of bone marrow contain blood vessels. There are two types of stem cells in the bone marrow: Hematopoietic and mesenchymal. This process, which consists of the production process of various erythrocytes and pluripotent stem cells, is known as hematopoiesis. The pluripotency of hematopoietic stem cells can be any cell type in the bloodstream. Under the influence of tissue and hormonal factors, in parallel with the differentiation or maturation process, these cells turn into the cells we know in the bloodstream(1).

Hematological cancers are neoplasms composed of cells originating from the bone marrow. . Most of these malignancies contain structural or numerical chromosomal abnormalities. The first anomaly detected in humans in this regard is the Philadelphia chromosome (2). After the philadelphia chromosome, which is an significant marker of chronic myloid leukemia (CML), the value of translocation, deletion and inversion of different chromosomes in the diagnosis of diseases and evaluation of prognosis in different types of hematological cancers has been understood.

Bone marrow examination is a valuable examination that is mostly performed in peripheral blood smear samples to show the cellular features of the bone marrow, tumors and participation of hematological diseases in suspected cases. For the first time in 1890, German pathologist David Paul Von Hansmann defined nuclear and mitotic structure irregularities in cancer biopsy materials and reported that these findings may be important in the development of cancer(3).

FISH applications, developed as a complement to classical cytogenetic methods, have an important place in cancer studies. The FISH technique is applied to metaphases (metaphase FISH-mFISH) or interphase cells (interphase FISH-iFISH) depending on the situation(4).

In this study, we retrospectively analyzed the results of bone marrow materials of patients diagnosed with hematological malignancy from various clinics who applied to Dicle University Faculty of Medicine, Department of Medical Biology and Genetics between 01/01/2021 and 30/11/2021, and analyzed using the FISH technique. Our aim is to evaluate the detailed examination and analysis of the prevalence of abnormalities in our patient population with the implementation of the FISH method.

MATERIAL & METHODS

A total of 109 patients with the diagnosis of hematological malignancy were included in this retrospective study, from the Department of Hematology, Department of Pediatrics, Hematology, and other clinics, between January 1, 2021 and November 30, 2021, to Dicle University Faculty of Medicine, Department of Medical Biology and Genetics.

FISH analysis results of bone marrow samples of 14 patients in the CML patient group (3 women and 11 men), 27 patients in the ALL patient group (12 women and 15 men), 40 patients in the AML patient group (17 women and 23 men), 6 patients in the CLL patient group (2 women and 4 men), 22 patients in the Multiple Myeloma patient group (13 women and 9 men) and 109 patients in total were evaluated retrospectively(table I). Considering the genetic analysis results of the patients, the FISH method was applied with different FISH probes (table 2) in the samples.

The data of all patients were searched through the closed registry system of the Department of Medical Biology and Genetics. Age, gender and prediagnosis of hematological malignancy of the patients were recorded. Using this information, a database was created in the excel program in computer environment. Cases with missing data were excluded from the study.

Ethics committee approval was obtained for this study from the Dicle University Clinical Research Ethics Committee at the meeting dated 21.01.2022/15

Statistical Evaluation

The data were recorded in the SPSS (Statistical Packages of Social Sciences, SPSS for Windows, Version 10.0, Inc, Chicago, IC, USA) program. Error controls, tables and statistical analyzes were also performed in this program, the relationship between the parameters obtained from the age, gender and diseases of the individuals in the patient groups was made according to the correlation and regression analysis. The comparison of the parameters between the groups was made according to the t test and their arithmetic mean was shown with standard deviation.

RESULTS

Of the 109 patients who participated in our study, 47 were female and 62 were male. The mean age of women was 50±22.02, and the mean age of men was 47±21.3 (table 1). The distribution of the patients participating in the study according to their preliminary diagnoses is CML(n=14), AML(n=40), CLL (n=6), ALL (n=27), M. Myeloma (n=22) (table 2).

Table 1: *Distribution of patients*

	PD (% value)	Age (AVG, %)	Gender (%) F/M
ALL	26(%23,9)	33.0±23.4	42.3/57.7
AML	40(%36,7)	46.5±19.2	45/55
CLL	7(%6,4)	52.5±13.6	28.6/71.4
CML	14(%12.8)	52.0±16.0	36.4/63.6
MM	22(%20,2)	68.6±9.7	56/44

PD: Patient Distribution F: female, M: male

The median age was 33.0±23.4 years in 12 (42.3%) female and 15 (57.7%) male patients diagnosed with Acute Lymphocytic Leukemia and aged 2-77 years. In the FISH study; Of the 27 interphase nuclei examined, 18 were normal, and chromosomal anomaly was detected in at least one sample type in 9 of them. Translocation specific to 8q24, 9q34, 12p13 and 4q21 regions, in FISH study using dual fusion probe, 2 of 15 male patients had 4q21, 2 had 8q24.9q34 and 12p13, 2 had 9q34.1(ABL1)/22q11.2(BCR) regions-specific translocation was observed, while 9 of them did not. Translocation specific to the 9q34.1(ABL1)/22q11.2(BCR) region was observed in 3 of 12 female patients, while no translocation was observed in 9 of them. In the iFISH study using the 13q14 region-specific deletion probe, it was found that the 13q14.3(DLEU2) region was deletion in 2 female patients. In the FISH study using the 11q23.3(MLL) region-specific rearrangement and deletion probe, 11q23.3(MLL)(trisomy7) was observed in 1 male patient and deletion of the 3'MLL region (11q23.3) in 1 male patient. In the FISH study using centromeric probes specific to 7p11 and 8p11 regions, 8p11 (monosomy8) was observed in 1 male patient, 7p11 (trisomy7) in 1 male patient, and both 7p11 and 8p11 (tetrasomy 7.8 tetraploidy) in 1 male patient.

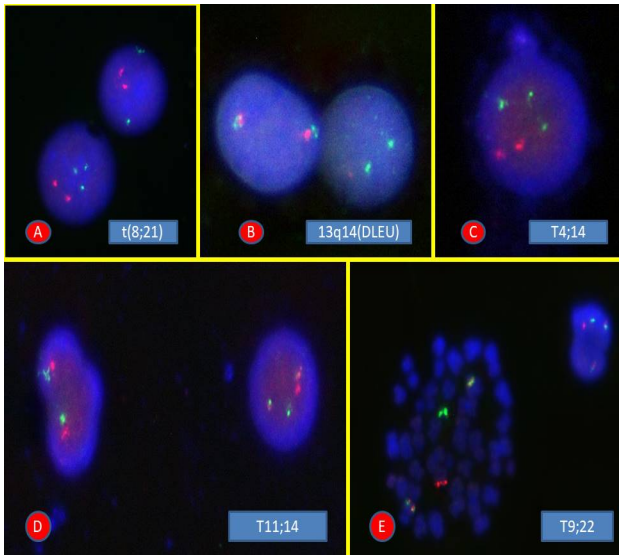
Table 2: *Site-specific centromeric FISH probes used in interphase cells obtained from uncultured bone marrow from patients*

Diseases	Region-Specific Centromeric Probes in Interphase Cells
Acute Lymphocytıc Leukemıa (ALL) (Probe used: ALL Panel / Diagen)	**A)** 8q24.21(MYC)/14q32.33(IGH), 9q34.1(ABL1)/22q11.2(BCR), 12p13.2(TEL)/21q22.12(AML) and 4q21.3-4q22.1)(AFF1)/11q23.3(MLL) region-specific translocation, dual fusion; **B)** 13q14.3(DLEU2)/13q34(LAMP1) region-specific deletion; **C)** 11q23.3(MLL) region-specific reorganization; **D)** 7p11.1-q11.1(D7Z1) ve 8p11.1-q11.1(D8Z2)
Acute Myeloid Leukemia (AML) (Probe used: AML Panel / Diagen)	**A)** 15q24.1(PML)/17q21.1(RARA), 8q21.3(ETO)/21q22.12(AML1) and 16p13.11(MYH11)/16q22.1(CBFB) region-specific translocation, dual fusion; **B)** 5q31.2(EGR1), 7q22.1(RELN)/7q31.2(TES) ve 17p13.1(P53) region-specific deletion; **C)** 11q23.3(MLL)
CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) (Probe used: CLL / Diagen)	**A)** 11q13.3(CCND1)/14q32.33(IGH) and 14q32.33(IGH)/18q21.33(BCL2) region-specific translocation, dual fusion; **B)** 17p13.1(P53) and 13q14.3(DLEU2)/13q34(LAMP1) region-specific deletion; **C)** 12p11.1-q11.1(D12Z3)
Chronic Myeloid Leukemia (CML) (Probe used: BCR-ABL t(9;22)/Diagen)	**A)** 9q34.1(ABL1)/22q11.2(BCR) site-specific translocation, dual fusion probe
Multiple Myeloma (MM) (Probe used: MM Panel/Diagen, Cytocell)	**A)** 4p16.3(FGFR3)/14q32.33(IGH) and 11q13.3(CCND1)/14q32.33(IGH) region-specific translocation, dual fusion; **B)** 17p13.1(P53) and 13q14.3(DLEU2)/13q34(LAMP1) region-specific deletion; **C)** 7p11.1-q11.1(D7Z1) ve 8p11.1-q11.1(D8Z2)

The median age was 46.5±19.2 in 17 (45%) female and 23 (55%) male patients diagnosed with Acute Myeloid Leukemia and aged between 21-87 years. In the FISH study; While 1 of 40 interphase nuclei could not be found to be

evaluated, results were obtained in 39 of them. According to these results, 27 were normal and 12 were anomaly. Translocation specific to 15q24, 8q21 and 16p13 regions, in FISH study using dual fusion probes, specific translocations to regions 15q24.1(PML)/17q21.1(RARA) were observed in 1 male patient, 8q21.3(ETO)/21q22.12(AML1) in 4 male and 2 female patients (fig.1A) ,16p13.11(MYH11)/16q22.1(CBFB) in 1 male and 1 female patient In the iFISH study using deletion probes specific to 5q31 , 7q22 and 17p13 regions, deletion of 7q22.1(RELN)/7q31.2(TES) region was detected in 4 male patients, while deletion specific to 5q31.2(EGR1) and 17p13.1(P53) regions was detected (fig 2A). 11q23.3(MLL)(trisomy7) was observed in 1 male patient as a result of iFISH examinations using the 11q23.3(MLL) region-specific rearrangement probe.

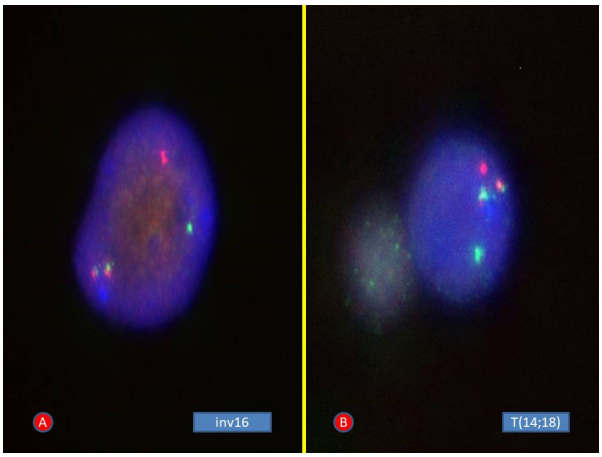
Figure 1: *FISH with different types of probes and partial metaphases.*



A) *t(8;21) Signal pattern (3 green, 2 red signals) consistent with the trisomy of region 8q21.(ETO) was detected.* ***B)*** *Signal pattern consistent with the deletion of the 13q14.3(DLEU2) region was detected* ***C)*** *Signal pattern consistent with the rearrangement of region 14q32.33(IGH) was detected in 33% of region t(4;14).* ***D)*** *Typical double fusion hybridization appearance specific to t(11;14)(q13.3;q32) IGH/CCND1 translocation was detected.* ***E)*** *t(9;22)(q34.1;q11.2)ABL1/BCR translocation was detected*

The median age was 52.5±13.6 years in 2 (28.6%) female and 4 (71.4%) male patients diagnosed with Chronic Lymphocytic Leukemia, aged 36-71 years. In the FISH study, 2 of the 6 interphase nuclei examined were normal and 4 had chromosomal structure anomaly. Translocation specific to 11q13, 14q32, 18q21 regions, in FISH study using dual fusion probe, 14q32(IGH) region-specific translocation was observed in 1 of 4 male patients, and 18q21 region-specific translocation was observed in 1, while no translocation was observed in 2 female patients(fig 2B). In the iFISH study using deletion probes specific to 17p13, 13q14 regions, deletion of 13q14.3(DLEU2) region was detected in 1 of 2 female patients and 2 of 4 male patients (fig 1B). No deletion of the 17p13 region was observed in the analyzed cells. As a result of iFISH examinations using 12p11 region-specific centromeric probes, trisomy 12 was not detected in any of the 6 cases.

Figure 2: *FISH with different types of probes and partial metaphases*



A) *A double fusion hybridization was detected, which may be compatible with the inv(16)(p13.11;q22.1) region.* ***B)*** *Typical double fusion hybridization appearance specific to t(14;18)(q32.33;q21.33) translocation was detected.*

The median age was 52.0±16.0 years in 3 (36.4%) female and 11 (63.6%) male patients, aged 25-79 years, diagnosed with Chronic Myeloid Leukemia. In the FISH study, 5 of the 14 interphase nuclei examined were normal and 9 were translocation.

Translocation specific to 9q34.1(ABL1)/22q11.2(BCR) regions, in FISH study using dual fusion probe, typical double fusion hybridization appearance specific to t(9;22)(q34.1;q11.2)ABL1/BCR translocation was detected in 2 of 3 female patients and 7 of 11 male patients in total 9 people (fig 1E), No translocation was observed in 1 female and 4 male patients.

The median age was 68.6±9.7 years in 13 (56%) female and 9 (44%) male patients diagnosed with Multiple Myeloma, aged between 53 and 83. In the FISH study, 1 of 22 interphase nuclei could not be found to be evaluated, while results were obtained in 21 of them. According to these results, 15 normal and 6 chromosome number and structural anomalies were observed. Translocation and

trisomy11 specific to 11q13, 14q32 regions were detected in 4 female patients in the iFISH study using dual fusion probes(fig 1C-1D). No deletions were detected in 17p13 and 13q14 gene regions. Trisomy 7 was detected in 3 female patients in the iFISH study using centromeric probes specific to 7p11 and 8p11 regions. Cells analyzed from 1 female patient were evaluated for hyperdiploidy, with trisomy 17 in 11% and trisomy 7 in 9%. No chromosomal abnormality was found in any of the 9 male patients examined.

DISCUSSION

Hematological cancers are more common in men, In our study, 47 (43.1%) of 109 cases with hematological malignancy were female and 62 (56.9%) were male, and the M/F ratio was found to be approximately 1.32. In a large retrospective study of 5013 patients with hematological cancer, 69.2% were male (n = 3468) and 30.8% were female (n = 1545) patients, and the M/F ratio was found to be 2.2 The high number of male patients in hematological cancer cases in our study is consistent with the literature.(5) In our study, in accordance with the literature, the most common AML patient group was observed, while the least CLL patient group was detected. Accordingly, while the ALL patient group consists of younger patients, Multiple Myeloma draws attention as a disease of advanced age.

Acute Myeloblastic Leukemia (AML), Acute Lymphoblastic Leukemia (ALL) are the two main groups of acute leukemias. Chronic Myelocytic Leukemia (CML) and Chronic Lymphocytic Leukemia (CLL) are classified as chronic leukemias. Multiple Myeloma (MM); It is a disease characterized by an increase in plasma cells in the bone marrow, the presence of M serum proteins secreted by these cells in the serum and/or urine, and lytic bone lesions (6).

Determination of chromosome aberrations in hematological cancers originating from bone marrow is valuable in terms of diagnosis and prognosis. Fluorescence In Situ Hybridization technique is accepted as a fast, easy and reliable method for detecting such changes. While chromosomal anomalies of 2000 and 3000 kbase can be detected by classical cytogenetic methods, it is possible to detect regions of 0.5 kb by FISH method (7). In the FISH method, the nucleic acid sequence with a complementary label to the target DNA/RNA molecule is called a "probe". There are 35 specific (locus-specific and/or translocation-specific) probes used for diagnosis in hematological cancer diseases, as well as all chromosome, telomere and α-satellite probes specific to 24 chromosomes. These probes are available in single and/or double color probe sets according to their usage patterns and features; they can be marked with three and/or five different colors(8). One of the disadvantages of the technique is that it allows the disease-specific analysis of only special panels to be performed in the FISH technique and that other aberrations cannot be detected at the same time(7). There are many literature reports stating that the results obtained with the FISH technique are more sensitive and specific than the classical cytogenetic method.

Özbey et al. compared chromosomal abnormalities in CML patients with cytogenetic and FISH techniques, interphase Dual-FISH (D-FISH) is an effective technique that is reliable and gives results in a short time, in detecting BCR/ABL reorganizations in patients with CML at the time of diagnosis, They reported that D-FISH could be considered as the first test to be used in the diagnosis of patients with Ph(+) CML (9) .In our study, typical double fusion hybridization appearance specific to the 9q34.1(ABL1)/22q11.2(BCR) region-specific translocation was detected in the majority of patients who underwent bone marrow iFISH with a preliminary diagnosis of CML.

More than 50 recurrent chromosomal anomalies have been detected in acute myeloid leukemia (AML). These specific cytogenetic translocations that can be diagnosed by FISH analysis; t(8;21)(q22;q22) (AML1/ETO) AML-M2, t(15;17)(q22;q11-12) (PML/RARα)AML-M3/M3V, inv(16)(p13q22) or t(16;16)(p13;q22) (CBFβ/MYH11) AML-M4/M4eo, 11q23 translocations (MLL) have been reported(10). Cytogenetic changes that can be diagnosed by FISH are mostly observed in the 5th and/or 7th chromosomes. 15-20% of all AML patients have a complex karyotype consisting of multiple numerical and structural chromosomal abnormalities. Mostly, 5q-, -7 and/or 3q-anomalies are primary anomalies(8). However, the karyotype was found to be normal in the majority of patients diagnosed with AML. Therefore, it should be kept in mind that the FISH technique is limited in the diagnosis of AML(11). Chromosomal number and structural anomalies were not observed in 27 of 40 patients with prediagnosis of AML included in our study, while

chromosomal anomaly was observed in at least one sample type compatible with the literature in the other 12 cases.

Chromosomal abnormalities that are effective in prognosis and treatment in acute lymphocytic leukemia (ALL) have been reported. Monosomy 7 and trisomy 8 have been reported as a rare (0.5%) primary chromosomal anomaly in ALL with isolated numerical anomaly in a single chromosome without structural or numerical anomaly(12). More than 40 recurrent structural chromosome rearrangements have been reported in adult ALL cases, and their incidence is less than 1%. Isochromosomes are unique among all structural chromosomal abnormalities, It creates a combination of loss and gain of genetic material. The isochromosomes observed in ALL are i(7q), i(9q) and i(17q)(13). BCR/ABL oncogene The most frequently observed (20-30%) translocation in adult ALL is t(9;22)(q34;q11), that is, Philadelphia (Ph) translocation. This translocation is characterized by a poor prognosis in ALL. Additional chromosome abrasions are observed in 41-86% of Ph-positive ALL cases. The most frequently observed ones are 9p anomalies, hyperdiploid karyotype and monosomy 7, respectively (14). MLL-fusion gene The second most common structural chromosomal abnormality is translocation t(4;11)(q21;q23) with 3-7%. Translocation t(12;21) TEL-AML1 is the most common translocation observed in pediatric ALL. Translocation is found in 25% of children diagnosed with Pre B ALL(15). In our study, chromosomal number and structural anomalies were not observed in 18 of 27 patients with a preliminary diagnosis of ALL, while chromosomal anomalies were observed in at least one sample type in the other 9 cases. In parallel with the literature, 8p11(monosomy8) chromosome number anomaly was observed in a male patient, 7p11(trisomy7) in a male patient, and both 7p11 and 8p11(tetrasomy 7,8 tetraploidy) in a male patient.

Interphase FISH analysis becomes very valuable in patients with chronic lymphocytic leukemia (CLL) since classical cytogenetic studies cannot yield results. FISH can reveal aberrations in 80% of CLL patients. FISH probes help us to show long arm deletions of chromosome 13, long arm deletions of chromosome 11, short arm deletions of chromosome 17, and presence or absence of trisomy 12, as well as IGH (14q32), BCL6(3q27), and rearrangements of chromosome 6. It can also be used to determine (13). Although the number of patients admitted to our study with a pre-diagnosis of CLL was less than expected, it was noted that mostly chromosomal anomaly was observed in accordance with the literature.

Since spontaneous mitotic activity is low in myeloma cells in Multiple Myeloma (MM) patients, classical cytogenetic techniques may be insufficient. In these cases, FISH is an effective screening tool. The most important chromosomal abnormalities are chromosome 13 abnormalities and immunoglobulin chain locus rearrangements on chromosome 14q32. Different probe options are available for the detection of chromosome 13 and IGH (14q32) rearrangements, and diagnosis can be made with FISH. Apart from this, FISH analysis can be performed to determine numerical anomalies for chromosomes 9, 11, 15(16).

Unlike the literature, in our patient group, results were obtained in 21 of the patients who applied with the pre-diagnosis of multiple myeloma, but no results were obtained in one sample.While chromosomal number and structural anomalies were not observed in 15 of 21 patients, chromosomal anomalies were observed in at least one sample type in the other 6 cases.

Genetic studies continue to occupy a large place in the diagnosis, treatment and follow-up of prognosis of many cancer types, especially in hematological malignancies. In genetic studies, bone marrow cytogenetic examination is more suitable for screening, and the FISH technique is a complementary and alternative method for differential diagnosis and prognosis in patients with pre-diagnosis. In particular, the FISH method is a powerful technique to reveal gene translocations, amplifications, chromosomal aneuploidies and deletions. The main advantage of this technique is that the FISH method also provides the opportunity to work in interphase cells, because there is no need to prepare metaphase cells as in the metaphase FISH study. The main disadvantage of the FISH technique is that it only makes an examination by suspecting a certain abnormality, and the necessity of finding a specific probe for each investigated abnormality is the limitation of this technique.

CONCLUSION

In this study, we evaluated the results obtained using the FISH method from bone marrow samples of our patients with prediagnosis of ALL, AML, CLL, CML and M. Myeloma,

which were analyzed retrospectively. Considering the difficulty of obtaining cells from the bone marrow according to the results of this study, we concluded that the FISH method is a powerful and effective technique used in cancer genetics, since it provides the opportunity to work even in interphase cells.

As a result, according to both our study results and the results of different study groups, it was concluded that the FISH method is an effective and preferred technique in investigating a specific chromosomal disorder, clarifying the diagnosis of diseases and prognosis. We also use this technique frequently in our clinic. We believe that studies on these techniques and probes should be supported.

Etik: Bu çalışmanın etik kurulu alınmıştır. 21.01.2022/15

Ethics committee approval had been taken. 21.01.2022/15

Yazar katkı durumu; Çalışmanın konsepti; LGÇ, MB, ST, DO, MB,İY, dizaynı; LGÇ, MB, ST, DO, MB,İY, Literatür taraması; LGÇ, MB, ST, DO, MB,İY, verilerin toplanması ve işlenmesi; LGÇ, MB, ST, DO, MB,İY, istatistik; LGÇ, MB, ST, DO, MB,İY, yazım aşaması; LGÇ, MB, ST, DO, MB,İY.

Author contribution status; The concept of the study; LGÇ, MB, ST, DO, MB,İY, design; LGÇ, MB, ST, DO, MB,İY, literature review; LGÇ, MB, ST, DO, MB,İY, collecting and processing data; LGÇ, MB, ST, DO, MB,İY, statistics; LGÇ, MB, ST, DO, MB,İY, writing phase; LGÇ, MB, ST, DO, MB,İY.

Yazarlar arasında çıkar çatışması yoktur.

The author declares no conflict of interest.

Finansal Destek: yoktur / Funding: none

doi: https://doi.org/10.33713/egetbd.1118486

REFERENCES

1. Gupta M, Malik S, Kalra R, Sharma N, Singh S, Gupta V, Jain P, Sen R. Etiological Profile of Plasmacytosis on Bone Marrow Aspirates. Dicle Tıp Dergisi. 2016; 43(1): 1-4.

2. Nowell PC, Hungerford DA. A minute chromosome in human chronic granulocytic leukemia. Science1960;132:1497-501.

3. Hansemann D. Über asymmetrische Zelltheilung in Epithelkrebsen und deren biologische Bedeutung. Virchow's Archiv für pathologische Anatomie und Physiologie und für klinische Medicin, 1890, 779: 299–326.

4. Garimberti E, Tosi S. Fluorescence in situ Hybridization (FISH) Basic Principles and Methodology. In: Bridger JM, Volpi EV. (eds). Fluorescence in situ Hybridization (FISH) Protocols and Applications. London, Springer Sicence;2010, 3-20.

5. Hossain MS, Iqbal MS. Diagnosed hematological malignancies in Bangladesh - a retrospective analysis of over 5000 cases from 10 specialized hospitals.BMC Cancer. 2014; 14: 438-9.

6. Rajkumar S, Kumar F S. Multiple Myeloma: Diagnosis and Treatment. Mayo Clin. Proc. 91, 101–119 (2016).

7. McNeil N, Ried T. Novel molecular cytogenetic techniques for identifying complex chromosomal rearrangements: technology and applications in molecular medicine. Expert Rev Mol Med 2000; 2000:1-14.

8. Durak B. Hematolojide FISH. Moleküler Hematoloji ve Sitogenetik Alt Komitesi Temel Moleküler Hematoloji Kurs Kitapcığı. Taksim International Otel 12-13 Mart 2005 , Mersin.

9. Özbey Ü, Yüce H, Elyas H. Kronik Myeloid Lösemili Hastalarda Kromozomal Anomalilerin Belirlenmesi için Sitogenetik ve FISH Tekniği Uygulamaları. F.Ü. Sağ.Bil.Derg. 2006: 20 (6): 383 – 389

10. Durak B. Akut Lösemilerde FISH Paneli ve Prognoz . Türk Hematoloji Derneği'nin Eğitim Çalışmalarından Bilimsel Alt Komite Kursları, Akut Lösemi Kursu, Anemon Otel 8-9 Nisan 2006, Aydın. Kurs Kitapcığı 15-18.

11. Fonatsch C, Krömer E. Myelogische Leukaemien. Medizinische Genetik, 2:100-107, 2002.

12. Ganten D, Ruckpaul K. Molekularmedizinische Grundlagen von haematologischen Neoplasien. Springer, Heidelberg. 2003.

13. Özdemir M, Durak B, Aslan V, Artan S, Gülbaş Z, Başaran N. Results of cytogenetics studies in patients with acute leukemia. European Human Genetics Conference 2000. 27-30May 2000, Amsterdam, the Netherlands. European Journal of Human Genetics, 8(Suppl. 1), 2000;P-369,

14. Özkalemkaş F. Akut Lenfoblastik Lösemi. Türkiye Klinikleri Journal of Hematology, 2:10-23.

15. Rieder H, Flohr T. Akute Lymphatische Leukaemien der Erwachsene. Medizinische Genetik, 2002;2:100- 107.

16. Rooney DE. Human Cytogenetics malignancy and acquired abnormalities (Thrid Edition). Oxford University Pres, New York, 2001