Detection of Hyperdiploidy from Cerebrospinal Fluid in B-Cell Acute Lymphoblastic Leukaemia

Sir,

In B cell acute lymphoblastic leukaemia (B-ALL), the identification of chromosomal rearrangements has resulted in significant advancements in the prediction of prognosis, risk stratification, and the creation of targeted therapies. High hyperdiploidy, TEL-AML fusion, mixed lineage lekaemia (MLL) rearrangements, BCR-ABL1, t(1;19) (q23;p13), intrachromosomal amplification of chromosome 21 (iAMP21), and hypodiploidies are some of the genetic chromosomal changes observed in B-ALL.[1] Genetic abnormalities can be detected in 75 to 80% of childhood ALL cases with standard chromosome analysis and interphase fluorescence *in situ* hybridisation (iFISH) analysis.[2]

A 14-year female patient with a diagnosis of B-ALL received IC-BCF chemotherapy protocol. At the time of diagnosis, the cytogenetic and iFISH methods detected a hyperdiploid karyotype >50 at chromosomes 8, 10, 11, 14, 17, and 21. Four years later, the patient complained of neck swelling and was considered a relapse of ALL. At that time, the cytogenetic analysis detected hyperdiploid karyotype >50 at chromosomes 8, 11, 14, and 21 again. The patient achieved remission with the FLAG chemotherapy protocol and then allogeneic stem cell transplantation was performed after fludarabine+ATG+TBI+cyclophosphamide preparation regimen. About one year after the transplantation, the patient presented with complaints of dizziness, headache, and diplopia. The patient's bone marrow sample was analysed cytogenetically and with FISH analysis, and the results were normal. Cerebrospinal fluid (CSF) sample was taken from the patient whose bone marrow was in remission. In the CSF sample, CD10(+), CD19(+), CD20(+), CD22(+), Tdt(+), MPO(-), HLA-DR(+) CD34(-), and CALLA(+) were detected through flow cytometry. At the same time, cytogenetic and iFISH analyses were performed on the CSF sample. iFISH analysis detected hyperdiploid karyotype >50 at chromosomes 8, 11, 14, and 21 (Figure 1).

Additionally, the polymerase chain reaction (PCR) method was used to perform BCR-ABL1 fusion gene analysis on the CSF sample, and the result was negative. The patient, who was thought to have isolated central nervous system involvement, received intrathecal methotrexate, cytarabine and dexamethasone treatment. The patient's clinical findings completely improved in the first week after intrathecal treatment. No leukaemia cells were observed in CSF in the first month of treatment. Sebsequently, systemic chemotherapy was started with methotrexate 3.5 g/m^2. Allogeneic stem cell transplantation was planned.

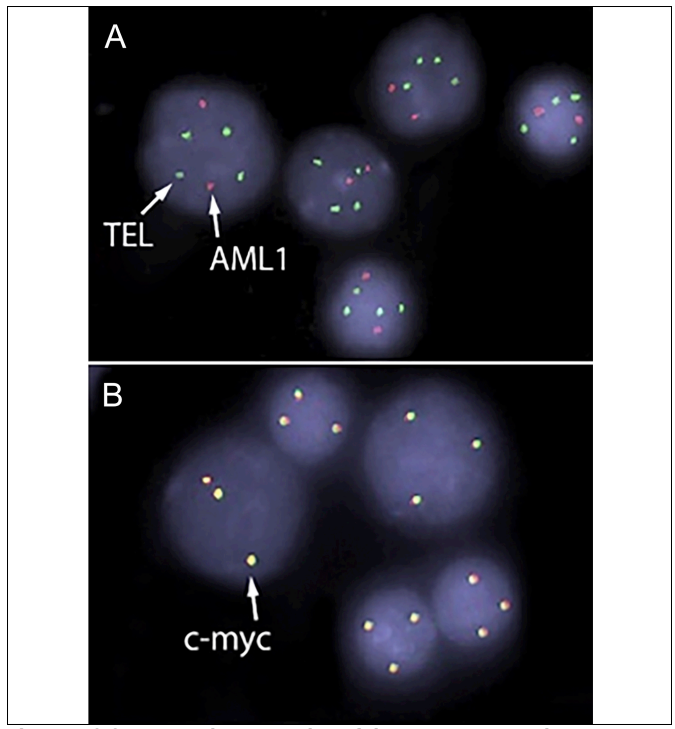

Figure 1: (A) Increased copy number of chromosome 21 or the *AML1* gene region. (B) Trisomy of the c-myc gene region or chromosome 8.

In order to achieve an accurate diagnosis of CNS involvement in ALL, it is essential to adopt a comprehensive approach. Techniques such as immunocytochemistry, flow cytometry, PCR, and iFISH are used to detect any residual leukaemic cells in the CSF. The quantity and quality of CSF cells are the limiting factors for PCR, flow cytometry, and immunocytochemical examinations. However, the FISH method is a fast, and economical technique that can detect small amounts of residual ALL cells.[3] In a study comparing cytology analysis and FISH analysis in CSF samples of ALL patients, approximately 9% of patients did not have sufficient cells for cytological examination. However, FISH analysis was still possible.[4]

In conclusion, CNS involvement was confirmed by performing FISH analysis on the CSF sample of an ALL patient whose bone marrow was in remission. Thus, the patient received the appropriate treatment and went into remission again quickly.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
EG: Contributed to data collection, drafted the text, conducted the related literature search, and did reference setting.
SD: Contributed to data collection and interpreted the data.
Both authors approved the final version of the manuscript to be published.

REFERENCES

1. Iacobucci I, Mullighan CG. Genetic basis of acute lymphoblastic leukemia. *J Clin Oncol* 2017; **35(9)**:975-83. doi: 10.1200/JCO.2016.70.7836.

2. Magatha LS, Scott JX, Subramaniam G, Chandrasekaran T, Paul SFD, Koshy T. Cytogenetic and fluorescence *in situ* hybridization profile of pediatric acute lymphoblastic leukemia in a university hospital in South India. *Med Princ Pract* 2021; **30(6)**:563-70. doi: 10.1159/000518280.
3. Karapetyan K, Gizhlaryan M, Kalinovskaia O, Hovhannisyan A, Tadevosyan G, Matinyan L, *et al*. Investigating residual leukemic cells in acute lymphoblastic leukemia: A practical approach using a streamlined interphase fluorescence *in situ* hybridization method on cerebrospinal fluid. *Mol Cytogenet* 2023; **16(1)**:17. doi: 10.1186/s13039-023-00649-x.
4. Hwang SM, Park HS, Park S, Kim S-M, Hong KT, Chang YH, *et al*. Application of fluorescence *in situ* hybridization on cerebrospinal fluid cytospins for the detection of residual leukemic cells in patients with childhood acute lymphoblastic leukemia. *Am J Clin Pathol* 2019; **151(4)**:416-23. doi: 10.1093/ajcp/aqy160.

Emine Goktas[1] and Sinan Demircioglu[2]

[1]Department of Medical Genetics, Faculty of Medicine, Necmettin Erbakan University, Konya, Turkiye
[2]Department of Internal Medicine Division of Haematology, Faculty of Medicine, Necmettin Erbakan University, Konya, Turkiye

Correspondence to: Dr. Emine Goktas, Department of Medical Genetics, Faculty of Medicine, Necmettin Erbakan University, Konya, Turkiye
E-mail: emineaktas88@hotmail.com

Received: June 28, 2024; Revised: August 01, 2024; Accepted: August 03, 2024
DOI: https://doi.org/10.29271/jcpsp.2024.11.1910