



First Case of Diffuse Large B-Cell Lymphoma Subtype of Monomorphic Post-Transplant Lymphoproliferative Disorder With 3q27 Translocation

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Dear Editor,

Post-transplant lymphoproliferative disorders (PTLDs) are a rare group of atypical lymphoid proliferations that develop as a result of immunosuppression in recipients of solid organ transplant or allogeneic hematopoietic stem cell transplant. According to the 4th edition of the World Health Organization Classification of Tumors of Haematopoietic and Lymphoid Tissues, PTLD is further divided into four categories on the basis of the histologic, immunophenotypic, and genetic characteristics: (1) early lesions consisting of plasmacytic hyperplasia and infectious mononucleosis-like, (2) polymorphic PTLD, (3) monomorphic PTLD, further classified according to the respective lymphoid or plasmacytic neoplasm they resemble in immunocompetent individuals, and (4) classic Hodgkin lymphoma-type PTLD [1]. The diagnosis and classification of PTLD are currently based on histologic criteria; hence, cytogenetic abnormalities have not been fully investigated. We report the first case of a monomorphic PTLD, diffuse large B-cell lymphoma (DLBCL) infiltrating spleen and bone marrow (BM) with t(3;6)(q27;p22) involving *BCL6*.

A 45-yr-old woman with a history of hepatocellular carcinoma secondary to hepatitis B virus (HBV)-associated liver cirrhosis,

who underwent living donor liver transplantation four years ago, visited our hospital with severe anemia and dizziness. Her hemoglobin level was 5.8 g/dL. Abdominal computed tomography (CT) scans showed splenomegaly and multiple intra-abdominal lymph node enlargements. Spleen biopsy revealed proliferation of large, oval cells with abundant cytoplasm (Fig. 1). In the immunohistochemical (IHC) examination, these atypical cells were positive for CD20, *BCL-2*, and *MUM-1* and negative for CD10, CD3, CD5, cyclin D1, and *BCL-6*. The result of *in situ* hybridization with Epstein Barr virus (EBV)-encoded small RNA (EBER) was negative; however, real-time quantitative PCR of peripheral blood sample showed 2,820 EBV copies/mL.

BM biopsy revealed the proliferation of large neoplastic B-cells that were positive for CD20 and negative for CD3 (Fig. 1). Final diagnosis was monomorphic PTLD, DLBCL subtype. Chromosomal analysis of the BM specimen revealed 46,XX,t(3;6)(q27;p22),del(14)(q31)[17]/46,XX[3] (Fig. 2). FISH analyses using dual-color *IGH* and *BCL6* (3q27) break-apart probes (Abbott Molecular Inc., Des Plaines, IL, USA) revealed *BCL6* rearrangements (22.5%) and heterozygous loss of 14q32 (9.7%) (Fig. 2).

The patient was treated with rituximab, cyclophosphamide,

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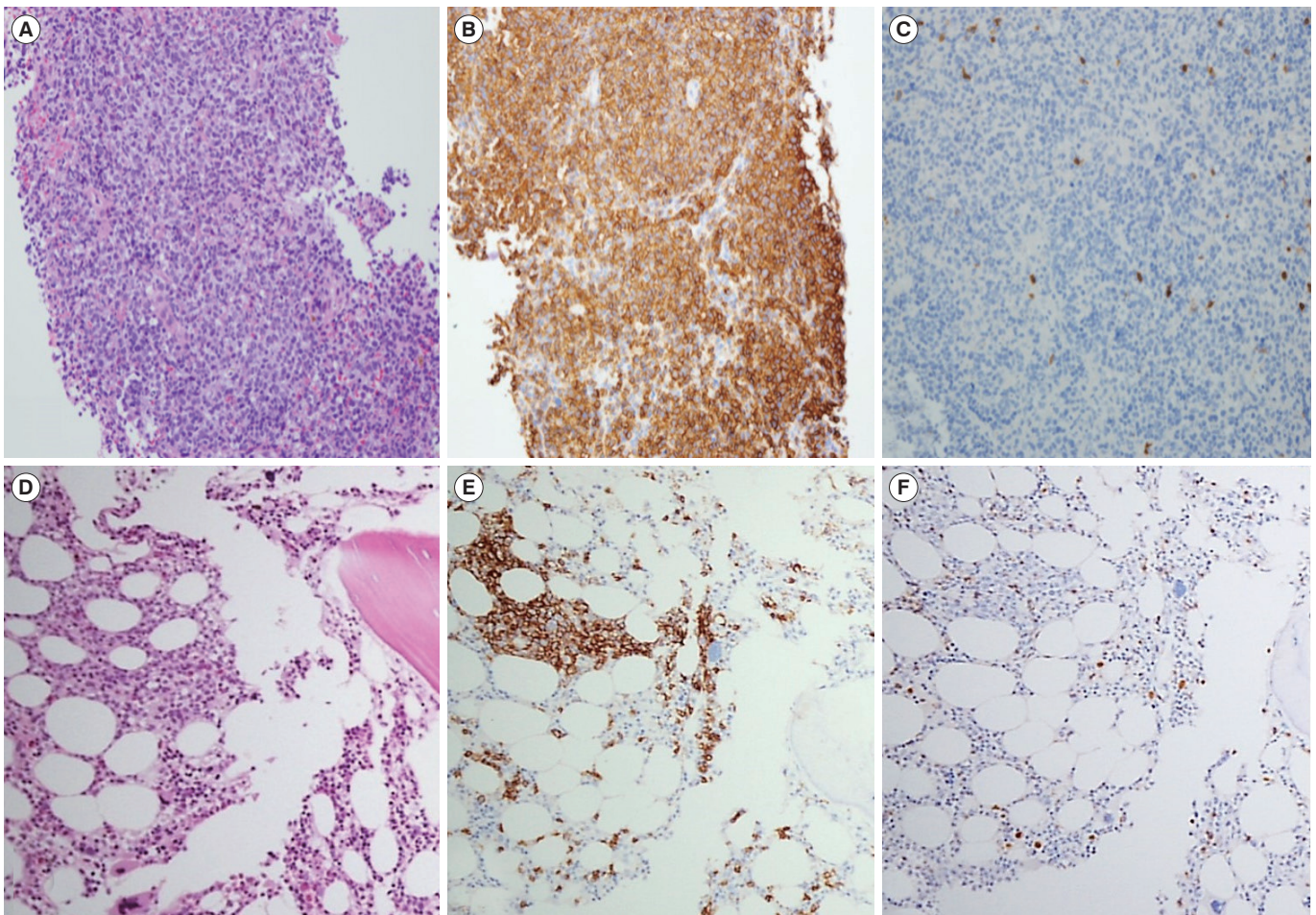


Fig. 1. Histopathologic findings of a monomorphic post-transplant lymphoproliferative disorder, diffuse large B-cell lymphoma subtype involving spleen (A, B, and C) and bone marrow (D, E, and F). (A) Hematoxylin and Eosin stain, $\times 40$. (B) CD20 stain, $\times 40$. (C) CD3 stain, $\times 40$. (D) Hematoxylin and Eosin stain, $\times 100$. (E) CD20 stain, $\times 100$. (F) CD3 stain, $\times 100$.

doxorubicin, vincristine, and prednisone (R-CHOP). Complete remission was achieved after six cycles of R-CHOP. After 14 months, brain magnetic resonance imaging demonstrated two lobulated enhancing masses at the posterior aspect of the medulla and nodule of vermis, suggesting central nervous system (CNS) lymphoma. The cytospin of cerebrospinal fluid revealed slightly increased cell counts ($18/\mu\text{L}$) and a few large lymphoid cells, suggestive of malignant lymphoma cells. Positron emission tomography-CT revealed marked hypermetabolic lesions on cerebellar vermis, consistent with lymphoma involvement. The patient was treated with five cycles of rituximab, methotrexate, vincristine, and procarbazine for the treatment of CNS lymphoma and achieved complete remission.

Among 18 clonal abnormalities in monomorphic B-cell PTLD, rearrangements of 8q24.1 (4 cases), 3q27 (2 cases), 14q32 (2 cases), and trisomy 9, 11, or both (5 cases) have been reported

[2]. Two PTLDs with 3q27 abnormalities showing DLBCL morphology have also been reported [2]. *BCL6* has been implicated in DLBCL, and *BCL6* rearrangements have been found in as many as 40% of DLBCLs and in 10% of a subset of follicular lymphoma. *BCL6* rearrangement is therefore one of the most frequent genetic abnormalities in B-cell non-Hodgkin's lymphomas (NHLs) [3]. The $t(3;6)(q27;p22)$ has been reported in six cases of B-cell NHLs, and four of these cases have been described as DLBCL [4-7]. However, the clinical implication of $t(3;6)(q27;p22)$ in B-cell NHLs has not been elucidated. Furthermore, PTLDs with $t(3;6)(q27;p22)$ have never been reported.

The 3q27/*BCL6* translocation is unique as it involves not only immunoglobulin genes but also non-immunoglobulin chromosomal loci as a partner. A comparative study suggested that non-immunoglobulin, *BCL6* translocation and concordant low

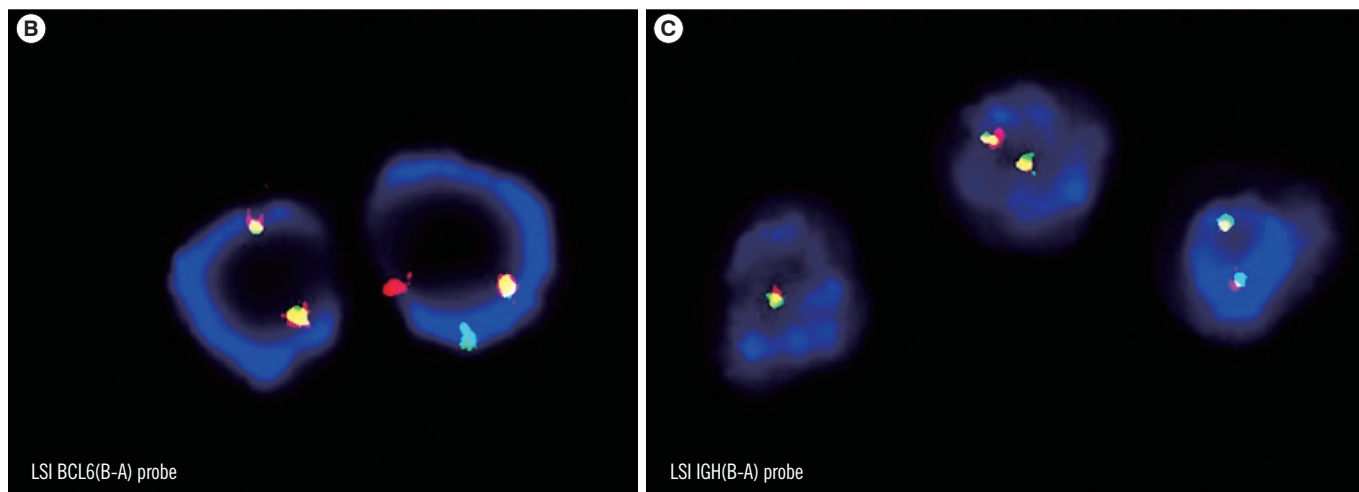
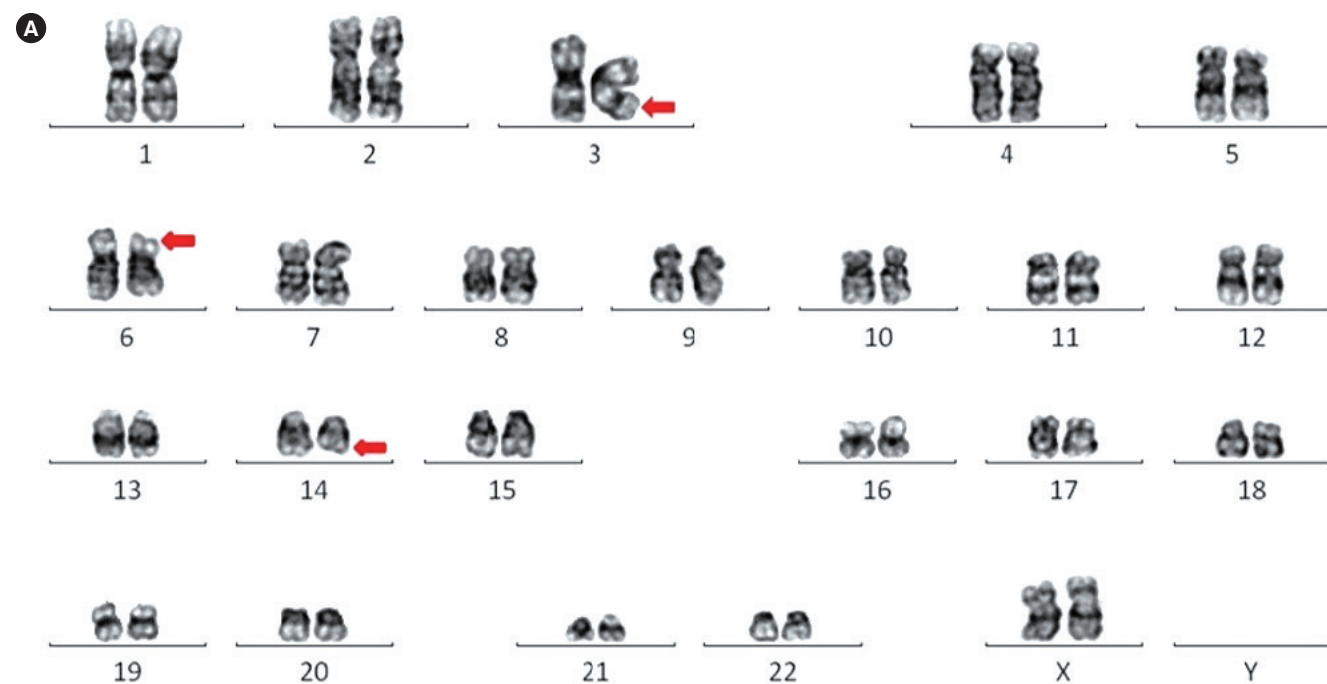


Fig. 2. Karyotype analysis of bone marrow specimen showing $t(3;6)(q27;p22)$ and $del(14)(q31)$ (A) and FISH results showing *BCL6* (3q27) rearrangement and loss of *IGH* (14q32) signals using dual-color, and break-apart probes, respectively (B and C).

BCL6 mRNA expression are indicators of poor clinical outcome in DLBCL cases [8].

Clinically, cases with CNS involvement show lower patient survival rate than those without CNS involvement [9, 10]. Therefore, pathogenetic and clinical implications, including effects of CNS involvement, prognosis, and treatment, of monomorphic PTLD, DLBCL subtype with 3q27 abnormality require further investigations.

To the best of our knowledge, this is the first report on mono-

morphic PTLD, DLBCL subtype with $t(3;6)(q27;p22)$. The $t(3;6)(q27;p22)$ might play a role in the pathogenesis and clinical outcome of this disease.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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