Loss of genomic DNA copy numbers in the p18, p16, p27 and RB loci in blastic plasmacytoid dendritic cell neoplasm

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a plasmacytoid dendritic cell precursor-derived aggressive neoplasm with a poor prognosis. BPDCN occurs as a reddish-brown, bruise-like, violaceous lesion, or reddish cutaneous nodules or plaques, which are often followed by bone marrow, lymph node, and blood involvement. A 74-year-old man was referred to us with an asymptomatic eruption on the right cheek and spreading asymptomatic eruptions on the trunk. The eruption on the right cheek had initially developed three months earlier. Physical examination revealed an asymptomatic, dark reddish, elastic, hard, subcutaneous lesion, 50 × 50 mm in size, on the right cheek (figure 1A) and numerous asymptomatic reddish plaques, 10 to 30 mm in diameter, on the trunk (figure 1B). There were no palpable lymph nodes. Atypical leukocytes were not present in the peripheral blood. Histopathological examination from the right cheek and left shoulder showed a diffuse, non-epidermotropic, monomorphous infiltrate of medium-sized blasts with irregular nuclei (figure 1C–D). The infiltrate occupied the dermis and upper subcutaneous tissue, but not the epidermis. Immunophenotype examination disclosed leucocyte common antigen (LCA)(+), CD56(+), CD123(+), terminal deoxynucleotidyl transferase (+), CD43(+), CD1a(-), CD2(-), CD3e(-), (LCA)(+), CD56(+), CD123(+), terminal deoxynucleotidyl transferase (+), CD43(+), CD1a(-), CD2(-), CD3e(-), CD4(-), CD5(-), CD7(-), CD8(-), CD19(-), CD20(-), CD30(-), CD45RO(UCHL-1)(-), CD138(-), ALK-1(-), and myeloperoxidase (+). Bone marrow aspiration revealed the involvement of 7.6% malignant cells showing the same immunophenotype as the atypical cells in the skin.

We performed array-comparative genomic hybridization (CGH) with a sample from the right cheek, to characterize the genomic alterations as described [1]. The patient provided written informed consent for participation in the study according to a protocol approved by the Genetic Ethics Committee of Kinki University. The array-CGH analysis revealed the loss of genomic DNA copy numbers in 1p31.3-33, 9p/q, 12p13.1-13.2, 13p/q, and the gain of 16p/q.

We believed that the patient had BPDCN with bone marrow involvement, referring to cases of CD4(-)CD56(+)CD123(+) BPDCN [2]. Treatment consisted of six courses of combination chemotherapy using pirarubicin, cyclophosphamide, vincristine and prednisolone, which resulted in complete remission. A bone marrow aspiration and a biopsy specimen from the right cheek after six courses of chemotherapy showed no malignant cells. Recurrent signs have not been detected for six months after chemotherapy.

Cases of CD4(-)CD56(+)/CD123(+) BPDCN might be explained either by genuine phenotypic variation in those neoplasms or by low levels of CD4 molecules within neoplastic cells [2]. BPDCNs commonly have abnormal tumor cell karyotypes with an average of six to eight [3]. The four most frequent common deleted regions (9q21.3, 12q12.1-q14.3, 12p13.2-p13.1, and 13q11-q12) contain several genes controlling G1/S transition cell-cycle, including, respectively, CDKN2A/CDKN2B, RB1, CDKN1B, and LATS2 [4]. The bi-allelic losses and/or multiple heterozygous deletions of genes regulating G1/S transition are almost identified in BPDCN patients [4]. These indicate...
that deletion events altering G1/S regulation are crucial for BPDCN oncogenesis [4-6].
In this case, we identified common chromosomal abnormalities, the loss of chromosome 9 including \(CDKN2A/p16-ARF-CDKN2B/p15\), 12p13.1-13.2 containing \(CDKN1B/p27\), and chromosome 13 including \(RB1\). We detected an additional chromosomal abnormality, the loss of the 1p31.3-33 region, including \(CDKN2C/p18\) (1p32) regulating G1/S transition, and other candidates of \(GADD45A\) (1p31.2), \(JUN\) (1p32-p31) and \(JAK1\) (1p32.3-p31.3) for tumor suppressor or promoter genes. Lucioni et al. reported that 3 of 21 BPDCN patients had losses in the overlapping region (1p32, 1p32.2, and 1p31.3-p31.2) [4].
The functional loss of \(CDKN2C/p18\) may be synergistically involved in the pathogenesis of BPDCN via damaging the control of the G1/S transition cell-cycle. In the present case, the deletion of the 1p31.3-33 region may be associated with aggressive Develop
In summary, we describe a case of BPDCN with chromosomal deletions, including the loci of \(CDKN2A/p16, CDKN1B/p27, RB1,\) and \(CDKN2C/p18\).

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