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REPORT ON THREE PATIENTS WITH BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

Brief Tittle: BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, clinically aggressive tumor that classified as a distinct entity among myeloid neoplasms in the 2016 WHO revision. Most patients present with cutaneous lesions with or without bone marrow involvement and leukemic dissemination. The tumor cells express CD4, CD56, CD123, TCL1(1). In general, ALL/lymphoma-type regimens were reported to show better survival outcomes than AML-type regimens. In detail, 7 of 26 patients complete remissions were registered after AML-type regimens, and 10 of 15 patients after ALL/lymphoma-type regimens, with a significant advantage for the ALL/lymphomatype approach(2,3). Patients who treated with hyperCVAD showed an objective response, but the duration of response was short so HSCT should be considered (4). Recent interest has been placed in a novel immunotherapy directed at SL-401 an IL-3R, notably overexpressed in BPDCN as well as other myeloid malignancies. This led to development of SL-401 an IL-3-diphtheria toxin conjugate that has

been demonstrated promise for BPDCN in early-phase trials(5-7,8). We aim to share our experience with BPDCN due to its rare entity and there is no consensus about treatment.

All three patients were male aged 19, 55 and 65, admitted to the hospital with fever, weight loss, weakness and lymphadenopathy. Physical examination revealed that all of them had lymphadenopathies, one of them had hepatosplenomegaly and two of them had skin lesions. Skin lesions were bruise-like"brown to violaceous infiltrated plaques on the back, extremities. One patient had brown-purple tumoral mass and also brown-purple nodular lesions on the head region. Bone marrow and lymph node biopsies showed diffuse infiltration by medium sized blasts with irregular nuclear contour, slightly large cytoplasm, high mitotic index and immunohistochemical expression CD4(+), CD56(+), CD123(+), TCL1(+). Skin biopsies revealed diffuse infiltration by similar cells. One patient had CNS involvement that pathologically proven by cerebrospinal fluid cytology. On one patient's bone marrow %36 TCF3 and %35 TEL genes deletions were detected by hybridization. HyperCVAD regimen was initiated to all patients. After one cycle of chemotherapy, two patients achieved complete remission (CR). One patient who achieved CR and the other patient who couldn't achieve CR died from sepsis. Other patient who achieved CR after one course of chemoterapy was treated with three cycles of HyperCVAD regimen as maintenance and afterwards he underwent transplantation with peripheral blood progenitor cells from a related one miss-matched donor. BuCy was administered for conditioning regimen before transplantation.

Two patients achieved CR with HyperCVAD regimen and one of them who underwent allogenic transplantation is still in CR 18 months after diagnosis. BPDCN can achieve a durable remission with HSCT regardless of the type of induction regimen. In particular, auto-HSCT in first CR appears to be a reasonable treatment option and may play an important role in improving the outcomes of BPDCN(9). On the other hand high-dose therapy followed by allo-SCT can provide durable disease control in up to 50% of patients and allo-SCT should be administered in first CR if possible(10). The allogeneic stem cell transplantation seems to improve the prognosis, but further studies are needed to confirm the place and the indication of this treatment strategy.

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Figure 1: Brown-purple tumoral mass of 3X3 centimeters in diameter on the right temporal region (A). After single cycle of chemotherapy skin lesions were regressed (B).