Blastic plasmacytoid dendritic cell neoplasm with skin, bone marrow and CNS involvement: a case report

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Case presentation

A 65-year-old man presented with constitutional symptoms and erythematous skin lesions. Blood analysis revealed pancytopenia, 2% circulating blasts, DIC, liver function abnormalities and elevated LDH. Skin biopsy revealed a dermal infiltration with a diffuse monomorphous infiltrate of medium-sized blast cells coexpressing CD4+/CD56+/CD123+. Bone marrow aspirate showed myeloid and erythroid dysplasia, with 10% blasts, and a specific immunophenotype, CD4w+/CD15+/CD56+/CD34+/CD117++/CD123+/CD7++/CD38+/HLA-DR+/CD45w+ suggesting underlying MDS-EB2. Bone marrow biopsy showed a markedly hypercellular marrow (90%) with CD4+/CD56+ small blasts negative for myeloid, NK- and lymphoid markers, and fibrosis grade 1. Cytogenetics revealed an aberrant karyotype with del(20q). Molecular analysis (NGS) of bone marrow revealed mutations in SRSF2 and ASXL1. Blastic plasmacytoid dendritic cell neoplasm (BPDCN) with cutaneous and bone marrow involvement was diagnosed. First AML induction therapy (cytarabine and idarubicine, 7+3) induced a complete morphological and flow cytometric remission on bone marrow examination as well as negative skin biopsy. Screening lumbar puncture was normal. Shortly after starting the second AML induction therapy (high dose cytarabine and idarubicine), he developed rapidly progressive motor and sensory symptoms of the lower limbs with sphincter impairment. Radiological findings were compatible with acute transverse myelitis over Th2 to Th10. Broad-spectrum antimicrobial therapy was given but extensive search for microbiological or leukemic aetiology remained negative. Neurological symptoms temporarily resolved during aplasia and reappeared after hematologic recovery. Finally, a repeat lumbar puncture revealed CNS relapse with cells expressing the initial flowcytometric phenotype. At that time the patient was rapidly deteriorating and palliative treatment was started.

Discussion

BPDCN is a rare disease, which should be recognized by its characteristic immunophenotype (triple positive CD4+/CD56+/CD123 phenotype without other lineage-specific markers). Because of its rarity, there are no prospective trials with respect to treatment. AML- as well as ALL-like therapies have been used, and allogeneic or autologous HSCT appear to provide some survival benefit (1-3). Occult CNS disease should be actively screened for at diagnosis, and intrathecal prophylaxis and treatment can improve outcomes (4). It seems wise to combine “lymphoid” drugs like methotrexate and L-asparaginase which are able to prevent CNS involvement with “myeloid” drugs such as idarubicine (2). A combination of L-asparaginase, methotrexate and dexamethasone seems to prolong survival and induce remissions (7). New therapeutic approaches are being tested such as bortezomib (5) and SL-401 (anti-CD123 interleukin-3 receptor inhibitor) (6).

Conclusion

BPDCN is a very rare and clinically aggressive disease with a median survival of 10-19 months. Most cases (80-90%) show an initial response to multiagent chemotherapy but relapses with resistance to drugs are regular. It has distinct immunophenotypic features (CD4+/CD56+/CD123+), with high frequency of cutaneous and bone marrow involvement, leukaemic dissemination and CNS involvement. CNS could be a persistent blast-cell sanctuary due to the limited penetration of cytostatic drugs across the blood-brain barrier in to the CSF and brain parenchyma (4). About 10-20% of cases of BPDCN are associated with or develop into other myeloid neoplasms such as CMML, MDS and AML. It is separately listed in the group of acute myeloid leukemias and related precursor neoplasms since WHO 2008.

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