Plasmacytoid Dendritic Cells Proliferation Coexisted with Acute Myeloid Leukemia

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To the Editor: Plasmacytoid dendritic cells (pDCs) represent a subset of dendritic cells. There are two distinct forms of neoplasms derived from pDCs; the one is blastic plasmacytoid dendritic cell neoplasm (BPDCN) and the other is mature pDCs proliferation coexisted with myeloid tumors. The mature pDCs in myeloid tumor are characterized by a lineage-negative human leukocyte antigen (HLA)-DR$^+$ CD56$^-$CD123$^+$CD11c$^-$ immunophenotype. Here, we describe an 83-year-old man who developed acute myeloid leukemia (AML) transferred from primary myelofibrosis (PMF) coexisted with monoclonal gammopathy of undetermined significance (MGUS) and mature pDCs proliferation; however, the immunophenotype results of bone marrow (BM) showed positive CD56 expression.

An 83-year-old male patient presented with pancytopenia in June 2016. Immunofixation electrophoresis revealed the IgG κ monoclonal immunoglobulin zone, and M protein quantitative value was 1.68 g/L. The BM aspirate was dry tap, and BM blood could only be attained for morphological analysis. Teardrop-like red blood cells could be seen in the BM morphology. Pathology of BM biopsy suggested that myelofibrosis with grade three. Gene screening suggested *JAK2V617* gene mutation. Pathological results of left inguinal lymph node biopsy suggested lymphadenosis, with immunophenotypic characteristics of CD20$^+$CD3$^+$CD30$^-$. Thus, the lymphoproliferative disease was excluded, and the patient was diagnosed as PMF coexisted with MGUS. Supportive therapy by blood transfusion was given.

From January 2017, BM morphology suggested that blast cells gradually increased to 46%, and dendritic cells were visible. Flow cytometry of the BM in April 2017 suggested that immature granulocytes and monoblast cells accounted for 12.5% and 14.1%, respectively, and abnormal pDCs accounted for 2.25%, with immunophenotypic characteristics of CD123$^+$HLA-DRst$^+$ CD13dim$^+$CD11bdim$^+$ CD56$^+$CD4$^+$BDCA4$^+$BDCA2$^-$. A diffuse distribution of immature cells was shown in BM biopsy. The patient was diagnosed as AML with pDCs proliferations. He refused chemotherapy, and only supportive treatments were given. He died of pneumonia in July 2017. The overall survival from diagnose was only 3 months.

Access this article online	
Quick Response Code:	Website: www.cmj.org
	DOI: 10.4103/0366-6999.237404

It is unambiguous that the diagnosis of the patient is AML transferred from PMF coexisted with MGUS. What is the reason of pDCs proliferation in the BM? Is it BPDCN or mature pDCs proliferation coexisted with myeloid tumor? A highly suspected diagnosis of BPDCN can be made when skin lesions exist, four antigens among CD4, CD56, CD123, TCL1, and CD303 are expressed by neoplastic cells and myeloid/lymphoid system specific markers such as CD117, MPO, CD20, and CD3 are negative.[1] This patient did not have skin lesions and the immunophenotypic characteristic of BPDCN. Mature pDCs proliferation coexisted with myeloid tumors is rare and affects predominantly male individuals (75%) with a median age of 69 years. Prognosis is usually poor, that is mainly due to the evolution of the myeloid neoplasm rather than expansion of pDCs. These mature pDCs show largely the same immunoprofile as their reactive counterparts, CD123, BDCA2, and TCL1 positive, but occasionally aberrantly express CD2, CD5, CD7, CD10, CD13, CD14, CD15, and CD33. CD56 is usually negative. Several cases with positive CD56 are summed in Supplementary Table 1.[2,3] We suspect that the advanced age and giving up chemotherapy may contribute to the poor prognosis of the patient reported here. The expression of CD56 suggests that the pDCs in these patients might be derived from monoblast cells.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that his name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Received: 08-04-2018 **Edited by:** Yuan-Yuan Ji
How to cite this article: Wang M, Chen YJ, Wang LR, Wang YZ, Lu J. Plasmacytoid Dendritic Cells Proliferation Coexisted with Acute Myeloid Leukemia. Chin Med J 2018;131:1866-7.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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Supplementary Table 1: Clinical information in nine cases of CD56$^+$ pDCs proliferation associated with myeloid tumor

Cases	Age (years)/ gender	Associated myeloid tumor	L	S	H	Skin lesions	Site of pDCs accumulation	Treatment	Survival (months)
1[2]	24/male	CMML	+	+	+	+	LN, SK	--	8 (DOD)
2[2]	50/male	AML-M4	+	+	+	+	LN, SK, BM	--	11 (AWD)
3[2]	63/female	U-CMP	+	+	–	–	LN, BM	--	15 (DOD)
4[2]	80/male	U-MDS/MP	+	+	+	+	LN, BM	--	43 (DOD)
5[2]	62/female	AML-M5	+	–	–	–	LN, BM	--	15 (DOD)
6[2]	52/male	CMML	+	+	–	–	LN, BM	--	13 (AWD)
7[3]	56/male	AML transferred from CD56$^+$ TdT$^+$ blastic tumor of skin	+	–	–	+	LN, SK, BM	Hyper-CVAD POMP maintenance troxacitabine/cytarabine	15 (DOD)
8[3]	73/male	AML transferred from CD56$^+$ TdT$^+$ blastic tumor of skin	+	–	–	+	LN, SK, BM	Hyper-CVAD and methotrexate/cytarabine salvage treatment	22 (DOD)
Our patient	83/male	AML-M4 transferred from PMF coexisted with MGUS	+	–	–	–	BM	Supportive treatment	3 (DOD)

pDCs: Plasmacytoid dendritic cells; CMML: Chronic myelomonocytic leukemia; AML: Acute myeloid leukemia; U-CMP: Unclassifiable chronic myeloproliferative disorder; U-MDS/MP: Unclassifiable myeloproliferative/myelodysplastic disorder; PMF: Primary myelofibrosis; MGUS: Monoclonal gammopathy of undetermined significance; L: Lymphadenopathy; S: Splenomegaly; H: Hepatomegaly; LN: Lymph node; BM: Bone marrow; SK: Skin; Hyper-CVAD: Hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone; POMP: Mercaptopurine, methotrexate, vincristine, and prednisone; DOD: Dead of disease; AWD: Alive with disease; +: Yes; -: No; --: No clear information.